THOMSON REUTERS INTEGRITY^{SM}

USER GUIDE - OVERVIEW

RELEASE 10.1

THOMSON REUTERS

CONTENTS

INTRODUCTION TO THOMSON REUTERS INTEGRITY^{SM}

Thomson Reuters Integrity^{SM} is a unique knowledge solution integrating biology, chemistry and pharmacology data on more than 320,000 compounds with demonstrated biological activity and almost 140,000 patent family records. It provides you with reliable, detailed information across multiple disciplines to empower your discovery and development activities.

Integrity includes key interlinking knowledge areas:

- Drugs & Biologics
- Targets & Pathways
- Genomics
- Biomarkers*
- Organic Synthesis
- Experimental Pharmacology
- Pharmacokinetics/Metabolism

- Clinical Studies
- Disease Briefings
- Companies & Research Institutions
- Literature
- Patents

* – Requires additional subscription.

(The Biomarkers Module brings a new dimension to *Integrity* – linking drugs, targets and genes to biomarkers information from a diverse range of sources.)

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Integrity offers a depth and breadth of content unmatched by any other resource:

- More than 320,000 bioactive compounds
- Target-based approaches to disease diagnosis and therapeutic intervention for more than 2,350 precedented targets with pathway information
- More than 9,600 genomics records with gene-related studies
- More than 92,000 organic synthesis intermediates and reagents from over 20,000 synthesis schemes
- More than 855,000 numerical values from experimental pharmacological studies describing drug/receptor and enzyme/target cell interactions
- More than 440,000 numerical values on pharmacokinetics/metabolism with data on parent compounds and active metabolites
- Comprehensive information on more than 105,000 references to clinical trials of compounds currently under study and/or in use in humans
- A background reference to more than 115 disease briefings with full-color multimedia illustrations and web enhancements
- Information on more than 4,450 companies and research institutions active in drug discovery and development, including sales information on more than 365
- More than 1,075,000 references to current literature, abstracts and proceedings from congresses and symposia, as well as company communications
- More than 139,500 patent families from 4 leading sources (EP, JP, US and WO)

Updated daily, expertly refined drug information is integrated within Integrity into a single, flexible resource that can help drive innovation, and support earlier decision-making.

With *Integrity* you can:

- Rapidly access recent, relevant and refined scientific information
- Make better decisions faster, with advanced knowledge management tools
- Lower risk and prioritize your projects using information integrated from multiple fields of drug R&D
- Stay at the cutting edge of drug research and development with daily updates

A key strength of *Integrity* is that it is developed, populated and supported by a cross-section of the scientific community. Our scientists provide an unparalleled depth of industry expertise that means we can add the features and content you value most – from concise product summaries to chemical structures emerging from the most recent patent and biomedical literature and congresses.

Integrity enables you among other things to:

- Identify new targets and leads
- View new compounds emerging from patent literature
- Create structure activity relationships at the click of a button

ACCESS AND PLUG-INS

Integrity is available for consultation 24 hours a day, 7 days a week and 365 days a year. The Integrity portal offers the option of using either a standard Internet connection:

http://thomsonreutersintegrity.com

or a Secure Sockets Layer (SSL) connection:

https://thomsonreutersintegrity.com

SSL encrypts queries to and replies from the system, for secure online communication.

TECHNOLOGY
Integrity utilizes the latest database technology for managing text, data and image information. Chemical structures made available within *Integrity* are managed using CambridgeSoft Corporation CS ChemOffice™ Webserver and ChemAxon JChem™ applications. In order to guarantee the highest quality of user experience and levels of reliability, *Integrity* servers operate from a secure, temperature-controlled environment with on site power back-up. Incorporation of the latest redundant and hotswap hardware prevents hardware failures from compromising access to the portal.

SYSTEM REQUIREMENTS
To access the *Integrity* portal on the Internet, you must have a standard computer with an Internet connection. Speed of access will depend on the type of Internet connection that you use. We recommend you install Microsoft Office 2000 or higher (for handling data exported from *Integrity* in Word and Excel formats) and a chemical structure database management program (capable of handling SDFiles; e.g., CS ChemFinder™, MDL[(R)] ISIS™).

Following are the minimum recommended system requirements needed to work effectively within *Integrity*:

Browser Requirements
To access *Integrity* you must have an Internet connection and one of the following Web browsers: Microsoft[(R)] Internet Explorer, version 6 or higher or Mozilla Firefox, version 2 or higher.

Display Settings
Integrity is best viewed at a minimum monitor resolution of 1024 by 768 pixels or higher, and at 256 colours or more (High Color or True Color recommended). You can modify the appearance of your Windows desktop by accessing the **Display Properties** via **Control Panel**, then choosing **Settings**.

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- Drag the **Screen resolution** slider to adjust your monitor display; drag to the right to increase the resolution or drag to the left to decrease the resolution.
- Select the number of colors to display from the **Color quality** menu; available options include Medium (16 bit) and Highest (32 bit).
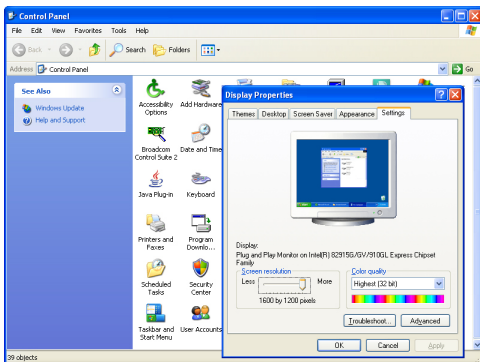
Internet Options

When exporting from *Integrity*, results are downloaded into a separate browser window. You must therefore ensure that you temporarily disable/turn off any pop-up blockers on your computer, since the content will not export when a pop-up blocker is active. The Web browser must also be configured to accept cookies.

Javascript

Integrity uses JavaScript for defining menus and navigation, opening new windows and for the processing of requests. You must therefore enable the JavaScript option within your Web browser to use *Integrity* successfully.

Java

Chemical structure search functionality can be provided using the ChemAxon Marvin applet; however, this requires that Java is installed on your machine. To install this free software, go to the Java website. (Here, you can also test your Java Virtual Machine (JVM) and verify the current version of the JRE (Java Runtime Environment) installed on your machine, if any.)

Adobe Flash Player

Integrity uses a variety of charts to make data accessible visually; these allow you to view the contents of records and results and to filter on specific parameters. To be able to view the charts and visualization features successfully you must have the latest version of Adobe Flash player (version 9 or higher) installed on your machine. To download the free **Adobe Flash player**, go to the Adobe website. (Here, you can also test and verify the current version of Adobe Flash Player installed on your machine, if any.)

Adobe Reader

Integrity makes certain information available in PDF format to enable easy viewing and printing. This requires the free **Adobe Reader**, which can be

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downloaded from the Adobe website.

Chemical Structure Search Plug-ins
Integrity now includes compatibility with four different programs for drawing structures to submit for chemical structure searches in the portal. You can select any option at any time; and the last option you select becomes your new default. These options are available in all Knowledge Areas enabled for structure searching:

Symyx(R) Draw
Structure queries can be incorporated using Symyx Draw (the replacement for MDL Draw/ISIS Draw). You must have an existing license and installation of the Symyx(R) Draw software in order to use this option.

Symyx(R) MDL ISIS/Draw + Symyx(R) MDL Chime
You must have an existing license and installation of the Symyx MDL(R) ISIS/Draw software in order to use this option. You also must have installed the Symyx MDL(R) ChimePro or Symyx MDL(R) Chime plug-in. The Symyx MDL(R) Chime plug-in can be downloaded free of charge (subject to licensing agreement) from the Symyx website download center (http://www.symyx.com/downloads) or by following the link inside *Integrity*.

Please note that Symyx no longer offer or support the Chime plug-in for Macintosh machines.

ChemAxon Marvin Applet
The ChemAxon Marvin Applet installs automatically when you select

this structure drawing option from within *Integrity*. No previous license or installation is required for this option; however, your computer must be Java-enabled.

CambridgeSoft CS ChemDraw™ Plug-in
You must have installed the CambridgeSoft CS ChemDraw™ Pro plug-in or the CS ChemDraw™ Net plug-in to use this option. The CS ChemDraw™ Net plug-in can be downloaded free of charge (subject to license agreement) from the CambridgeSoft website:

http://www.cambridgesoft.com

or by following the link inside *Integrity*. The *Integrity* portal detects which program is needed for your computer configuration and assists in installing the correct version.

To install the chemical structure search plug-in: log on to *Integrity*, go to the Drugs & Biologics Knowledge Area and click the Structure Search bar to display the Structure Search Options. Check under Programs to see if a CS ChemDraw™ plug-in is already installed on the computer (it may be an option under ChemOffice or CS ChemOffice). If so, determine if the version installed works in Integrity by executing a simple structure search.

If there is not a prior installation of the plug-in or if the structure search does not appear to work correctly, click the Structure Editor link that appears just below the structure drawing window and use the links provided in the pop-up window to download the CambridgeSoft CS ChemDraw™ Net plug-in for

Windows or Macintosh, as appropriate.

For Windows, go to: http://www.cambridgesoft.com/cdpn110/cdpn110.exe

For Macintosh, go to: http://www.cambridgesoft.com/cdpn110/cdpn1101.dmg

Follow any instructions that appear. If there are any questions during this procedure or the structure search does not appear to work correctly, please contact Integrity Support.

Note: If the CS ChemDraw™ toolbar does not appear when you display the Structure Search Form, move your mouse pointer over the structure drawing window and right-click; then select **View, Main Tools**. The toolbar appears.

The CS ChemDraw™ plug-in does not have a separate manual. Information on structure drawing conventions can be found in the standard CS ChemDraw™ Manuals. To display or download this manual in PDF format, first verify which version of the plug-in you have installed (this can be found in any Structure Search Form in *Integrity*: right-click in the structure drawing window, select **Help**, then **About ChemDraw...**; note the version number that appears). Then go to:

http://www.cambridgesoft.com/services/documentation/manuals_desktop.cfm

and click the appropriate version number in the ChemDraw™ line in the ChemDraw™ Manuals table.

Other Plug-ins

Other plug-ins may prove useful for certain aspects of Integrity, including RealPlayer (www.real.com) and Windows Media Player (www.microsoft.com).

LOGIN SCREEN

Welcome

Registered Users

If you already have a User Name and Password to use Thomson Reuters Integrity, enter them here and click Login

User Name

Password   Login

Forgotten your password? Please click here
Use of this service is offered to Authorized Users on the condition that they accept the Terms of Use

First-time Users

If your company/institution has licensed Thomson Reuters Integrity under the self-registration mode, click here to register   Self-Register

The *Integrity* login screen is reached using the following Internet address or URL: http://thomsonreutersintegrity.com (or alternatively, https://thomsonreutersintegrity.com for an SSL connection).

Depending on the type of access licensed by your organization, you will either be provided with a User Name and Password combination by Thomson Reuters or will be able to self-register the first time you use *Integrity*.

Registered Users
To use *Integrity* after you have registered the first time or if you have been provided with a User Name/Password combination by your system administrator, simply type your User Name and Password details in the boxes provided and then click **Login**.

Note: Before using Integrity for the first time, please click on Terms of Use. Ensure you have read and are in agreement with the terms and conditions as outlined before you continue to log on.

Self-Registration
To register to use *Integrity*, click **Self-Register** under First-time Users on the Welcome screen. Review the Terms of Use and click to accept them. Then click **Continue**. Complete the registration form. To register successfully, all fields must be completed.

- **First Name –** Enter your first name
- **Last Name –** Enter your last name
- **Company/Institution –** Enter your organization name
- **Department** – Enter your department name
- **City** – Enter your location
- **Country** – Select your country location from the alphabetical list of all countries
- **Email address** – Enter your e-mail address; name@company.com. The entry must be a valid e-mail address (i.e. contain a single '@', at least one '.', etc). Case sensitive.

  Please note – You are required to supply your current corporate e-mail address (rather than a personal e-mail address).

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- **Telephone Number** – Enter your contact telephone number
- **User Name** – Enter your user name
- **Password** – Enter your password
- **Confirm Password** – Confirm your password by re-typing it, exactly as above. Case sensitive.

Check the information, particularly your e-mail address. The text entered in the Password and Confirm Password fields must be identical. Make a note of your chosen User Name and Password and keep them safe.

Click **Send** Send to proceed to the next stage of the process and register your details or click **Reset** Reset to clear the contents of the form and start again.

Registration for *Integrity* is immediate.

If registration is not successful, a message displays indicating that information is missing from one or more fields of the registration form. Click **OK** to accept this message and then enter the information requested in the required field(s) and click **Send**.

If registration is successful, the Login screen appears. You can now log on by entering your newly created User Name and Password and clicking Login. This takes you to the *Integrity* Home Page.

Forgotten password
If you have forgotten your password, click on the link below the login boxes,

enter your User Name and E-mail Address in the boxes provided and then click **Send**. Your *Integrity* password will be sent to you by e-mail. (If you enter only your e-mail address, then you will be sent both your username and email.)

If you do experience any difficulties gaining access to *Integrity*, please contact Integrity Support, integritysupport@thomsonreuters.com.

Password Usage & Confidentiality
Integrity user names and passwords are personal and non-transferable under the *Integrity* Terms of Use. A user name/password combination defines an individual user account in *Integrity*, and each account may have a single e-mail address entered for receiving Alerts. Sharing a user name/password combination is not permitted and violates the confidentiality of the original user's Saved Queries and Alerts and prevents the other user from using the Alerts feature. If two users attempt to use a user name/password combination simultaneously, they will be ejected from the system.

Terms of use
Access to *Integrity* is offered on condition that you accept without modification the terms, conditions and notices contained in the Terms of Use document. Use of *Thomson Reuters Integrity*^{SM} constitutes agreement to all such terms, conditions and notices. Registered users may consult the Terms of Use by clicking the link on the *Integrity* Login page or, if inside *Integrity*, by clicking Support/Help and then on Terms of Use.

Thomson Reuters is the creator, compiler, producer and publisher of *Thomson*

Reuters Integrity^SM and therefore is the exclusive holder worldwide of all intellectual property rights, copyrights, trademark rights and database sui generis rights on *Thomson Reuters Integrity*^SM and on any of its elements in any language, including but not limited to any know how, operating, source code, database, data, design, image, audio and literary elements accessible through *Thomson Reuters Integrity*^SM and/or through which *Thomson Reuters Integrity*^SM operates, except where expressly stated otherwise.

BOOKMARKING INTEGRITY
You can bookmark the *Integrity* internet page for future use.

In Microsoft® Internet Explorer:
Click on **Favorites** and then **Add to Favorites**. Click **Add** to save in your Favorites list, alternatively navigate to the desired folder or create a new folder to save the bookmarked page in.

An *Integrity* icon appears in your Favorites list; you can drag and place this on your toolbar for easy access.

In Mozilla Firefox®:
Click on **Bookmarks** and then **Bookmark This Page**. Click **OK** to save in your Bookmarks list, alternatively navigate to the desired folder or create a new folder to save the bookmarked page in.

Note that it is important when bookmarking *Integrity* that you use the simple url without anything more after the .com, otherwise the bookmark may not function correctly after new releases.

SETTING INTEGRITY AS YOUR DEFAULT HOME PAGE

Alternatively, you may wish to make *Integrity* your browser default home page.

In Microsoft® Internet Explorer:
Click on **Tools**, **Internet Options**, insert the *Integrity* Internet address into the address field, and then click on **OK**.
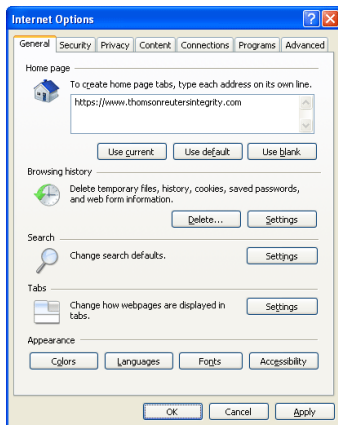
In Mozilla Firefox®:
Click on **Tools**, **Options**, insert the *Integrity* internet address into the home page field, and then click on **OK**.
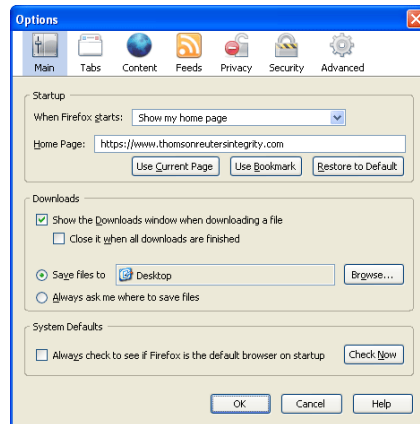
GENERAL NAVIGATION

Navigating in Integrity is simple and intuitive, using the Navigation bar, which is located just below the *Integrity* portal banner, the quick access links found on the Integrity Home Page or on the Knowledge Area pages, and the paging links, Options menu and Filter by Statistics feature found on the results page.

When you navigate through to an *Integrity* record, from the quick access links on the *Integrity* Home Page, or when you perform a database search and display the results list or click through to the record level, the Options menu presents you with the most commonly performed actions needed to process your output further, for example Keep me Posted, display options, Export Center and Integrity Reports.

Quick Search

The Quick Search feature allows you to see at a glance the information available in all Knowledge Areas of *Integrity*. Quick Search searches across the most relevant text-based fields in each Knowledge Area. Access to all other

search options is via the Quick Access searches on the Home Page or the Search forms found in each Knowledge Area. Quick Search is located to the center of the Navigation bar at the top of each page in *Integrity*.

Navigation Bar



The Navigation bar is always visible, regardless of your location within Integrity. It provides quick navigation to all of the main areas:

- **Knowledge Areas** – Displays the associated Search form. Knowledge Areas are the entry points to searching and retrieving information in *Integrity*. The type of results you would like to view first determines which Knowledge Area you should choose. This does not affect your access to the complete set of data in *Integrity* as all data is integrated.

- **Quick Search** – Search and retrieve terms across all Knowledge Areas in *Integrity*. Access lists of records and see which Knowledge Areas contain related information which may be relevant to your search.

- **Home** – Displays the *Integrity* Home Page.

- **Support/Help** – Quick access links to the Help Request/Suggestion Form, Terms of Use, Frequently Asked Questions, User Guide and the *Integrity* Learning Center

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- **Query Manager/Alert Center** – Displays the Query Manager and Alert Center, which includes your Saved Queries, Keep me Posted, Controlled Vocabulary and Session History.

- **Reports** – Displays the status and details of recently generated Integrity Reports.

- **Exit** – Exit *Integrity*; this closes the current session and returns you to the Login screen. This option is available only from the *Integrity* Home Page. You must therefore return to the Home Page first to close a session.

Quick Access Links

These links found on the *Integrity* Home Page or on the left hand side of the Knowledge Area pages provide direct access to specific information in the database. The quick access links include:

- Today's News

- Today's Featured Patents

- Conferences

- The Starting Line

- Pipeline on the Move

- Gateways to Gene-related Studies

- Gateways to Patents

- Gateways to Clinical Trials

- Gateways to Development Status

Filter by Statistics
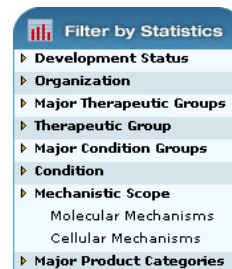
Searches can be refined by using the Filter by Statistics charts on the right hand side of the results page. Charts are Knowledge Area and results display specific and offer the option to refine the search or view the number of results grouped under the same criteria. A visual representation of the results is presented in a bar chart (you can change to another display format from the Filter by Statistics chart page), allowing you to view a breakdown by the selected criteria and select subsets of data, export the chart results, or take a screen capture of the chart. Rollover the chart bars to reveal the exact number of results represented by each bar. Use the check boxes to the left of the bars and click View Subset to refine and navigate to a subset of results.

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SUPPORT, TRAINING AND FEEDBACK

Thomson Reuters aims to provide comprehensive support for all its customers. As a valued customer and user of *Thomson Reuters Integrity*^{SM}, a number of complimentary resources are provided for you.

GENERAL INFORMATION
Integrity is part of the ongoing commitment of Thomson Reuters to empower knowledge-based drug discovery and development. To find out more about *Integrity* and for the latest information, please visit:

science.thomsonreuters.com/products/integrity

GETTING HELP/SUPPORT
Integrity includes a Help Request/Suggestion Form. For *Integrity*, Technical Support is also Integrity Support. Contact Integrity Support for technical assistance, to request information on content or features, or to forward suggestions for *Integrity*.

From within *Integrity*:

1. On the **Navigation bar**, click on **Support/Help**, and then click **Help Request/Suggestion Form**. The Help Request form displays, pre-populated with your contact details.

2. Enter the specific details of your help or support request in the space provided, and then click **Send**.

Alternatively, you may wish to consult *Integrity* Frequently Asked Questions which is available as a PDF download under Getting Started on the Home Page or from Support/Help. Finally, enquiries can be sent directly to integritysupport@thomsonreuters.com.

When submitting a request for technical support, please include the following information: Operating System in use (e.g. Windows 2000, Windows XP, Mac OS 9.2.2); browser type and version, including any service packs (e.g. Internet Explorer v. 6.0), together with details on the search that was run and any results obtained, including the wording of any error messages that appear. If your question relates to structure searching, please specify which structure editor you are using.

CUSTOMER SUPPORT
The Thomson Reuters Global Customer Support Center provides you with a single point of access for all available support materials and reference tools for Thomson Reuters' products, including Product Training and Support:science.thomsonreuters.com/support:

science.thomsonreuters.com/support

Select a product to get started, or choose *Integrity* from the Other Product Support options.

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CUSTOMER TRAINING

Global Customer Training provides a wide range of training opportunities in Thomson Reuters products. For further details of available training visit:

science.thomsonreuters.com/training

Should you need to contact the Thomson Reuters Training Team directly, please use the online form to submit your request; this can be found at:

science.thomsonreuters.com/info/contacttraining

The *Integrity* Learning Center contains links to all the latest training opportunities and resources available for *Integrity*, including Live Sessions, E-Learning short sessions (pre-recorded; Getting Started, Home Page Overview, Using the Search Forms, Chemical Structure Searching), Use Cases, and Materials (Product Information, Integrity Factsheet, Biomarkers Module Factsheet and Biomarkers Module FAQs).

PROVIDING FEEDBACK

At Thomson Reuters, we are always interested to hear from you and we welcome and value your feedback, since it helps us to provide you with the very the best tools possible for all your information needs. Please send your comments and suggestions, tell us about any problems you experience when using *Integrity* or any discrepancies you may find:

Integritysupport@thomsonreuters.com

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THOMSON REUTERS

THOMSON REUTERS INTEGRITY^{SM}

USER GUIDE - HOME PAGE

RELEASE 10.1

THOMSON REUTERS

CONTENTS

INTEGRITY HOME PAGE

When you log on to *Integrity*, you are taken to the *Integrity* Home Page, which provides direct links to recent and relevant content in Integrity and access to the Knowledge Areas that are the entry points to searching and retrieving information in the portal.

QUICK ACCESS SEARCHES

The Quick Access Searches found on the *Integrity* Home Page provide direct access to Key Drugs & Biologics, and to Pipeline Information.

- **Quick Access to Key Drugs & Biologics** – Use the Browse Index to select one or more Drug names, and then click **Go** to display matching search results from the Drugs & Biologics Knowledge Area. (Drug names in *Integrity* include code, brand or generic names.)

- **Quick Access to Pipeline Information** – A link to all compounds launched or under active development for a specific condition.
  - Use the Condition Lookup to select one or more conditions (broad groups and/or subgroups can be selected) and click **OK**. Results are displayed as a program list, known as Gateways to Development

Status display in Integrity. Details include: Entry Number, Main Name, Mechanism of Action, Organization, Condition, Phase, Country, Admin. Route and Formulation.

– Click an underlined column header to sort data in ascending alphabetical/numerical order.

– Use the Options menu to choose alternative display formats, link to related information in other Knowledge Areas or to display the results in Printer Friendly Format.

– Click on an Entry Number link to display the corresponding record from the Drugs & Biologics Knowledge Area.

– Click on an Organization link to display the corresponding record from the Companies & Research Institutions Knowledge Area.

QUICK ACCESS LINKS

The Quick Access Links found on the *Integrity* Home Page or on the Knowledge Area pages provide direct access to specific information in the database.

• Highlights are updated daily and include Today's News, Today's Featured Patents, and Conferences.

• Weekly Insights provides one-click access to recent and relevant information found in *Integrity*, updated each Monday, and includes The Starting Line, Pipeline on the Move, Gateways to Gene-Related Studies, Gateways to Patents, and Gateways to Clinical Trials.

Today's News

Presents a sampling of current news in drug R&D. Links are provided to the 5-10 most significant news items added to the database in the last 24 hours.

• Click on an Article title link to display the corresponding News Article.

Today's Featured Patents

Presents Today's featured patent family entries in *Integrity*. A link is provided to a selection of patents analyzed in the last 24 hours.

• Click on the link under Today's Featured Patents to display the Patent results.

Conferences

Presents a summary of the latest conferences added to the database. Links are provided to selected references from recent conferences in the field of drug R&D.

- Click on a Citations link to display a list of references for a particular conference from the Literature Knowledge Area. (For ongoing conferences, citations are being added daily and so the number of available citations through the link will increase daily as more are added.)
- Click on a Report link (where present) to view highlights for a particular conference from the Literature Knowledge Area

The Starting Line

A link to a table, updated weekly, of the most promising compounds (NME/ New Molecular Entities). These compounds are usually lead compounds or else known entities with new mechanisms of action that have been cited for the first time in Literature references.

- Click on the link to display The Starting Line; 'A selection of new molecular entities and targets ready to enter the R&D arena'. Details include: Company, Product, Condition and Comments.
- Use the paging links to view all of the data, or click Print Full Table to print out the full table contents.
- Click on a Product link to display the corresponding record from the Drugs & Biologics Knowledge Area.

Pipeline on the Move

A link to a table, updated weekly, of changes detected in the status of drugs currently under active development. Presented in database format, with access to previous weeks' data and the ability to sort and export data.

- Click on the link to display Pipeline on the Move; 'Milestones for drugs under active development'. Details include: Organization, Main Name, Condition, Milestone, Area and Notes.
- Click an underlined column header to sort data in ascending alphabetical order.
- Use the paging links or the First, Previous, Next, Last links to view all of the data.

- Use the Options menu to export data in a spreadsheet (Excel) or word processor (Word) format, display a Product List or to display the results in Printer Friendly Format.
- Click on an Organization link to display the corresponding record from the Companies & Research Institutions Knowledge Area.
- Click on a Main Name link to display the corresponding record from the Drugs & Biologics Knowledge Area.

Gateways to Gene-Related Studies

A link to a list of new studies on targets added to *Integrity* during the previous business week.

- Click on the link to display Gateways to Gene-Related Studies; 'Studies delineating new areas of potential therapeutic intervention'. Details include: Gene Name, Organism, Condition, Study Type, Model and Links to References.
- Click an underlined column header to sort data in ascending alphabetical order.
- Use the Options menu to export data in a spreadsheet (Excel) or word processor (Word) format, link to related information in other Knowledge Areas, choose alternative display formats or to display the results in Printer Friendly Format.

- Click on a Reference link to display the associated reference.

Gateways to Patents
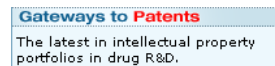
A link to the list of Featured patents from the previous business week.

- Click on the link to display Gateways to Patents; 'The latest in intellectual property portfolios in drug R&D'. Details include: Patents (Applicants), Title, Subject Matter, Condition and Lead Compound.
- Use the paging links to view all of the data.
- Use the Options menu to set up a Keep me Posted alert, export data in a spreadsheet (Excel), word processor (Word), BizInt or RDFile, link to related information in other Knowledge Areas, choose alternative display formats or to display the results in Printer Friendly Format.
- Click on a Title link to display the corresponding record from the Patents Knowledge Area.
- Click on a Lead Compound link to display the corresponding record from the Drugs & Biologics Knowledge Area.

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Gateways to Clinical Trials

A link to a table of new Clinical Studies references added to *Integrity* during the previous business week.

- Click on the link to display Gateways to Clinical Trials; 'Clinical studies cited in the most recent biomedical literature and at congresses'. Details include: Study, Design, Pop. No., Conclusions/Objectives and Details.
- Use the tab headers to display results for Journal/Congress or Other Sources. Use the paging links or the First, Previous, Next, Last links to view all of the data within a tab.
- Click an underlined column header to sort data in ascending alphabetical/ numerical order.
- Use the Options menu to export data in a spreadsheet (Excel) or word processor (Word) format, link to related information in other Knowledge Areas, choose alternative display formats or to display the results in Printer Friendly Format.
- Click on a Ref. link to display the associated reference.

GETTING STARTED
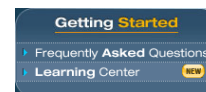
Includes links to Frequently Asked Questions and to the *Integrity* Learning Center.

Frequently Asked Questions
The *Integrity* FAQs provides answers for many of the most frequently asked questions, plus numerous definitions relating to the content found in *Integrity*.

Integrity Learning Center
The *Integrity* Learning Center provides case studies on how to use the Integrity portal efficiently and obtain the maximum benefit from data retrieved. Periodically, the Learning Center adds detailed case studies for *Integrity*, explaining search strategies, data links and other utilities using practical examples.

NEW FEATURES
The new features section of the *Integrity* Home Page presents the latest enhancements in *Integrity*, ranging from new content to technological innovations and new features.

KNOWLEDGE AREAS

Access to the Knowledge Areas search pages is provided at the top left of the *Integrity* Home Page.

Healthcare & Science Offices

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USER GUIDE - KNOWLEDGE AREAS

RELEASE 10.1

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INTEGRITY KNOWLEDGE AREAS

HOW TO CHOOSE A KNOWLEDGE AREA

When you log on to *Integrity*, you are taken to the *Integrity* Home Page, which provides gateways to the most recent and relevant content in *Integrity* and access to the Knowledge Areas that are the entry points to searching and retrieving information. Choosing a Knowledge Area determines a starting point for your search and the type of results you will view first; it does not affect your access to the complete set of data in *Integrity* because the data is fully integrated. Results displayed are linked to additional information that can be found in the other Knowledge Areas. You can go to a new Knowledge Area at any point: from the *Integrity* Home Page, from the Search Forms and from the Results Displays.

To begin searching *Integrity*:

- Click a Knowledge Area on the *Integrity* Home Page.

DEFINITION OF KNOWLEDGE AREAS

Each Knowledge Area search form is composed of sections that allow you to develop search strategies to retrieve data of interest. For example, the Drugs & Biologics Knowledge Area search form allows you to combine search criteria from four sections: Product, Reference, Targets & Pathways and Patent.

The Knowledge Areas available for searching and retrieving information in Integrity are:

Knowledge Area	Information Type	Used to Search For
Drugs & Biologics	Essential general and chemical information, and the development status of bioactive compounds in the drug development pipeline.	Information on bioactive compounds. Searches can include criteria for targets, literature or patent references associated with the compounds.
Targets & Pathways	Coverage of genes and their related proteins as precedented targets for drug discovery.	Information on gene, proteins and physiopathologic processes as targets for therapeutic intervention. Searches can include criteria for products, literature or patent references associated with the targets.

Definition of Knowledge Areas continued...

Knowledge Area	Information Type	Used to Search For
Genomics	Covers the relationships between genes and diseases to provide insights into underlying biological mechanisms and identify potential new drug targets.	Information on genes, diseases and underlying biological mechanisms as targets for therapeutic intervention. Searches can include criteria for literature or patent references associated with the genomics.
Biomarkers*	Covers a wide range of biomarker types from genomic, proteomic and biochemical to cellular, physiological and imaging.	Information on biomarker uses at every stage of drug R&D, including disease risk detection, diagnosis, target identification, proof-of-mechanism, proof-of-concept, treatment/safety monitoring, and outcome measurement. Searches can include criteria for product, literature or patent references associated with the biomarkers.

Knowledge Area	Information Type	Used to Search For
Organic Synthesis	Routes of synthesis (schemes, intermediates, reagents, end products) for drugs currently on the market or in development. Includes routes of synthesis for end products in biological testing published from patents selected for DDR.	Information on drug synthesis routes, chemical intermediates, reagents and end products of synthesis processes. Searches can include criteria for end products, literature or patent references associated with the syntheses.
Experimental Pharmacology	Data from experimental studies that delineate drug/receptor and enzyme/target cell interactions.	Information on pharmacological activity screens and assays of bioactive compounds. Searches can include criteria for bioactive compounds tested, associated literature and patent references.

* – Requires additional subscription.

Definition of Knowledge Areas continued...

Knowledge Area	Information Type	Used to Search For
Pharmacokinetics/ Metabolism	Data from experimental and clinical studies that delineate the absorption, distribution, metabolism and excretion (ADME) profile of a drug.	IInformation on pharmacokinetics studies of bioactive compounds. Searches can include criteria for bioactive compounds tested or associated literature references.
Clinical Studies	Information on clinical trials of drugs currently under study or in use in humans.	Information on clinical studies of bioactive compounds. Searches can include criteria for bioactive compounds tested or associated literature references.
Disease Briefings	Dynamic executive summaries on the current status of and future trends in drug therapy for specific diseases.	Disease briefings by name or content (full text). Searches can include bioactive compound criteria.

Knowledge Area	Information Type	Used to Search For
Companies & Research Institutions	Essential information on public and private companies, academic centers and research institutions active in the field of pharmaceuticals and biotechnology.	Information on overall company sales/revenues, sales of launched products, products in development and new patents. Searches can include criteria for products or patent references associated with the companies.
Literature	References to current biomedical literature, abstracts and proceeding from congresses and symposia and company communications.	Information on biomedical literature, congresses and company communications. Searches can include bioactive compound criteria.
Patents	References to the most recent patent literature reflecting drug research activity throughout the world	Information on patent literature related to drug discovery and development. Searches can include bioactive compound criteria

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SEARCHING INTEGRITY

There are four ways of searching in *Integrity*:

- Advanced Search forms (found in each Knowledge Area)
- Quick Search (found on each page in *Integrity*)
- Quick access links (e.g. Pipeline on the Move, Today's Patents, etc...)
- Disease Briefings (searching based on a medical condition or disease)

SEARCHING INTEGRITY

After logging on to *Integrity* and selecting a Knowledge Area you are taken to the Advanced Search form for that Knowledge Area.

- Each Advanced Search form contains a series of search fields that are grouped into Sections such as Product, Targets & Pathways, Reference, Patent, Organic Synthesis, Experimental Pharmacology, Pharmacokinetics/Metabolism, Clinical Studies, Companies & Research Institutions and Disease Briefings.
- Each Knowledge Area contains a combination of two or more Sections that can be used for simple or complex searching schemes using Boolean logic search operators (AND/OR).
- The top section of each Advanced Search form is a set of search fields specific to the Knowledge Area selected (for example, fields such as Applicant in Patents and Author in Literature) and in most cases one of the other Sections will be the Product section of search fields. Some Knowledge Areas will also have additional sections of search fields, where

this is relevant to the content of the Knowledge Area

Each section includes a total of 3 search fields. On the left of each search field line is a menu (with the default heading Select Value or Optional Value) that allows you to choose a specific search field. Next to the menu is a search field box where you can enter search terms manually or select from a Browse Index. To the right of each field is an Index button that opens a Browse Index of associated vocabulary for the search field chosen. To the right of the Index button is an inter-field operator button that allows you to combine search fields using Boolean logic (AND/OR).

At the top right corner of the Advanced Search Form are a Clear button for resetting the Search Form contents and a Start button for launching the search.

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BROWSE INDEXES

Most search fields in *Integrity* have an associated Browse Index of search terms available for use in that field. Fields that do not have a Browse Index have a tip indicating how searches should be set up (e.g. YES/NO fields or date formats). Consult the Browse Index for assistance in choosing search terms to use in your search strategies. The Lookup function on the left can be used to obtain a short list of available search terms. Selecting specific terms in this way, those used in *Integrity*, ensures that if what you are searching for is in Integrity, you will get results. For example, *Integrity* standardizes to one term for all masterlists and controlled vocabulary indexes, so using abbreviations, alternate terms, or alternate spellings of a given term will result in missing results, whereas selecting from the index will retrieve them all.

- There are four basic types of Browse Index in *Integrity*:
- Tip – offers hints on the format for entering criteria (e.g. Available Since)
- Masterlist – contains the complete database content (e.g. Drug Name)
- Controlled Vocabulary – unique terms for given criteria (e.g. Phase)
- Controlled Vocabulary: hierarchical – unique terms for given criteria searchable by hierarchy (e.g. Mechanism of Action)

Terms are displayed in a pop-up window, depending on the content type of the List; Masterlist, Controlled Vocabulary: Hierarchical List, Controlled Vocabulary: Non-Hierarchical List, Free Text Fields, YES/NO fields, or Numeric (date) Fields.

Masterlist

Used for example:

- Drug Name, Pharmacological Activity, Organization, etc...

Masterlists contain the complete database content and allow alphabetical browsing of terms and term lookup.

1. Click on the **Index** button to select terms.
2. Use the text entry box to display a short list of matching terms – simply type in text and then press Enter or click **Lookup**. It is not necessary to use truncation.
3. Alternatively, click a letter from the A-Z browse index links (options are 0-9, and all individual letters A through to Z) to display a short list of terms starting with a particular letter.
4. Select one or more terms from the list of terms and click **OK** to copy the term(s) to the search field. When selecting multiple terms from the same index a logical OR operator is placed automatically between terms. However, you can change this to AND by typing directly into the search boxes, as required.
   - **Ctrl+click** – hold down the control key and click-select individual (non-contiguous) terms.
   - **Shift+click** – hold down the shift key and click-select start and end terms to define a (contiguous) range or span.
5. Optional. Click the **Print** icon ⎙ to print off the List of Values.

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Controlled Vocabulary: Hierarchical List

Used for example:

- Condition, Mechanism of Action, Classification, Product Category, etc...

Hierarchical lists consist of a controlled set of terms organized into a hierarchy that allows browsing of related concepts to identify more specific terms and term lookup.

1. Click on the **Index** button to select terms from the hierarchical indexes.

   The indexing tree opens displaying the top level terms.

2. Use the text entry box to locate a term directly within the hierarchy – simply type in text and then press Enter or click **Lookup**. It is not necessary to use truncation.

   The hierarchy is expanded and any matching terms appear highlighted. The tree opens at all points where matching terms appear.

3. Use the [+] or [–] alongside a term to expand or collapse the tree below a term, and to navigate through the hierarchy. Browse and locate the terms you want; browsing can also be useful since it allows you to see how all the terms are grouped together under the various subject headings. (Subject headings appear listed alphabetically.)

4. Use the scroll bar in combination with the First, Previous, Next and Last buttons to locate specific terms within the hierarchy.

5. Click **Order alphabetically** to switch views between Hierarchical and Alphabetical lists.

6. Click on the desired terms to add them to your search. For the Alphabetical list view, selection of multiple terms is possible (then click **OK** to copy the term(s) to the Search Form):

   - **Ctrl+click** – hold down the control key and click-select individual (non-contiguous) terms.
   - **Shift+click** – hold down the shift key and click-select start and end terms to define a (contiguous) range or span.

7. Optional. Click the **Print** icon 🖶 to print off the List of Values.

When selecting multiple terms from the same index a logical OR operator is placed automatically between terms. However, you can change this to AND by typing directly into the search boxes, as required.

Controlled Vocabulary: Non-hierarchical List

Used for example:

- Phase, Administration Route, Milestone, etc...

Controlled Vocabulary: Non-hierarchical lists consist of a controlled set of terms that allows alphabetical browsing of terms and term lookup.

1. Click on the **Index** button to select terms.

2. Use the text entry box to display a short list of matching terms – simply

type in text and then press Enter or click **Lookup**. It is not necessary to use truncation.

3. Alternatively, click a letter from the A-Z browse index links (options are 0-9, and all individual letters A through to Z) to display a short list of terms starting with a particular letter.

4. Select one or more terms from the list of terms and click **OK** to copy the term(s) to the search field.

   - **Ctrl+click** – hold down the control key and click-select individual (non-contiguous) terms.
   - **Shift+click** – hold down the shift key and click-select start and end terms to define a (contiguous) range or span.

   When selecting multiple terms from the same index a logical OR operator is placed automatically between terms. However, you can change this to AND by typing directly into the search boxes, as required.

5. Optional. Click the **Print** icon 🖨 to print off the List of Values.

Free Text Fields
Used for example:

- Chemical Name/Description, Molecular Formula, etc…

Provides hints and advice on the format for entering search criteria in free text fields, including details of intra-field operators that can be used (AND, OR, NOT) and search examples.

YES/NO Fields
Used for example:

- New Molecular Entity, Basic Patent, Under Active Development, etc…

Provides hints and advice on the format for entering search criteria in YES/NO fields. Yes and No are the only permitted values in these fields; type Y for Yes, N for No.

Numeric Fields
Used for example:

- Entry Number, Available Since, Year Launched/Registered, CAS Registry No., etc…

Provides hints and advice on the format for entering search criteria in numeric (date) fields, including details of intra-field operators that can be used, plus ranges, greater than and less than.

Browse Indexes Summary
The tables below summarize which fields/browse indexes are found within each of the Sections on the Search Forms in Integrity.

Product
Found in the Drugs & Biologics, Targets & Pathways, Biomarkers, Experimental Pharmacology, Pharmacokinetics/Metabolism, Clinical Studies, Disease

Briefings, Companies & Research Institutions, Literature, and Patents Knowledge Areas.

Search Field		Index Type	Additional Details
Entry Number		Hint (number)	Provides details on the format for entering search criteria
Drug Name		Masterlist	Lookup and A-Z browse links display
Chemical Name/ Description		Hint (free text)	Provides details on the format for entering search criteria
Standard InChI		Hint (free text)	Provides details on the format for entering search criteria
Standard InChIKey		Hint (free text)	Provides details on the format for entering search criteria

Search Field		Index Type	Additional Details
CAS Registry No.		Hint (number)	Provides details on the format for entering search criteria
Molecular Formula		Hint (free text)	Provides details on the format for entering search criteria
Molecular Weight		Hint (number)	Provides details on the format for entering search criteria
Highest Phase		Controlled: Non-hierarchical	Lookup and A-Z browse links display
Year Launched/ Registered		Hint (date)	Provides details on the format for entering search criteria
Organization		Masterlist	Lookup and A-Z browse links display

Definition of Knowledge Areas (Product) continued...

Search Field		Index Type	Additional Details
Organization (+ Related Orgs.)		Masterlist	Lookup and A-Z browse links display
Condition		Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
Therapeutic Group		Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
Mechanism of Action		Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
Product Category		Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display

Search Field		Index Type	Additional Details
Prescription/ Indication Type		Controlled: Non-hierarchical	Lookup and A-Z browse links display
New Molecular Entity (Y/N)		Hint (Yes/No)	Provides details on the format for entering search criteria
Metabolites (Y/N)		Hint (Yes/No)	Provides details on the format for entering search criteria
Natural Source (Y/N)		Hint (Yes/No)	Provides details on the format for entering search criteria
Development Status	Phase	Controlled: Non-hierarchical	Lookup and A-Z browse links display
	Condition	Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display

Search Field		Index Type	Additional Details
Development Status continued...	Organization	Masterlist	Lookup and A-Z browse links display
	Brand Name	Masterlist	Lookup and A-Z browse links display
	Under Active Development (Y/N)	Hint (Yes/No)	Provides details on the format for entering search criteria
	Administration Route	Controlled: Non-hierarchical	Lookup and A-Z browse links display
	Formulation	Hint (free text)	Provides details on the format for entering search criteria
Milestone	Milestone	Controlled: Non-hierarchical	Lookup and A-Z browse links display
	Milestone Date	Hint (date)	Provides details on the format for entering search criteria

Search Field		Index Type	Additional Details
Milestone continued...	Condition	Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
	Organization	Masterlist	Lookup and A-Z browse links display
Natural Source	Scientific Name	Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
	Common Name	Masterlist	Lookup and A-Z browse links display
	Organism Part	Controlled: Non-hierarchical	Lookup and A-Z browse links display
	Geographic Area	Controlled: Non-hierarchical	Lookup and A-Z browse links display
Last Updated		Hint (date)	Provides details on the format for entering search criteria

Definition of Knowledge Areas (Product) continued...

Search Field		Index Type	Additional Details
Available Since		Hint (date)	Provides details on the format for entering search criteria

Targets & Pathways

Found in the Drugs & Biologics and Targets & Pathways Knowledge Areas.

Search Field		Index Type	Additional Details
Classification		Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
Target Name	Name	Masterlist	Lookup and A-Z browse links display
	Type	Controlled: Non-hierarchical	Lookup and A-Z browse links display
Description		Hint (free text)	Provides details on the format for entering search criteria
GenBank ID		Masterlist	Lookup and A-Z browse links display
Entrez Gene ID		Masterlist	Lookup and A-Z browse links display
PDB ID		Masterlist	Lookup and A-Z browse links display

Definition of Knowledge Areas (Targets & Pathways) continued...

Search Field		Index Type	Additional Details
Swiss-Prot		Masterlist	Lookup and A-Z browse links display
EC Classification		Masterlist	Lookup and A-Z browse links display
Condition	Condition	Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
	Status	Controlled: Non-hierarchical	Lookup and A-Z browse links display
Targetscape		Hint (Yes/No)	Provides details on the format for entering search criteria
Images & Pathways		Hint (Yes/No)	Provides details on the format for entering search criteria

Search Field		Index Type	Additional Details
Images & Pathways Title		Hint (free text)	Provides details on the format for entering search criteria
Available Since		Hint (date)	Provides details on the format for entering search criteria

Genomics

Found in the Genomics Knowledge Area only.

Search Field			Index Type	Additional Details
Classification			Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
Gene Name			Masterlist	Lookup and A-Z browse links display
Protein Name			Masterlist	Lookup and A-Z browse links display
Gene/Protein Name			Masterlist	Lookup and A-Z browse links display
EC Classification			Masterlist	Lookup and A-Z browse links display
PDB ID			Masterlist	Lookup and A-Z browse links display
Swiss-Prot			Masterlist	Lookup and A-Z browse links display
GenBank ID			Masterlist	Lookup and A-Z browse links display

Search Field			Index Type	Additional Details
Entrez Gene ID			Masterlist	Lookup and A-Z browse links display
Condition			Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
Sequence			Hint (text)	Provides details on the format for entering search criteria
Sequence Type			Controlled: Non-hierarchical	Lookup and A-Z browse links display
Organism			Masterlist	Lookup and A-Z browse links display
Gene Variants	Variation Type		Controlled: Non-hierarchical	Lookup and A-Z browse links display
	Disease Association		Controlled: Non-hierarchical	Lookup and A-Z browse links display

Definition of Knowledge Areas (Genomics) continued...

Search Field			Index Type	Additional Details
	Variation Name		Masterlist	Lookup and A-Z browse links display
	Gene Variant Diseases	Condition	Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
		Effect	Controlled: Non-hierarchical	Lookup and A-Z browse links display
Gene-Related Studies	Condition		Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
	Model		Masterlist	Lookup and A-Z browse links display
	Study Type		Controlled: Non-hierarchical	Lookup and A-Z browse links display

Search Field			Index Type	Additional Details
	Polymor-phism (Y/N)		Hint (Yes/No)	Provides details on the format for entering search criteria
Last Updated			Hint (date)	Provides details on the format for entering search criteria
Available Since			Hint (date)	Provides details on the format for entering search criteria

Biomarkers

Found in the Biomarkers Knowledge Area only; the fields appear grouped as Biomarker or Biomarker Use.

Biomarker				
Search Field			Index Type	Additional Details
Name			Masterlist	Lookup and A-Z browse links display
Type			Controlled: Non-hierarchical	Lookup and A-Z browse links display
Biological Process			Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
Description			Hint (free text)	Provides details on the format for entering search criteria
Product Modifier			Masterlist	Lookup and A-Z browse links display

Search Field			Index Type	Additional Details
Mechanism Modifier			Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
Highest Validity			Controlled: Non-hierarchical	Lookup and A-Z browse links display
Methods Papers	Type		Controlled: Non-hierarchical	Lookup and A-Z browse links display
	Stage		Controlled: Non-hierarchical	Lookup and A-Z browse links display
	Reference		Hint (free text)	Provides details on the format for entering search criteria
Review Type			Controlled: Non-hierarchical	Lookup and A-Z browse links display

Definition of Knowledge Areas (Biomarkers) continued…

Search Field			Index Type	Additional Details
Review Title			Hint (free text)	Provides details on the format for entering search criteria
Last Update			Hint (date)	Provides details on the format for entering search criteria
Available Since			Hint (date)	Provides details on the format for entering search criteria

Biomarker Use				
Search Field			Index Type	Additional Details
Use ID			Hint (number)	Provides details on the format for entering search criteria
Indication	Condition		Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
	Safety/Tox.		Controlled: Non-hierarchical	Lookup and A-Z browse links display
	Experimental Pathology		Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
Population			Masterlist	Lookup and A-Z browse links display
Role			Controlled: Non-hierarchical	Lookup and A-Z browse links display

Definition of Knowledge Areas (Biomarkers) continued...

Search Field			Index Type	Additional Details
Validity			Controlled: Non-hierarchical	Lookup and A-Z browse links display
Parameter			Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
Technique			Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
Substrate			Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
Kit	Name		Masterlist	Lookup and A-Z browse links display
	Organization		Masterlist	Lookup and A-Z browse links display
	All Related Organiza-tions		Masterlist	Lookup and A-Z browse links display

Search Field			Index Type	Additional Details
	Regulatory Authority		Controlled: Non-hierarchical	Lookup and A-Z browse links display
	Country		Masterlist	Lookup and A-Z browse links display
	Status		Controlled: Non-hierarchical	Lookup and A-Z browse links display
	Milestone	Country	Masterlist	Lookup and A-Z browse links display
		Name	Controlled: Non-hierarchical	Lookup and A-Z browse links display
		Date	Hint (date)	Provides details on the format for entering search criteria
Genetic Variation	Gene Name (including synonyms)		Masterlist	Lookup and A-Z browse links display

Definition of Knowledge Areas (Biomarkers) continued...

Search Field			Index Type	Additional Details
Correlates to...			Controlled: Non-hierarchical	Lookup and A-Z browse links display
Product Name			Masterlist	Lookup and A-Z browse links display
Mechanism of Action			Controlled: Non-hierarchical	Lookup and A-Z browse links display
Product Category			Controlled: Non-hierarchical	Lookup and A-Z browse links display
Therapeutic Group			Controlled: Non-hierarchical	Lookup and A-Z browse links display
Authority			Controlled: Non-hierarchical	Lookup and A-Z browse links display

Organic Synthesis
Found in the Organic Synthesis Knowledge Area only.

Search Field		Index Type	Additional Details
Synthesis Text		Hint (free text)	Provides details on the format for entering search criteria
Drug (End Product) Name		Masterlist	Lookup and A-Z browse links display
End Product Entry Number		Hint (number)	Provides details on the format for entering search criteria
Scheme Number		Hint (number)	Provides details on the format for entering search criteria
Available Since		Hint (date)	Provides details on the format for entering search criteria

Definition of Knowledge Areas (Organic Synthesis) continued...

Search Field		Index Type	Additional Details
Intermediate	Number	Hint (number)	Provides details on the format for entering search criteria
	Chemical Name	Hint (free text)	Provides details on the format for entering search criteria
	Standard InChl	Hint (free text)	Provides details on the format for entering search criteria
	Standard InChlKey	Hint (free text)	Provides details on the format for entering search criteria

Search Field		Index Type	Additional Details
	CAS Registry No.	Hint (number)	Provides details on the format for entering search criteria
	Molecular Formula	Hint (free text)	Provides details on the format for entering search criteria
	Molecular Weight	Hint (number)	Provides details on the format for entering search criteria
	Supplier	Masterlist	Lookup and A-Z browse links display
Reagent	Number	Hint (number)	Provides details on the format for entering search criteria

Definition of Knowledge Areas (Organic Synthesis) continued...

Search Field		Index Type	Additional Details
	Chemical Name	Hint (free text)	Provides details on the format for entering search criteria
	Standard InChI	Hint (free text)	Provides details on the format for entering search criteria
	Standard InChIKey	Hint (free text)	Provides details on the format for entering search criteria
	CAS Registry No.	Hint (number)	Provides details on the format for entering search criteria

Search Field		Index Type	Additional Details
	Molecular Formula	Hint (free text)	Provides details on the format for entering search criteria
	Molecular Weight	Hint (number)	Provides details on the format for entering search criteria
	Supplier	Masterlist	Lookup and A-Z browse links display
	Representation	Hint (free text)	Provides details on the format for entering search criteria

Experimental Pharmacology

Found in the Experimental Pharmacology Knowledge Area only.

Search Field	Index Type	Additional Details
Pharmacological Activity	Controlled: Non-hierarchical	Lookup and A-Z browse links display
Parameter	Controlled: Non-hierarchical	Lookup and A-Z browse links display
Unit	Controlled: Non-hierarchical	Lookup and A-Z browse links display
Method	Controlled: Non-hierarchical	Lookup and A-Z browse links display
Material	Controlled: Non-hierarchical	Lookup and A-Z browse links display
Available Since	Hint (date)	Provides details on the format for entering search criteria

Pharmacokinetics/Metabolism

Found in the Pharmacokinetics/Metabolism Knowledge Area only.

Search Field		Index Type	Additional Details
Model		Controlled: Non-hierarchical	Lookup and A-Z browse links display
Condition		Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
Administered Product	Drug Name	Masterlist	Lookup and A-Z browse links display
	Formulation	Controlled: Non-hierarchical	Lookup and A-Z browse links display
	Administration Route	Controlled: Non-hierarchical	Lookup and A-Z browse links display
	Interacting Agent	Controlled: Non-hierarchical	Lookup and A-Z browse links display
Measured Product	Drug Name	Masterlist	Lookup and A-Z browse links display
	Compartment	Controlled: Non-hierarchical	Lookup and A-Z browse links display

Definition of Knowledge Areas (Pharmacokinetics/Metabolism) continued...

Search Field		Index Type	Additional Details
	Measured As	Controlled: Non-hierarchical	Lookup and A-Z browse links display
	Parameter	Controlled: Non-hierarchical	Lookup and A-Z browse links display
Available Since		Hint (date)	Provides details on the format for entering search criteria

Clinical Studies

Found in the Clinical Studies Knowledge Area only.

Search Field	Index Type	Additional Details
Condition	Controlled: Non-hierarchical	Lookup and A-Z browse links display
Study Design	Controlled: Non-hierarchical	Lookup and A-Z browse links display
Study	Hint (free text)	Provides details on the format for entering search criteria
Intervention Type	Controlled: Non-hierarchical	Lookup and A-Z browse links display
Population No.	Hint (number)	Provides details on the format for entering search criteria
Journal or Congress	Hint (Yes/No)	Provides details on the format for entering search criteria
Available Since	Hint (date)	Provides details on the format for entering search criteria

Disease Briefings

Found in the Disease Briefings Knowledge Area only.

Search Field	Index Type	Additional Details
Disease Briefing	Masterlist	Lookup and A-Z browse links display
Text	Hint (free text)	Provides details on the format for entering search criteria
Available Since	Hint (date)	Provides details on the format for entering search criteria
Last Updated	Hint (date)	Provides details on the format for entering search criteria

Companies & Research Institutions

Found in the Companies & Research Institutions Knowledge Area only.

Search Field		Index Type	Additional Details
Organization Name		Masterlist	Lookup and A-Z browse links display
Organization (+ Related Orgs.)		Masterlist	Lookup, hierarchical, alphabetical and A-Z browse links display
Headquarters (Country)		Masterlist	Lookup and A-Z browse links display
Main Activity		Controlled: Non-hierarchical	Lookup and A-Z browse links display
Product Economic Data	Product Annual Sales	Hint (number)	Provides details on the format for entering search criteria
	Drug Name	Masterlist	Lookup and A-Z browse links display

Definition of Knowledge Areas (Companies & Research Institutions) continued...

Search Field		Index Type	Additional Details
	Year	Hint (year)	Provides details on the format for entering search criteria
	Geographic Area	Masterlist	Lookup and A-Z browse links display
Company Economic Data	Number of Employees	Hint (number)	Provides details on the format for entering search criteria
	R&D (% of Sales)	Hint (number)	Provides details on the format for entering search criteria
	Total Sales	Hint (number)	Provides details on the format for entering search criteria

Search Field		Index Type	Additional Details
	Total Revenues	Hint (free text)	Provides details on the format for entering search criteria
	Total Sales/Revenues	Hint (number)	Provides details on the format for entering search criteria
	Year	Hint (number)	Provides details on the format for entering search criteria
Last Updated		Hint (date)	Provides details on the format for entering search criteria
Available Since		Hint (date)	Provides details on the format for entering search criteria

Reference

Found in the Drugs & Biologics, Targets & Pathways, Genomics, Biomarkers, Organic Synthesis, Experimental Pharmacology, Pharmacokinetics/ Metabolism, Clinical Studies, and Literature Knowledge Areas.

Search Field		Index Type	Additional Details
Title		Hint (free text)	Provides details on the format for entering search criteria
Text		Hint (free text)	Provides details on the format for entering search criteria
Title/Text		Hint (free text)	Provides details on the format for entering search criteria
Author		Masterlist	Lookup and A-Z browse links display

Search Field		Index Type	Additional Details
Source		Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
Year		Hint (date)	Provides details on the format for entering search criteria
Volume		Hint (number)	Provides details on the format for entering search criteria
Issue/Number		Hint (number)	Provides details on the format for entering search criteria
News Date		Hint (date)	Provides details on the format for entering search criteria

Definition of Knowledge Areas (Reference) continued...

Search Field		Index Type	Additional Details
Congress	Source	Masterlist	Lookup and A-Z browse links display
	Year	Hint (date)	Provides details on the format for entering search criteria
	Congress Edition	Hint (number)	Provides details on the format for entering search criteria
	City	Masterlist	Lookup and A-Z browse links display
	Country	Masterlist	Lookup and A-Z browse links display
Last Updated		Hint (date)	Provides details on the format for entering search criteria

Search Field		Index Type	Additional Details
Available Since		Hint (date)	Provides details on the format for entering search criteria

Patent

Found in the Drugs & Biologics, Targets & Pathways, Genomics, Biomarkers, Organic Synthesis, Experimental Pharmacology, Companies & Research Institutions, and Patents Knowledge Areas.

Search Field		Index Type	Additional Details
Title		Hint (free text)	Provides details on the format for entering search criteria
Integrity Abstract		Hint (free text)	Provides details on the format for entering search criteria
Original Abstract		Hint (free text)	Provides details on the format for entering search criteria
Title/Abstracts		Hint (free text)	Provides details on the format for entering search criteria

Search Field		Index Type	Additional Details
Condition		Controlled: Hierarchical	Lookup, hierarchical, alphabetical and A-Z browse links display
Subject Matter		Controlled: Non-hierarchical	Lookup and A-Z browse links display
Application Data	Application Data	Masterlist	Lookup and A-Z browse links display
	Application Name (+ All Related)	Masterlist	Lookup and A-Z browse links display
	Country	Masterlist	Lookup and A-Z browse links display
	State	Masterlist	Lookup and A-Z browse links display
	Research Institution (Y/N)	Hint (Yes/No)	Provides details on the format for entering search criteria

Definition of Knowledge Areas (Patent) continued...

Search Field		Index Type	Additional Details
Inventor		Masterlist	Lookup and A-Z browse links display
Patent	Patent Number	Hint (free text)	Provides details on the format for entering search criteria
	Publication Date	Hint (date)	Provides details on the format for entering search criteria
	Expiration Date	Hint (date)	Provides details on the format for entering search criteria
	Basic Patent (Y/N)	Hint (Yes/No)	Provides details on the format for entering search criteria

Search Field		Index Type	Additional Details
Priority	Priority Data	Hint (free text)	Provides details on the format for entering search criteria
	Priority Date	Hint (date)	Provides details on the format for entering search criteria
Last Updated		Hint (date)	Provides details on the format for entering search criteria
Available Since		Hint (date)	Provides details on the format for entering search criteria

COMBINING SEARCH TERMS

AND ▸

You can combine search fields using the appropriate inter-field (AND/OR) button on the far right of each search field box on the search screen. Where your search query includes several fields it is important to ensure that you specify the relationships between fields, since this will affect the composition of your results.

- Use the inter-field Boolean operator button(s) to combine search fields using Boolean logic (AND/OR)

AND ▸
AND
OR

Multiple fields are automatically linked with the Boolean AND operator; however, you can change this to OR if you wish. Using the AND operator searches for the occurrences that meet the criteria of all the fields linked with this operator; using the OR operator searches for the occurrences that meet the criteria for at least one field where a term has been entered.

You can combine terms within a search field to create a logical statement by using the operators and wildcards listed below.

AND – All of the search terms linked with this operator (intra-field or inter-field) must be present in the field (e.g. in the Authority field: "ASCO" AND "European Group on Tumor Markers (EGTM)").

- Using the Boolean AND operator effectively narrows your search, making it more focused. Typically, the more search terms or concepts you combine in a search using AND logic, the smaller the results set.

OR – Any of the search terms linked with this operator (intra-field or inter-field) can be present in the field (e.g. in the Development Status Phase field: "Phase III" OR "Pre-Registered").

- Using the Boolean OR operator keeps your search broad and ensures the most comprehensive retrieval. Typically, the more search terms or concepts you combine in a search using OR logic, the larger the results set.

A logical OR is automatically placed between multiple terms selected from the same Browse Index; however, you can change this to logical AND by typing directly into the search boxes, as required.

From – From indicates the starting point of a search that is based on numerical or date values (e.g. in the Patent Publication Date field: From 20050101).

From... To... – From ... To ... indicates the starting and ending points of a search that is based on numerical or date values (e.g. in the Patent Publication Date field: From 20050101 to 20050201).

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* – The asterisk (*) symbol replaces any number of characters in the search term. It can be used either as a truncation symbol at the start, end or both the start and end of a search term (e.g. in the Drug Name field: val*; *sartan; *alsart*), or as a wildcard symbol within a search term.

? – The question mark (?) symbol replaces a single character and can be repeated and used as a wildcard symbol anywhere in the search term (e.g. in the Drug Name field: Aprov?l; Aprov??).

GENERAL TEXT/DATA SEARCHING

Take the following steps to run a text or data search in *Integrity*:

1. Go to a Knowledge Area.
2. Choose a Section.
3. Enter your text or search terms into one or more search boxes.
   - Select a field to search from the list of available field values (the menus have the default headings Select Value or Optional Value).
   - Click the **Index** button to open the Browse Index for the search field chosen and select terms (recommended) or type words or phrases directly. (Use the Windows Maximize icon to expand the Browse Index to see more terms at once.)
   - **Browse Indexes:** Some Browse Indexes offer a choice of an alphabetical or a hierarchical display. The Lookup function on the left can be used to obtain a short list of available search terms. Select one or more terms in the index on the right and click **OK** to close the Browse Index window and copy the term(s) to the Search Form. If you wish to add another term to the field, click the Index button again and choose a new term.
   - Where multiple terms are selected within a single field, a logical OR operator is inserted automatically to separate the terms; however, you can change this manually to AND if you wish.
   - Not all the search fields have an associated Browse Index of terms. Some fields provide a description of the type of search term that should be entered manually within the field, which format to use, and

which operators and wildcards are valid.

- If you wish to add other criteria to your search strategy, repeat the process using the next search field line down within the same Section or go to the first free search field line in any other Section of the Search Form. You must complete at least one search field to perform a search; however, it is not obligatory to enter terms in more than one field.

4. Specify the relationship between the search boxes; choose to retrieve 'all terms' or 'any terms' by selecting AND or OR inter-field Boolean operators, as desired. (AND is selected by default.)

5. Optional. If your search includes fields selected from the Product, Organic Synthesis or Experimental Pharmacology Sections:

- For Product, choose to filter by Lead Compound and/or Under Active Development; initially, neither option is selected.

- For Organic Synthesis, choose to display Schemes or Intermediates or Reagents; initially, Schemes is selected.

(For Intermediate sub-fields, available choices are Schemes or Intermediates; for Reagent sub-fields, available choices are Schemes or Reagents.)

- For Experimental Pharmacology, choose to Include Literature Results and/or Include Patent Results; initially, both options are selected.

6. Click the **Start** button at the top of the Search Form to run the search and view your results, or click **Clear Form** at any point to clear the entire search query and start afresh. The results of your search appear in a table, list or record format depending on the number of records retrieved by the search.

7. Optional. Use the Session History to retrace queries and results obtained during the past 24 hours. The functionality is identical to that of the Session History tab within the Query Manager/Alert Center; you can re-run a previous search to generate a new results list, edit a search strategy and then either re-run or save it, or save a query for future use and (optionally) set the search as an e-mail alert, if desired.

Notes:
- Each search field can contain up to 300 characters maximum (includes search terms and any Boolean logic operators; for example, Phase = "Phase III" or "Pre-Registered" or "Recommended Approval" or "Registered").
- Searching is not case sensitive – typing words in upper case, lower case or mixed case produces exactly the same results.
- Logic operators (Boolean AND, OR) can be used to define the relationship

between search terms you enter, both within and between fields (intra-field or inter-field).

• Wildcard truncation can be used at the start, within, or at the end of search terms; you can also combine or use symbols multiply in a single word or term.

 * – The asterisk (*) symbol replaces any number of characters and can be used at the start, end, both the start and end, or within a search term.

 ? – The question mark (?) symbol replaces a single character and can be repeated and used anywhere in the search term.

RECORD COUNT

Integrity displays information on the number of records in each Knowledge Area and, additionally, the number of records with a chemical structure for the Drugs & Biologics Knowledge Area. This provides you with a quick overview of the product database content.

324122 Records in Drugs & Biologics
302354 Records with chemical structure

CHEMICAL STRUCTURE SEARCHING

Structure Search Options · Structure Search

Search Type
○ Substructure
○ Exact Structure
○ Similarity (0-100%) 80

Structure Representation
○ Normal
○ Standardized

Search Options
☐ Match Stereochemistry

Guide to Structure Search Options

You are using Symyx MDL ISIS/Draw. Double-click in the structure drawing window above to launch Symyx MDL ISIS/Draw. When you have drawn your structure, click Transfer to copy the structure into the Integrity Structure Drawing Window.

Click here to change to another structure editor.

Integrity has a chemical structure search feature that allows you to search by product substructure in the Product Section of the Drugs & Biologics, Experimental Pharmacology, Pharmacokinetics/Metabolism, Clinical Studies, Companies & Research Institutions, Disease Briefings, Literature and Patents Knowledge Areas and for products or chemical intermediates in the Organic Synthesis Knowledge Area. You can combine substructure searches with text and data searches.

One of the chemical structure search features of *Integrity* is a CS ChemOffice™ Webserver application. To utilize this chemical structure search function, you must have the CS ChemDraw™ Pro plug-in or the CS ChemDraw™ Net plug-in

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installed on your computer. The Net plug-in can be downloaded at no charge via the link provided in *Integrity*. Use this plug-in to run substructure searches in the Drugs & Biologics, Organic Synthesis, Experimental Pharmacology, Pharmacokinetics/ Metabolism, Clinical Studies, Disease Briefings, Companies & Research Institutions, Literature and Patents Knowledge Areas.

An alternative chemical structure search feature available in the Drugs & Biologics Knowledge Area is a ChemAxon Jchem™ application. To utilize this chemical structure search function, you must have the Marvin applet installed on your computer. The Marvin applet downloads automatically when you connect to the Marvin structure search page inside *Integrity*.

Take the following steps to run a substructure or combined search in *Integrity*:

1. Go to a Knowledge Area. (Structure Search is available in all Knowledge Areas except Targets & Pathways, Genomics, and Biomarkers.)
2. Click the Structure Search bar that is next to the Product or Organic Synthesis Section.

Structure Search

3. The Structure Search Form opens. If you are in the Drugs & Biologics Knowledge Area, you are taken to the structure search editor that you last used (Symyx(R) Draw, Symyx MDL(R) ISIS/Draw, CS ChemDraw™ plug-in or Marvin applet). If you wish to change to another structure editor, click the link below the drawing window.

4. Use the toolbar to draw a structure or import the structure from an existing file.
5. Depending on the structure search tool in use, there are a variety of right-click options, toolbar options and menu options available for determining your structure search strategy.
6. Specify the type of searching using the Structure Search Options: Search Type (Substructure, Exact Structure, or Similarity (0-100%)) , Structure Representation (Normal or Standardized), and Search Options (Match Stereochemistry). The Match Stereochemistry option allows you to consider or ignore stereochemistry when running Exact or Substructure searches. For more information, click on the Guide to Structure Search Options link.
7. To add text or data criteria to your search strategy, go to a search field line and enter term(s) as described under General Text/Data Searching.
8. When your search strategy is complete on screen, click the **Start** button at the top of the Search Form. The results of your search appear on screen in a table or record format depending on the number of records retrieved by the search.

SEQUENCE SEARCHING

You can search by protein or gene sequence in the Genomics Knowledge Area of *Integrity*.

Take the following steps to run a sequence search in *Integrity*:

1. Go to the Genomics Knowledge Area.
2. Choose the Genomics Section.
3. In the first search field line, select Sequence from the list of available field values.
4. Type or paste a gene or protein sequence or sequence fragment in the search field box to the right of the menu (this search field is not case-sensitive).
5. Do not use wildcards. Truncation is automatic on the left and the right of the sequence.
6. If you wish to add other criteria to the search strategy, go to the next search field line in the Genomics Section or go to the first free search field line in any other Section of the Search Form and enter the necessary data.
7. When your search strategy is complete on screen, click the **Start** button at the top of the Search Form. The results of your search appear on screen in a table or record format depending on the number of records retrieved by the search.

QUICK SEARCH

The Quick Search feature can be used to retrieve terms across all *Integrity* Knowledge Areas. Quick Search, which is found on each page in *Integrity* – is located to the center of the Navigation bar.

To perform a search using Quick Search:

1. Type the keyword(s) or search terms you wish to find into the search box, and then click **Go**.

A scheme appears showing the results found in the various Knowledge Areas.

2. Click a Knowledge Area bar to view the results for that Knowledge Area; click the Related Info button next to each Knowledge Area to display the set of related information associated with the record set retrieved for that Knowledge Area. For Related Info, use the Next and Back buttons to navigate or retrace your steps.

(You can also use the 'All Related via Quick Search' option from search results to access related information associated with the record set for that Knowledge Area.)

You can search single words or phrases in Quick Search. If you enter more than one word, separated by spaces, then the words will be searched as a phrase, i.e. appearing next to each other in the order you typed them.

- Quick Search is not case-sensitive – typing words in upper case, lower case or mixed case produces exactly the same results.
- Logic operators (Boolean AND, OR) can be used to define the relationship between search terms you enter.
- Wildcard truncation can be used at the start, within, or at the end of search terms; you can also combine or use symbols multiply in a single word or term.
  * – The asterisk (*) symbol replaces any number of characters and can be used at the start, end, both the start and end, or within a search term.
  ? – The question mark (?) symbol replaces a single character and can be repeated and used anywhere in the search term.

- Avoid using hyphens or apostrophes in Quick Search; instead, use an asterisk to substitute for one or more characters.
- When entering a company code drug name, omit the hyphen; e.g. FK506, CDP870.
- Quick search searches across the most relevant text-based fields in each Knowledge Area; it does not search across date fields or Y/N fields and it does not search fields that are not directly applicable to the Knowledge Area (i.e. does not search condition in Companies & Research Institutions because there is no condition field in a Company & Research Institutions full record).

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USER GUIDE - ADVANCED SEARCH

RELEASE 10.1

THOMSON REUTERS

ADVANCED SEARCH

There is an Advanced Search form associated with each of the Knowledge Areas in *Integrity*.

To begin searching *Integrity* using Advanced Search:

• Click a Knowledge Area on the *Integrity* Home Page.

You can go to a new Knowledge Area at any point: from the *Integrity* Home Page, from the Search Forms and from the Results. The type of results you would like to view first determines which Knowledge Area you should choose. This does not affect your access to the complete set of data in *Integrity* as all data are integrated. The focus of *Integrity* is on products in discovery or development since 1988.

DRUGS & BIOLOGICS

The Drugs & Biologics Knowledge Area includes essential chemical and pharmacological information, and the development status of bioactive compounds in the drug development pipeline. Use to search for information on bioactive compounds. Searches can include criteria for targets or literature or patent references associated with the compounds.

• Information in the Drugs & Biologics Knowledge Area dates back to 1988,

with more than 1,500 selected back records added (e.g. aspirin).

The Drugs & Biologics Advanced Search includes the following Sections:

• Product (includes ability to filter by Lead Compounds and/or Under Active Development) + Structure Search
• Reference
• Targets & Pathways
• Patent

The number of records included in the Drugs & Biologics Knowledge Area and, additionally, the number of records with a chemical structure is displayed at the top left hand side of the screen. The Quick Access Links below the record count provide direct access to specific information in the database:

• **The Starting Line** – A link to a table, updated weekly, of the most promising compounds entering preclinical development. These compounds are usually lead compounds or with new mechanisms of action that have been cited for the first time in Literature references.
• **Pipeline on the Move** – A link to a table, updated weekly, of changes detected in the status of drugs currently under active development. Presented in database format, with access to previous weeks' data and the ability to sort and export data.
• **Gateways to Development Status** – A series of links to compounds launched or under active development for a specific condition (either a broad group or one or more 'subgroups' can be selected). Includes a

Quick Access Search facility to display pipeline information for a specific condition.

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TARGETS & PATHWAYS

The Targets & Pathways Knowledge Area provides coverage of genes and their related proteins as precedented targets for drug discovery. Use to search for information on gene, proteins and physiopathologic processes as targets for therapeutic intervention. Searches can include criteria for product, literature or patent references associated with the targets.

- Information in the Targets & Pathways Knowledge Area dates back to 2004.

Targets & Pathways Advanced Search includes the following Sections:

- Targets & Pathways
- Product (includes ability to filter by Lead Compounds and/or Under Active Development)
- Reference
- Patent

The number of records included in the Targets & Pathways Knowledge Area is displayed at the top left hand side of the screen. The Quick Access Links below the record count provide direct access to specific information in the database:

- **Targetscapes** – A series of links to molecular landscapes related to a specific condition (either a broad group or one or more 'subgroups' can be selected).

GENOMICS

The Genomics Knowledge Area covers the relationships between genes and diseases to provide insights into underlying biological mechanisms and identify potential new drug targets. Use to search for information on genes, diseases and underlying biological mechanisms as targets for therapeutic intervention. Searches can include criteria for genomics or literature or patent references associated with the genomics.

• Information in the Genomics Knowledge Area dates back to 2001.

The Genomics Advanced Search includes the following Sections:

• Genomics
• Reference
• Patent

The number of records included in the Genomics Knowledge Area is displayed at the top left hand side of the screen. The Quick Access Links below the record count provide direct access to specific information in the database:

• **Gene-Related Studies** – A series of links to studies delineating new areas of potential therapeutic intervention (either a broad group or one or more 'subgroups' can be selected; alternatively, choose 'All Conditions'). Includes a Quick Access Search facility to display gene-related studies for a specific condition.

BIOMARKERS

The Biomarkers Knowledge Area links drugs, targets and genes to biomarkers information from a diverse range of sources. Covers a wide range of biomarker types from genomic, proteomic and biochemical to cellular, physiological and imaging. Use to search for information on biomarker uses at every stage of drug R&D, including disease risk detection, diagnosis, target identification, proof-of-mechanism, proof-of-concept, treatment/safety monitoring, and outcome measurement. Searches can include criteria for biomarker, product or literature or patent references associated with the biomarkers.

- Information in the Biomarkers Knowledge Area dates back to 2007, with selected back records added.
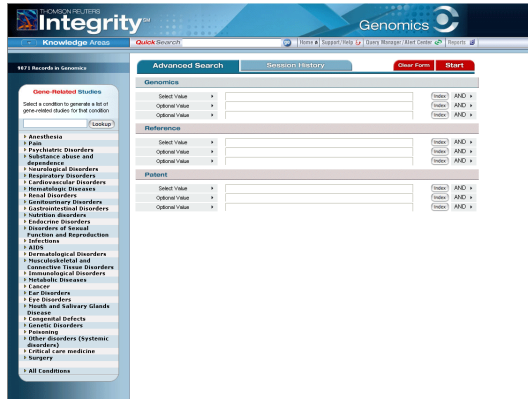
The Biomarkers Advanced Search includes the following Sections:

- Biomarker
- Product (includes ability to filter by Lead Compounds and/or Under Active Development)
- Reference
- Patent

The number of records included in the Biomarkers Knowledge Area is displayed at the top left hand side of the screen. The links below the record count provide access to the Biomarkers User Resources that assist you in using the *Biomarkers Module*, including the *Biomarkers Module* factsheet, Biomarker Knowledge Area FAQs and Latest Enhancements.

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ORGANIC SYNTHESIS

The Organic Synthesis Knowledge Area covers routes of synthesis (schemes, intermediates, reagents, end products) for drugs currently on the market or in development. Use to search for information on drug synthesis routes, chemical intermediates, reagents and end products of synthesis processes. Searches can include criteria for end products or literature or patent references associated with the syntheses.

• Information in the Organic Synthesis Knowledge Area dates back to the 1970s.

The Organic Synthesis Advanced Search includes the following Sections:

• Organic Synthesis (includes ability to display schemes/intermediates/reagents) + Structure Search
• Product (includes ability to filter by Lead Compounds and/or Under Active Development)
• Reference
• Patent

The number of records included in the Organic Synthesis Knowledge Area is displayed at the top left hand side of the screen.

EXPERIMENTAL PHARMACOLOGY

The Experimental Pharmacology Knowledge Area covers data from experimental studies that delineate drug/receptor and enzyme/target cell interactions. Use to search for information on pharmacological activity screens and assays of bioactive compounds. Searches can include criteria for bioactive compounds tested or associated literature references.

• Information in the Experimental Pharmacology Knowledge Area dates back to 1998.

The Experimental Pharmacology Advanced Search includes the following Sections:

• Experimental Pharmacology (choose to Include Literature Results and/or Include Patent Results)
• Product (includes ability to filter by Lead Compounds and/or Under Active Development)
• Reference
• Patent

The number of records included in the Experimental Pharmacology Knowledge Area is displayed at the top left hand side of the screen.

PHARMACOKINETICS/METABOLISM

The Pharmacokinetics/Metabolism Knowledge Area covers data from experimental and clinical studies that delineate the absorption, distribution, metabolism and excretion (ADME) profile of a drug. Use to search for information on pharmacokinetics studies of bioactive compounds. Searches can include criteria for associated literature references.

- Information in the Pharmacokinetics/Metabolism Knowledge Area dates back to 2000.

The Pharmacokinetics/Metabolism Advanced Search includes the following Sections:

- Pharmacokinetics/Metabolism
- Reference
- Product (includes ability to filter by Lead Compounds and/or Under Active Development) + Structure Search

The number of records included in the Pharmacokinetics/Metabolism Knowledge Area is displayed at the top left hand side of the screen.

CLINICAL STUDIES
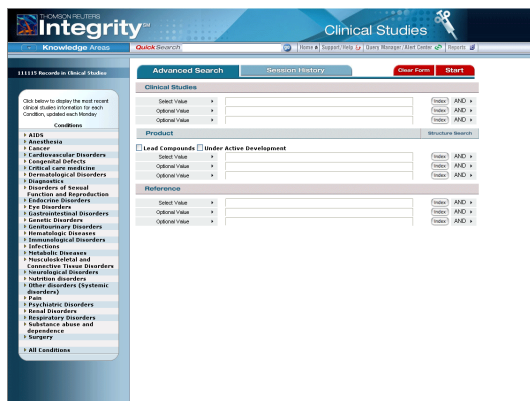
The Clinical Studies Knowledge Area covers data from clinical trials of drugs currently under study or in use in humans. Use to search for information on clinical studies of bioactive compounds. Searches can include criteria for bioactive compounds tested or associated literature references.

• Information in the Clinical Studies Knowledge Area dates back to 2000.

The Clinical Studies Advanced Search includes the following Sections:

• Clinical Studies
• Product (includes ability to filter by Lead Compounds and/or Under Active Development) + Structure Search
• Reference

The number of records included in the Clinical Studies Knowledge Area is displayed at the top left hand side of the screen. The Quick Access Links below the record count provide direct access to specific information in the database:

• **Clinical Studies** – A series of links to the most recent clinical studies references added to the database for each condition (either a broad group or one or more 'subgroups' can be selected; alternatively, choose 'All Conditions'). Content is updated each Monday.

DISEASE BRIEFINGS

The Disease Briefings Knowledge Area provides dynamic executive summaries on the current status of and future trends in drug therapy for specific diseases. Use to search disease briefings by name or content (full text). Searches can include bioactive compound criteria.

• Information in the Disease Briefings Knowledge Area dates back to 2000.

The Disease Briefings Advanced Search includes the following Sections:

• Disease Briefings
• Product (includes ability to filter by Lead Compounds and/or Under Active Development) + Structure Search

The number of records included in the Disease Briefings Knowledge Area is displayed at the top left hand side of the screen. The Quick Access Links below the record count provide direct access to specific information in the database:

• **Disease Briefings** – A series of links to Integrity disease briefings containing information on the current status and future trends in drug therapy for specific diseases.

COMPANIES & RESEARCH INSTITUTIONS

The Companies & Research Institutions Knowledge Area provides essential information on public and private companies, academic centers and research institutions active in the field of pharmaceuticals and biotechnology. Use to search for information on overall company sales/revenues, sales of launched products, products in development and new patents.

• Information in the Companies & Research Institutions Knowledge Area dates back to 2000.

The Companies & Research Institutions Advanced Search includes the following Sections:

• Companies & Research Institutions
• Product (includes ability to filter by Lead Compounds and/or Under Active Development) + Structure Search
• Patent

The number of records included in the Companies & Research Institutions Knowledge Area is displayed at the top left hand side of the screen.

LITERATURE

The Literature Knowledge Area provides references to current biomedical literature, abstracts and proceeding from congresses and symposia and company communications. Use to search for information on biomedical literature, congresses and company communications. Searches can include bioactive compound criteria.

• Information in the Literature Knowledge Area dates back to 1988.

The Literature Advanced Search includes the following Sections:

• Reference
• Product (includes ability to filter by Lead Compounds and/or Under Active Development) + Structure Search

The number of records included in the Literature Knowledge Area is displayed at the top left hand side of the screen. The Quick Access links below the record count provide direct access to specific information in the database:

• **Conferences** – A tabbed summary list of the latest conferences added to the database and forthcoming conferences. Citations links are provided to selected references; Report links (where present) display highlights for a particular conference. The 'More conferences…' links display the respective full conference lists.

PATENTS

The Patents Knowledge Area provides references to the most recent patent literature reflecting drug research activity throughout the world. Use to search for information on patent literature related to drug discovery and development. Searches can include bioactive compound criteria.

• Information in the Patents Knowledge Area dates back to 1988.

The Patents Advanced Search includes the following Sections:

• Patent
• Product (includes ability to filter by Lead Compounds and/or Under Active Development) + Structure Search

The number of records included in the Patents Knowledge Area is displayed at the top left hand side of the screen. The Quick Access links below the record count provide direct access to specific information in the database:

• **Patents** – A series of links to the most recent patent information added to the database for each condition (either a broad group or one or more 'subgroups' can be selected; alternatively, choose 'All Conditions'). Content is updated each Monday. Click the link in the panel below to display today's featured patent family entries in *Integrity*.

SEARCH FIELDS

Each Section in *Integrity* has three search field lines which can be set to any of the available field values (the menus have the default headings Select Value or Optional Value). Multiple fields are automatically linked with a Boolean AND operator; however, you can change this to OR using the appropriate inter-field (AND/OR) button – which is found on the far right of each search field line, to the right of the Index button. A search field can contain up to a maximum of 300 characters, allowing for the use of Boolean operators, AND or OR, within the field as well as between fields, e.g. Phase = ''Phase III'' or ''Pre-Registered'' or ''Recommended Approval'' or ''Registered''.

All Knowledge Areas have at least two Sections of search fields, one of which will be the Knowledge Area specific set of search fields (for example, fields such as applicant in Patents and author in Literature) and in most cases one will be the Product Section of Search fields.

1. Select the field to search from the list of available field values. (The list of field values for the *Biomarkers Module* is divided into two sections: Biomarker and Biomarker use.)

Menu items preceded by the ⊞ icon; for example Development Status, Milestone, and Natural Source in the Product Section, have submenus from which you may select

2. Click the **Index** button to open the Browse Index for the search field chosen and select terms (recommended) or type words or phrases directly. (Use the Windows Maximize icon to expand the Browse Index to see more terms at once.)
3. Where multiple terms are selected within a single field, a logical OR operator is inserted automatically to separate the terms; however, you can change this manually to AND if you wish.
4. If you wish to add other criteria to your search strategy, repeat the process using the next search field line down within the same Section or go to the first free search field line in any other Section of the Search Form. You must complete at least one search field to perform a search; however, it is not

obligatory to enter terms in more than one field.

- Each Section has three search field lines which can be set to any of the available field values; if more search fields are needed, or if there are not enough Knowledge Area specific fields, then the search can be refined by using the Filter by Statistics charts on the results page. (The charts are Knowledge Area specific and allow you to refine the search or view the results by many of the same criteria as the original search field choices.)

5. Specify the relationship between the search boxes; choose to retrieve 'all terms' or 'any terms' by selecting AND or OR inter-field Boolean operators, as desired. (AND is selected by default.)

6. Optional. If your search includes fields selected from the Product, Organic Synthesis or Experimental Pharmacology Sections:

- For Product, choose to filter by Lead Compound and/or Under Active Development; initially, neither option is selected.

☐ Lead Compounds ☐ Under Active Development

- For Organic Synthesis, choose to display Schemes or Intermediates or Reagents; initially, Schemes is selected.

Display ◉ Schemes ○ Intermediates ○ Reagents

(For Intermediate sub-fields, available choices are Schemes or Intermediates; for Reagent sub-fields, available choices are Schemes or

Reagents.)

- For Experimental Pharmacology, choose to Include Literature Results and/or Include Patent Results; initially, both options are selected.

☑ Include Literature Results ☑ Include Patent Results

Please note that terms may appear more than once within a particular list of field vales. The provision of related criteria search in Integrity allows you to specify exactly what a specific term relates to. For example, Condition appears three times as a product search field, once in the main list (the condition is associated to the compound in a general sense), once under Development Status (to search phase information for the condition) and once under Milestones (to search for milestones related to the condition).

SEARCH FIELDS DETAIL

Details of the search fields available within each Section are provided below.

PRODUCT

Found on the Drugs & Biologics, Targets & Pathways, Biomarkers, Experimental Pharmacology, Pharmacokinetics/Metabolism, Clinical Studies, Disease Briefings, Companies & Research Institutions, Literature, and Patents Advanced Search. Includes the following choice of fields:

- Entry Number
- Drug Name
- Chemical Name/Description
- Standard InChl
- Standard InChlKey
- CAS Registry No.
- Molecular Formula
- Molecular Weight
- Highest Phase
- Year Launched/Registered
- Organization
- Organization (+ Related Orgs.)
- Condition
- Therapeutic Group
- Mechanism of Action
- Product Category

- Prescription/Indication Type
- New Molecular Entity (Y/N)
- Metabolites (Y/N)
- Natural Source (Y/N)
- Development Status
  - Phase
  - Condition
  - Organization
  - Brand Name
  - Under Active Development (Y/N)
  - Administration Route
  - Formulation
- Milestone
  - Milestone
  - Milestone Date
  - Condition
  - Organization
- Natural Source
  - Scientific Name
  - Common Name
  - Organism Part
  - Geographic Area
- Last Updated
- Available Since

The Product section of search fields has the option to filter by Lead Compound and/or Under Active Development:

• Choose to filter by Lead Compound and/or Under Active Development; initially, neither option is selected.

☐ **Lead Compounds** ☐ **Under Active Development**

The Under Active Development option restricts searches to include only those compounds that are under active development; alternatively, use the Under Active Development (Y/N) search field to link this search criterion with other criteria (example: Under Active Development = ''Y'' AND Highest Phase = ''Phase I'' AND Condition = ''Neuroblastoma'').

The Under Active Development label appears on records for products that are actively moving through the drug R&D pipeline from preclinical stages through registration (i.e. preclinical, IND filed, phase I, phase I/II, phase II, phase II,III, phase III, preregistered, recommended approval and registered).

The criteria for labeling a compound Under Active Development include the following, which must have occurred over the last 12-18 months:

• The company is actively informing the public on the development of the product via press releases, mention in annual reports, citation on the company's website (particularly, if the company publishes a 'pipeline' and the product is included in it)
• References to the compound that indicate its progress are being published in the biomedical literature (journals and congresses)

Under Active Development is indicated in the Full Product Record, and the entry numbers of UAD products appear in red and are marked with an asterisk.

• Compounds in very early stage development are not considered to be Under Active Development and will therefore be excluded from searches using the Under Active Development filter.
• Compounds that are launched and that are not being investigated for new conditions, in new regions or by new organizations are not considered Under Active Development and will be excluded from searches using the Under Active Development filter.

The Lead Compound option restricts searches to include only lead compounds. This feature is particularly useful when searching on compounds in the earliest stage of development (i.e. Biological Testing).

When a series of 'sister' compounds are derived from a single patent or literature reference, the series has a designated 'lead compound'. If there is only one specifically claimed compound in the patent, this will be the lead compound. Or, in a case where pharmacology data are presented (e.g., IC50 values), the most active compound will be designated the lead compound in the series (other things such as administration routes cited or any toxicity data being equal). However, the use of the term 'lead compound' by Thomson Reuters is not a prediction of which compound from the series will go into preclinical or later development. It is simply a tool that allows those searching

large volumes of data to pull out a single representative compound from a series.

Entry Number
A numeric field which searches the Entry Number, a 6-digit compound ID number assigned to every bioactive compound found in the *Thomson Reuters* databases. The Entry Number serves as a unique compound identifier throughout a drug's life. ENs are assigned sequentially; in results lists, where an Entry Number is shown in red and flagged with an asterisk, this denotes that the associated bioactive compound is currently under active development. The Under Active Development label appears on records for products that are actively moving through the drug R&D pipeline from preclinical stages through registration (i.e. preclinical, IND filed, phase I, phase I/II, phase II, phase II, III, phase III, preregistered, recommended approval and registered). Use the Under Active Development checkbox as a filter to restrict searches to retrieve only those compounds that are under active development. Type a 6-digit number. Operators: OR, From, From … To …; no wildcards. Examples: 176436; From 176436; From 176436 to 178099; 176436 OR 178099.

Drug Name
An indexed field which searches the drug name (this includes Code Names, Generic Names, and Brand Names). Includes a Browse Index of available terms from which you may select. Examples: Rosiglitazone, N-Acetylglucosamine, GAB-532, Tagamet, C-type natriuretic peptide.

Chemical Name/Description
A free text field which searches the chemical name/description. Type a fragment of a chemical name (for bioactive compounds with a chemical name representation) or other descriptive term (for bioactive compounds not represented by a chemical name, such as monoclonal antibodies). Operators: AND, OR, NOT, *, ?. Examples: imidazoline; imidazolin*; imidazoline AND *chloro*; monoclonal; interferon; gamma.

Standard InChI
A free text field which searches the standard InChI. The International Chemical Identifier (InChI) is a non-proprietary identifier for chemical substances that can be used in printed and electronic data sources; InChI was developed in cooperation of IUPAC and NIST and is the newest way of describing chemical structures in text. Type a fragment of a Standard InChI. Operators: AND, OR, *, ?. Examples: 1S/C47H51NO14*; *38,24-58-33)62-27*.

Standard InChIKey
A free text field which searches the standard InChIKey. InChIKey is a fixed-length format derived directly from InChI. The 27 characters long InChIKey is made of three parts connected by hyphens. The first part is 14 characters long and is based on the connectivity and proton layers of an InChI string. The second part contains 9 characters that are related to all other InChI layers (isotopes, stereochemistry, etc.) and also contains the version of InChI and its standard/non-standard property in the last two characters. The third part is one letter, describing the (de)protonation layer of the original InChI. Type a

Standard InChIKey or a fragment of a Standard InChIKey. Operators: AND, OR, *, ?. Examples: RCINICONZNJXQF-MZXODVADSA-N; RCI*.

CAS Registry No.

A numeric field which searches the CAS Registry Number, a sequentially assigned accession number from the CAS Registry – the world's largest substance database. The CAS Registry Number (RN) is made of three parts connected by hyphens and has the format: 123456-78-9. The first part can be from two to seven digits long. The second part contains 2 digits. The third part is a single check-digit. The CAS RN has no chemical or structural meaning in itself. It is simply an identifier for a specific substance that CAS has registered during the process of indexing the literature or added from another source. The shorter the first part, the older the registration and therefore the more common (and probably better described) the compound is. Type a CAS Registry Number or part thereof. Operators: OR, NOT, *. Examples: 138402-11-6; 138402*.

Molecular Formula

A free text field which searches the molecular formula of a compound or substance. Type a molecular formula or part thereof. Operators: OR, NOT; * (on both the right and the left). Examples: C25H28*; C25H28N6O.

Molecular Weight

A numeric field which searches the molecular weight of a compound or drug. Type a number. Operators: From, From … To …; no wildcards. Examples: From 10000; From 451 to 452.

Highest Phase

A controlled text field which searches the highest phase of development for a compound or drug; valid options are:

- **Not Determined** – Development status is unknown.
- **Discontinued** – Development of the product has stopped before a registration dossier has been filed.
- **Withdrawn** – The product is withdrawn from the market after launch.
- **Biological Testing** – Products from patents are entered into this phase. Synthesis and preliminary pharmacology (in vitro testing) data may be available. Movement to a higher phase occurs only if there is information published to show that they have moved. Over 80% of all compounds in Integrity are in Biological Testing.
- **Preclinical** – In vivo testing; testing in animals has started.
- **IND Filed** – Application has been filed with the competent authority requesting permission to test the drug in humans (IND = Investigational New Drug Application in U.S.).
- **Phase 0** – An FDA approved trial which tests small quantities of experimental drugs on humans.
- **Clinical** – Used when it is known that the drug is in clinical testing, but the exact phase is not known.
- **Phase I** – Initial studies to determine the metabolism and pharmacologic actions of drugs in humans, the side effects associated with increasing doses, and to gain early evidence of effectiveness have started; usually conducted in healthy volunteers.

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- **Phase I/II** – Studies that combine certain aspects of phase I trials and phase II trials; for example, a safety study in patients.
- **Phase II** – Controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks have started.
- **Phase II/III** – Studies that combine certain aspects of phase II trials and phase III trials.
- **Phase III** – Expanded controlled and uncontrolled trials have started after preliminary evidence suggesting effectiveness of the drug has been obtained. These are intended to gather additional information to evaluate the overall relationship of the drug and provide an adequate basis for physician labelling benefit-risk.
- **Pre-Registered** – Application to market the drug (e.g. New Drug Application or Marketing Authorisation Application) has been filed.
- **Recommended Approval** – Approval of the drug has been recommended by the corresponding FDA Advisory Committee or a Positive Opinion has been issued by the CHMP.
- **Registered** – The competent regulatory authority has approved the drug for marketing, but the drug is not yet available on the market.
- **Launched** – The drug is being marketed.
- **Suspended** – The product is stopped when undergoing regulatory review.
- **Not Applicable** – The product is withdrawn from the market after launch.

Each compound has only one highest phase. Use this field to retrieve all compounds that have reached a specified phase. For example, if you are interested in micro-dosing studies, choose Phase 0; alternatively, if you wish to focus on proof-of-efficacy trials, choose Phase 3. Includes a Browse Index of available terms from which you may select.

Year Launched/Registered
A numeric field which searches the year the drug was launched or registered. Format is YYYY; operators: From, From … To …; no wildcards. Examples: 1999; From 1999; From 1999 to 2000.

Organization
An indexed field which searches the organization(s) – the names of companies, institutes, universities and other entities related to the product. Includes a Browse Index of available terms from which you may select. Examples: Bayer, GlaxoSmithKline, Indiana State University, King's College London.

Organization (+ Related Orgs.)
An indexed field which searches the organization plus any related organization(s). For example, a search for Roche will also retrieve Genentech, Chugai, etc. Includes a Browse Index of available terms from which you may select. Examples: Daiichi Sankyo, Genentech, Oklahoma State University, Sanofi-Aventis.

Condition
A controlled text field which searches the condition or type of disorder the bioactive compound treats. Includes a Browse Index of available terms (with

both Alphabetical and Hierarchical display) from which you may select. Examples: Chronic obstructive pumonary disease (COPD), Leukemia, acute myeloid, Crohn's disease, Hepatitis B.

Therapeutic Group

A controlled text field which searches the pharmacological/therapeutic groups into which bioactive compounds can be classified. These can be broad groups (for example, Cardiovascular Drugs, Neurologic Drugs) or more specific groups (for example, Antihypertensive Drugs, Antiarrhythmic Drugs). This field does not include terminology for mechanisms of action (inhibitors, agonists, antagonists, potentiators, sensitizers, etc.). The Therapeutic Group search field is useful for retrieving compounds that are relevant to a specific (broad or narrow) condition where all types of mechanism of action are of interest – for example, a search for Therapeutic Group = Antihypertensive Drugs finds compounds that are ACE inhibitors, calcium antagonists, endothelin ETB antagonists, angiotensin AT1 antagonists, etc. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select.

Mechanism of Action

A controlled text field which searches the mechanism of action for bioactive compounds – for example, Angiotensin-I Converting Enzyme (ACE) Inhibitors, Calcium Channel Blockers, Angiotensin Receptor Antagonists, Dopamine D1 Agonists, etc. There are two types of Mechanism of Action in *Integrity*: Cellular Mechanisms and Molecular Mechanisms. Any one compound

can have multiple mechanisms of either or both types. The Mechanism of Action search field is useful for retrieving very specific groups of compounds that work by the same mechanisms. It can also be used with the Boolean operator AND to search for compounds with a dual mechanism of action – for example, "Angiotensin-I Converting Enzyme (ACE) Inhibitors" AND "Neprilysin (Enkephalinase, Neutral Endopeptidase, NEP) Inhibitors". Activity is described by Mechanism of Action in Integrity by the use of terms such as Ligand and Modulator.

- **Ligands** are products that bind to a receptor (they have an affinity constant for a given receptor) but it is not known if they act as agonists or antagonists.
- **Modulators** are products that bind to an allosteric site rather than the orthosteric site of the receptor and modulate the effect of orthosteric ligands.
  (Modulator is also used to describe mechanisms that are not acting on receptors. This is a wide definition meaning that a product modulates the activity of an effector (e.g. an enzyme or protein) without the exact mechanism being specified.)

- The terms "drugs acting on X receptors" are used when products act on a family of receptors (for example acetylcholine receptors) but information on which receptor is being bound is not specified.

Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select.

Product Category
A controlled text field which searches the various groupings into which bioactive compounds can be classified in terms of what they are rather than how they work or what they are used for. These groups include Chemical Categories, Biological Factors, Biotechnology Medicines (Antibodies, Vaccines, etc), Delivery Systems, Hormones, etc. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select.

Prescription/Indication Type
A controlled text field which searches the prescription/indication type; valid options are:

- **Emergency Use Authorization** – Allows the U.S. Food and Drug Administration (FDA) to sanction use of unapproved medical products during a public health emergency.
- **Nutraceutical** – Any substance that is a food or a part of a food and provides medical or health benefits, including the prevention and treatment of disease
- **Orphan Drug** – There are many diseases and conditions which affect such small numbers of individuals that they are considered rare and where adequate drugs have not been developed. Drugs for these diseases and conditions are commonly referred to as "orphan drugs".
- **Pediatric** – FDA approved drugs for pediatric use.

Includes a browse Index of available terms from which you may select.

New Molecular Entity (Y/N)
A Yes/No field which searches for new molecular entities. A new molecular entity in *Integrity* is a compound described for the first time in the biomedical literature, at a congress or in a company communication that is identified by an investigational code or chemical name. The NME status is retained for 4 months. Yes and No are the only values permitted in this field. Type Y for yes; type N for no.

Metabolites (Y/N)
A Yes/No field which searches for the presence of metabolites. Yes and No are the only values permitted in this field. Type Y for yes; type N for no.

Natural Source (Y/N)
A Yes/No field which searches for bioactive compounds from a natural source. Yes and No are the only values permitted in this field. Type Y for yes; type N for no.

Development Status
There are seven available choices for Development Status: Phase, Condition, Organization, Brand Name, Under Active Development (Y/N), Administration Route, and Formulation.

Development Status – Phase
A controlled text field which searches the Phase column in the Development Status table for a compound or drug; valid options are: Not Determined, Discontinued, Withdrawn, Biological Testing, Preclinical, IND Filed, Phase 0,

Clinical, Phase I, Phase I/II, Phase II, Phase II/III, Phase III, Pre-Registered, Recommended Approval, Registered, Launched, Suspended, or Not Applicable. See Highest Phase above for definitions.

The Development Status Summary in the full product record shows the highest phase reached for each condition, and the Details button in the table header opens the Development Status table. The Development Status table often contains multiple repeated phases, since each line corresponds to a development program.

A product can be developed by different organizations, for different conditions and in different regions and each of these can have separate development programs which may be in a different phase. A Development Status Phase search will pick up all lines in the table that match the criteria.

Includes a Browse Index of available terms from which you may select.

Development Status – Condition
A controlled text field which searches the Condition column in the Development Status table for a compound or drug. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select. Examples: Bronchitis, Panic disorder, Renal failure, Cardiomyopathy.

Note: The Gateways to Development Status Quick Access Links found below the record count on the left of the Drugs & Biologics Advanced Search provide direct access to compounds launched or under active development for a

specific condition (either a broad group or one or more 'subgroups' can be selected).

Development Status – Organization
An indexed field which searches the Organization column in the Development Status table for a compound or drug. Includes a Browse Index of available terms from which you may select. Examples: Bayer, GlaxoSmithKline, Indiana State University, King's College London.

Development Status – Brand Name
An indexed field which searches the Brand Name column in the Development Status table for a compound or drug. Includes a Browse Index of available terms from which you may select. Examples: Bactrim, Anafranil, Sambucol, Vancomycin Enterocaps.

Development Status – Under Active Development (Y/N)
A Yes/No field which searches the Development Status table for compounds or drugs under active development. Yes and No are the only values permitted in this field. Type Y for yes; type N for no.

The Under Active Development label appears on records for products that are actively moving through the drug R&D pipeline from preclinical stages through registration (i.e. preclinical, IND filed, phase I, phase I/II, phase II, phase II/III, phase III, preregistered, recommended approval and registered).

The criteria for labeling a compound Under Active Development include the following, which must have occurred over the last 12-18 months:

- The company is actively informing the public on the development of the product via press releases, mention in annual reports, citation on the company's website (particularly, if the company publishes a 'pipeline' and the product is included in it)
- References to the compound that indicate its progress are being published in the biomedical literature (journals and congresses)

Under Active Development is indicated in the full product record, and the entry numbers of UAD products appear highlighted in red and marked with an asterisk in the results.

Development Status – Administration Route
A controlled text field which searches the Administration Route column in the Development Status table for a compound or drug. Includes a Browse Index of available terms from which you may select. Examples: oral, topical, transdermal, parenteral.

Development Status – Formulation
A free text field which searches the Formulation column in the Development Status table for a compound or drug. Type one or more words. Enclose adjacent words in double quotes. Operators: AND, OR, NOT, *. ?. Examples: tablets, capsules, "nasal spray".

Note: The Development Status search fields allow for increased specificity and targeted results; however, not all products have a Development Status table, as products that never move out of the early phases are determined to not have a development history.

Milestone
There are four available choices for Milestone: Milestone, Milestone Date, Condition, and Organization.

Milestone – Milestone
A controlled text field which searches the Milestone column in the Milestones table for a compound or drug; valid options are:

- **Acquired** – A product is acquired by a new company, usually by acquisition/merger with another company.
- **ANDA Filed or Approved** – (Only applicable for the U.S. Food and Drug Administration, ANDA stands for Abbreviated New Drug Application.) Contains data that, when submitted to FDA's Center for Drug Evaluation and Research, Office of Generic Drugs (ANDA Filed), provides for the review and ultimate approval of a generic drug product. Generic drug applications are called "abbreviated" because they are generally not required to include preclinical (animal) and clinical (human) data to establish safety and effectiveness. Instead, a generic applicant must scientifically demonstrate that its product is bioequivalent (i.e., performs in the same manner as the innovator drug). Once approved (ANDA Approved), an applicant may manufacture and market the generic drug product to provide a safe, effective, low-cost alternative.
- **Application Withdrawn** – An application for approval (NDA filed, sNDA filed, BLA filed, sBLA filed, ANDA filed in US; MAA filed in EU; pre-

registered in other countries) is withdrawn when the Company is unable to satisfy the Administration requirements. If an applicant withdraws an original application for approval or supplement before FDA has completed its review, the review clock stops on the date FDA receives the letter notifying it of the withdrawal. As an example, if new data are required by the Administration before giving the approval and the Company is unable to perform the trials in time, it withdraws the application and resubmits it later with the entirety of data available.

- **Approvable Letter** – (Only applicable for the U.S. Food and Drug Administration.) An official communication from FDA to an application for approval sponsor that allows the commercial marketing of the product. An approvable letter informs the applicant that FDA has completed the scientific review of its application for approval and determined that it can be approved pending resolution of minor deficiencies identified in the letter or during FDA's inspection of the device's manufacturing facilities. No longer being issued as of August 2008 (see Complete Response Letter).
- **Available for outlicensing** – A product which is available for licensing.
- **BLA Filed or Approved** – (Only applicable for the U.S. Food and Drug Administration, BLA stands for Biologic License Application.) Biological products are approved for marketing under the provisions of the Public Health Service (PHS) Act. The Act requires a firm who manufactures a biologic for sale in interstate commerce to hold a license for the product. A biologic license application is a submission (BLA filed) that contains specific information on the manufacturing processes, chemistry, pharmacology, clinical pharmacology and the medical affects of the biologic product. If the information provided meets FDA requirements, the application is approved (BLA Approved) and a license is issued allowing the firm to market the product.
- **Clinical** – Used when it is known that the drug is in clinical testing, but the exact phase is not known.
- **Codeveloped** – A product which is being developed by more than one company.
- **Complete Response Letter** – In August 2008, the FDA began issuing complete response letters when communicating a decision to a drug company that a new drug application (NDA) or abbreviated new drug application (ANDA) to market a new or generic drug will not be approved in its present form. Currently FDA issues either approvable or not approvable letters in these cases. Complete response letters will only be issued for applications that are not approved; this rule will not impact how FDA communicates decisions to approve an application.
- **CTA Filed** – (Only applicable for the E.U. European Medicines Agency – EMEA, CTA stands for Clinical Trial Authorization.) Application for authorization for the beginning of a clinical trial.
- **Discontinued** – Development of the product has stopped before a registration dossier has been filed.
- **Fast Track Designation** – (Only applicable for the U.S. Food and Drug Administration.) A designation that the US Food and Drug Administration (FDA) reserves for products intended to treat a serious or life threatening

condition, and that have the potential to address an unmet medical need. The FDA takes appropriate actions to expedite the development and review of the approval applications for fast track products. The Fast Track program enables a company to file an NDA on a rolling basis as data becomes available. This permits the FDA to review the filing as it is received, rather than waiting for the entire document prior to commencing the review process. With a Fast Track designation, there is an opportunity for more frequent interactions with the FDA and possibility of a priority review, which could decrease the length of a typical review period.

- **IDE Filed** – (Only applicable for the US Food and Drug Administration, IDE stands for Investigational Device Exemption.) An application for authorization for an investigational device to be used in a clinical study in order to collect safety and efficacy data required to support a Premarket Approval Application (PMA).
- **IND Filed** – (Only applicable for the US Food and Drug Administration, IND stands for Investigational New Drug.) An application for authorization for a drug product to be used in a clinical study in order to collect safety and efficacy data required to support a New Drug Application (NDA).
- **Launched** – The drug is being marketed.
- **Licensed** – A company licenses a drug when it sells all or part of the rights it holds from the drug to another company. As an example, the owner company can just sell rights for a certain condition or for development and/or marketing in certain countries, only.
- **Licensee agreement terminated** – When a previous license agreement

has expired or has been cancelled.
- **MAA Filed or Approved** – (Only applicable for the E.U. European Medicines Agency – EMEA, MAA stands for Marketing Authorization Application.) MAA filed is the submission that contains specific information on the manufacturing processes, chemistry, pharmacology, clinical pharmacology and the medical affects of the biologic product. If the information provided meets EMEA requirements, the application is approved (MAA Approved) and a license is issued allowing the firm to market the product.
- **NDA Filed or Approved** – (Only applicable for the U.S. Food and Drug Administration, NDA stands for New Drug Application.) When the sponsor of a new drug believes that enough evidence on the drug's safety and effectiveness has been obtained to meet FDA's requirements for marketing approval, the sponsor submits to FDA a new drug application (NDA Filed). The application must contain data from specific technical viewpoints for review, including chemistry, pharmacology, medical, biopharmaceutics, and statistics. If the NDA is approved (NDA Approved), the product may be marketed in the United States.
- **Negative Opinion** – (Only applicable for the E.U. European Medicines Agency – EMEA.) The Committee for Medicinal Products for Human Use (CHMP) of the EMEA is responsible for preparing the Agency's opinions on all questions concerning medicinal products for human use. In the "Community" or "centralized" procedure, the CHMP is responsible for conducting the initial assessment of medicinal products for which a

Community-wide marketing authorization is sought. If CHMP considers that the medicinal product is not approvable, it gives a Negative Opinion.

- **Not Approvable Letter** – (Only applicable for the U.S. Food and Drug Administration.) A not approvable letter informs the PMA applicant that FDA has completed the scientific review of the PMA and does not believe that the PMA can be approved because of the significant deficiencies identified in the letter. After the applicant receives a not approvable letter, he or she may: amend the PMA to address the deficiencies; withdraw the PMA; or consider this letter to be a denial of approval of the application.

  For original applications, a not approvable letter is issued after FDA has conducted a complete review of the application, including any recommendations by an FDA advisory panel, if applicable, and determines that the available data in the application do not support a determination of reasonable assurance of safety and effectiveness. Generally, before FDA issues a not approvable letter, the agency provides the applicant with an opportunity to address its concerns through a major deficiency letter. No longer being issued as of August 2008 (see Complete Response Letter).

- **Not Recommended Approval** – (Only applicable for the U.S. Food and Drug Administration.) In some cases, FDA seeks the recommendations of advisory committees made up of outside experts. These expert advisers add to FDA's understanding, so that final agency decisions will more likely reflect a balanced evaluation. Committee recommendations are not binding on FDA, but the agency considers them carefully when deciding drug issues. Not Recommended Approval means that the advisory committee considers that the drug is not approvable.

- **On Hold** – A product development is placed temporarily on hold by the company, usually as a voluntary measure. As an example, if the Data Monitoring Committee (DMC) has requested additional data, if protocol revisions are needed, etc.

- **On Hold Lifted** – A temporary, and usually voluntary by the company, hold on a product's development is lifted.

- **Orphan Drug Designation** – There are many diseases and conditions which affect such small numbers of individuals that are considered rare and adequate drugs for many of such diseases and conditions have not been developed. Drugs for these diseases and conditions are commonly referred to as "orphan drugs". It is in the public interest to provide incentives for the development of orphan drugs. In the EU, the term "Orphan Drug" refers to a product that treats a serious or life-threatening disease that affects fewer than five people per 10,000 population. In the US, the term "Orphan Drug" refers to a product that treats a disease that affects fewer than 200,000 people in the country. Orphan drug designation may qualify recipients for exclusive marketing rights in the United States for seven years and in the EU for ten years if the company is first to receive marketing approval for this product.

- **Phase 0** – An FDA approved trial which tests small quantities of experimental drugs on humans.

- **Phase I** – Initial studies to determine the metabolism and pharmacologic

actions of drugs in humans, the side effects associated with increasing doses, and to gain early evidence of effectiveness have started; usually conducted in healthy volunteers.

- **Phase I/II** – Studies that combine certain aspects of phase I trials and phase II trials; for example, a safety study in patients.
- **Phase II** – Controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks have started.
- **Phase II/III** – Studies that combine certain aspects of phase II trials and phase III trials.
- **Phase III** – Expanded controlled and uncontrolled trials have started after preliminary evidence suggesting effectiveness of the drug has been obtained. These are intended to gather additional information to evaluate the overall relationship of the drug and provide an adequate basis for physician labelling benefit-risk.
- **PMA Filed or Approved** – (Only applicable for the U.S. Food and Drug Administration, PMA stands for Premarket Approval Application.) Premarket approval by FDA is the required process of scientific review to ensure the safety and effectiveness of Class III devices. A Class III device is defined as one that supports or sustains human life or is of substantial importance in preventing impairment of human health or presents a potential, unreasonable risk of illness or injury. The applicant submits to FDA a PMA (PMA filed). If the license is granted (PMA approved), the

applicant is authorised for marketing a particular medical device.

- **Positive Opinion** – (Only applicable for the EU European Medicines Agency – EMEA.) The Committee for Medicinal Products for Human Use (CHMP) of the EMEA is responsible for preparing the Agency's opinions on all questions concerning medicinal products for human use. In the "Community" or "centralized" procedure, the CHMP is responsible for conducting the initial assessment of medicinal products for which a Community-wide marketing authorization is sought. If CHMP considers that the medicinal product is approvable, it gives a Positive Opinion.
- **Pre-Registered** – Application to market the drug (e.g. New Drug Application or Marketing Authorisation Application) has been filed.
- **Preclinical** – In vivo testing; testing in animals has started.
- **Recommended Approval** – (Only applicable for the U.S. Food and Drug Administration.) In some cases, FDA seeks the recommendations of advisory committees made up of outside experts. These expert advisers add to FDA's understanding, so that final agency decisions will more likely reflect a balanced evaluation. Committee recommendations are not binding on FDA, but the agency considers them carefully when deciding drug issues. Recommended Approval means that the advisory committee considers that the drug is approvable.
- **Registered** – The competent regulatory authority has approved the drug for marketing, but the drug is not yet available on the market.
- **sBLA Filed or Approved** – (Only applicable for the U.S. Food and Drug Administration, sBLA stands for Supplemental Biologic License

Application.) A supplemental biologic license application submission (sBLA filed) is required by the FDA for biologic products when changes are made in the manufacturing processes or label, for the marketing authorization of a new formulation, strength or indication. If the information provided meets FDA requirements, the application is approved (sBLA Approved).

- **sNDA Filed or Approved** – (Only applicable for the U.S. Food and Drug Administration, sNDA stands for Supplemental New Drug Application.) A supplemental new drug application submission (sNDA filed) is required by the FDA when changes are made in the manufacturing processes or label of a drug, and for the marketing authorization of a new formulation, strength or indication. If the information provided meets FDA requirements, the application is approved (sNDA Approved).
- **Suspended** – A trial is suspended (enrolment or patients treatments) usually following the recommendation of a Data Safety Monitoring Board (DSMB). The company temporarily suspends a trial as a precaution when adverse events are detected, new data are required, etc.
- **Withdrawn** – The product is withdrawn from the market after launch.

Includes a Browse Index of available terms from which you may select.

Milestone – Milestone Date

A numeric field which searches the Milestone Date column in the Milestones table for a compound or drug. Format is: YYYYMMDD; operators: From, From … To …; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

Milestone – Condition

A controlled text field which searches the Condition column in the Milestones table for a compound or drug. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select. Examples: Hypogonadism, Cancer, breast.

Milestone – Organization

An indexed field which searches the Organization column in the Milestones table for a compound or drug. Includes a Browse Index of available terms from which you may select. Examples: Bayer, GlaxoSmithKline, Indiana State University, King's College London.

Note: The Milestone search fields allow for increased specificity and targeted results; however, not all products have a Milestones table, as products that never move out of the early phases are determined to not have a milestone.

Natural Source

There are four available choices for Natural Source: Scientific Name, Common Name, Organism Part, and Geographic Area.

Natural Source – Scientific Name

An indexed field which searches the Scientific Name of the Natural Source. The scientific naming of an organism uses a binomial nomenclature. In this system, the two parts used to identify an organism are called the genus and the species. For example, *Homo sapiens* – the scientific name for humans; Homo is the genus and sapiens the species. The Scientific Name usually appears

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italicized and often only the first letter of the genus is given (i.e. *H. sapiens*). The taxonomic organization of species is hierarchical; each species belongs to a genus, each genus to a family, and so on through order, class, phylum, and kingdom.

Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select. The hierarchical display has systematic groupings into categories on the basis of evolutionary or structural (morphological and physiological) relationships between species up to the highest levels of classification, which are: Algae, Animals, Bacteria, Fungi, Lichens, Mosses, Plants, or Protozoa. Examples: Salix alba, Enterobacter sp., Cholorophyta (green algae), Protozoa.

Natural Source – Common Name
An indexed field which searches the Common Name of the Natural Source. Includes a Browse Index of available terms from which you may select. Examples: Dandelion, Oolong tea, Mango, Alfalfa.

Natural Source – Organism Part
A controlled text field which searches the Organism Part of the Natural Source. Includes a Browse Index of available terms from which you may select. Examples: Fruit rind, Stem bark, Resin, Venom.

Natural Source – Geographic Area
A controlled text field which searches the Geographic Area of the Natural Source. Includes a Browse Index of available terms from which you may select.

Examples: Europe, North America, Japan, Worldwide.

Last Updated
A numeric field which searches the date the record was last updated. Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

Available Since
A numeric field which searches the date the record was made available. Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

The table below summarizes the search fields available for Product:

Search Field	Field Type	Additional Details
Entry Number	Numeric	6-digit number; operators: OR, From, From ... To ... ; no wildcards
Drug Name	Indexed Field	Browse (alphabetical)
Chemical Name/ Description	Free Text	Operators: AND, OR, NOT, *, ?
Standard InChI	Free Text	Standard InChI or fragment; operators, AND, OR, *, ?
Standard InChIKey	Free Text	Standard InChIKey or fragment; operators, AND, OR, *, ?
CAS Registry No.	Numeric	CAS Registry Number or part thereof; operators, OR, NOT, *
Molecular Formula	Free Text	Molecular Formula or part thereof; operators, OR, NOT, * (on both the right and left)
Molecular Weight	Numeric	Operators: From, From ... To ... ; no wildcards
Highest Phase	Controlled Text	Browse (alphabetical)

Search Field	Field Type	Additional Details
Year Launched/Registered	Numeric (date)	YYYY; OR, From, From ... To... ; no wildcards
Organization	Indexed Field	Browse (alphabetical)
Organization (+ Related Orgs.)	Indexed Field	Browse (alphabetical)
Condition	Controlled Text	Browse (alphabetical/ hierarchical)
Therapeutic Group	Controlled Text	Browse (alphabetical/ hierarchical)
Mechanism of Action	Controlled Text	Browse (alphabetical/ hierarchical)
Product Category	Controlled Text	Browse (alphabetical/ hierarchical)
Prescription/Indication Type	Controlled Text	Browse (alphabetical)
New Molecular Entity (Y/N)	YES/NO	Yes and No are the only values; type Y for yes, N for no.
Metabolites (Y/N)	YES/NO	Yes and No are the only values; type Y for yes, N for no.

Search fields available for Product continued...

Search Field	Field Type	Additional Details
Natural Source (Y/N)	YES/NO	Yes and No are the only values; type Y for yes, N for no.
Dev. Status – Phase	Controlled Text	Browse (alphabetical)
Dev. Status – Condition	Controlled Text	Browse (alphabetical/ hierarchical)
Dev. Status – Organization	Indexed Field	Browse (alphabetical)
Dev. Status – Brand Name	Indexed Field	Browse (alphabetical)
Dev. Status – Under Active Development (Y/N)	YES/NO	Yes and No are the only values; type Y for yes, N for no.
Dev. Status – Administration Route	Controlled Text	Browse (alphabetical)
Dev. Status – Formulation	Free Text	Enclose adjacent words in double quotes. Operators: AND, OR, NOT, *, ?
Milestone – Milestone	Controlled Text	Browse (alphabetical)
Milestone – Milestone Date	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards

Search Field	Field Type	Additional Details
Milestone – Condition	Controlled Text	Browse (alphabetical/ hierarchical)
Milestone – Organization	Indexed Field	Browse (alphabetical)
Natural Source – Scientific Name	Indexed Field	Browse (alphabetical/ hierarchical)
Natural Source – Common Name	Indexed Field	Browse (alphabetical)
Natural Source – Organism Part	Controlled Text	Browse (alphabetical)
Natural Source – Geographic Area	Controlled Text	Browse (alphabetical)
Last Updated	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards
Available Since	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards

TARGETS & PATHWAYS

Found on the Drugs & Biologics and Targets & Pathways Advanced Search. Includes the following choice of fields:

- Classification
- Target Name
  – Name
  – Type
- Description
- GenBank ID
- Entrez Gene ID
- PDB ID
- Swiss-Prot
- EC Classification
- Condition
  – Condition
  – Status
- Targetscape
- Images & Pathways
- Images & Pathways Title
- Available Since

Classification
An indexed field which searches the classification of a target; available categories are: receptors, enzymes, ion channels, transmitter-gated channels, carriers, cytokines, growth factors, hormones, neurotransmitters, neurotrophic factors, transcription factors, translation factors, adapter proteins, adhesion molecules, angiogenic factors, lipoproteins, structural proteins, mitochondrial tRNAs, other proteins, bacterial proteins, viral proteins, protozoal proteins, alga proteins, fungal proteins, yeast proteins, plant proteins, archaeal proteins, insect proteins, and other targets. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select. Examples: Dopamine D2 Receptor, IFN-gamma, Peptide Hormones, Neurotransmitters, C-Reactive Protein.

Target Name
There are two available choices for Target Name: Name and Type.

Target Name – Name
An indexed field which searches the target name. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select. Examples: Interleukin-1 beta, Leucine-tRNA ligase, 12S ribosomal RNA, Triacylglycerol.

Target Name – Type
A controlled text field which searches the target type; available choices are Gene or Protein. Includes a Browse Index of available terms from which you may select.

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Description

A free text field which searches the description associated with a target. Type one or more words. Enclose adjacent words in double quotes. Operators: AND, OR, NOT, *. ?. Examples: hypertension; hypertens*, hypertension and ''congestive heart failure''.

GenBank ID

An indexed field which searches the GenBank identification code for a target. GenBank(R) is the NIH genetic sequence database, an annotated collection of all publicly available nucleotide sequences and their protein translations. GenBank is part of the International Nucleotide Sequence Database Collaboration, which is comprised of the DNA DataBank of Japan (DDBJ), the European Molecular Biology Laboratory (EMBL), and GenBank at the National Center for Biotechnology Information. For more information on GenBank, visit the GenBank website at NCBI.

Includes a Browse Index of available terms from which you may select. Examples: EU429475, W14812, NC_001416.

Entrez Gene ID

An indexed field which searches the Entrez Gene identification code for a target. Entrez Gene is a searchable database of genes, from RefSeq genomes. The NCBI Reference Sequences collection aims to provide a comprehensive, integrated, non-redundant, well-annotated set of sequences, including genomic DNA, transcripts, and proteins. For more information on Entrez Gene, visit the Entrez Gene web page at NCBI.

Includes a Browse Index of available terms from which you may select. Examples: Q30154, 10052, NM_001017995.

PDB ID

An indexed field which searches the Protein Data Bank identification code for a target. The PDB ID is the primary identifier by which entries can be retrieved from the RCSB Protein Data Bank. The PDB identification code consists of a single numeric digit followed by three alphanumeric characters. For more information on the Protein Data Bank, visit the RCSB Protein Data Bank website.

Includes a Browse Index of available terms from which you may select. Examples: 1A2K, 11GS, 6PAX.

Swiss-Prot

An indexed field which searches the Swiss-Prot code for a target. Swiss-Prot is a curated protein sequence database that provides a high level of annotation (such as the description of protein function, domain structures, post-translational modifications, variants, etc.), a minimal level of redundancy, and high level of integration with other databases. For more information on Swiss Prot/UniProt, visit the Swiss Prot website.

Includes a Browse Index of available terms from which you may select. Examples: A1X283, P02533, Q00796.

EC Classification

An indexed field which searches the EC Classification for a target where that

target is an enzyme. The EC Classification (EC), according to the Enzyme Nomenclature (IUBMB) is based on six major biochemical reactions with enzymes denoted by a sequence of four numbers separated by periods (EC X.X.X.X) according to the chemical reactions they catalyze: EC 1.X.X.X – Oxidoreductases, EC 2.X.X.X – Transferases, EC 3.X.X.X – Hydrolases, EC 4.X.X.X – Lyases, EC 5.X.X.X – Isomerases, and EC 6.X.X.X – Ligases. The remaining three numbers represent a progressively finer classification of the enzyme. For more information on Enzyme Nomenclature, visit the NC-IUBMB Enzyme Nomenclature web page.

- EC 1 – Oxidoreductases catalyze oxidation/reduction reactions; transfer of H and O atoms or electrons from one substance to another. Example enzymes (trivial name): dehydrogenase, oxidase.
- EC 2 – Transferases catalyze the transfer of a functional group from one substance to another. The group may be methyl-, acyl-, amino- or a phosphate group. Example enzymes (trivial name): transaminase, kinase.
- EC 3 – Hydrolases catalyze the formation of two products from a substrate by hydrolysis. Example enzymes (trivial name): lipase, amylase, peptidase.
- EC 4 – Lyases catalyze the non-hydrolytic addition or removal of groups from substrates. C-C, C-N, C-O or C-S bonds may be cleaved. Example enzymes (trivial name): decarboxylase.
- EC 5 – Isomerases catalyze intramolecule rearrangement, i.e. isomerisation changes within a single molecule. Example enzymes (trivial name): isomerise, mutase.
- EC 6 – Ligases catalyze the joining together of two molecules by synthesis

of new C-O, C-S, C-N or C-C bonds with simultaneous breakdown of ATP. Example enzymes (trivial name): synthetase.

EC numbers do not specify enzymes per se, but instead represent enzyme-catalyzed reactions. If different enzymes (e.g. from different organisms) catalyze the same reaction, then they are allocated the same EC number. By contrast, Swiss-Prot/Uni-Prot identifiers uniquely specify a protein by its amino acid sequence.

Condition
There are two available choices for Condition: Condition and Status.

Condition – Condition
A controlled text field which searches the condition or type of disorder associated with the target. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select. Examples: diabetes type 2, infection, HIV, graft-versus-host disease, inflammation.

Condition – Status
A controlled text field which searches the status of the condition or type of disorder associated with the target; available choices are Candidate or Validated. An algorithm is used to give an indication of how valid a target is for a condition by labelling the condition validated if a product acting on the target and associated with the condition has been tagged Under Active Development. The Candidate label is used if there are associated products

for that condition but they are not Under Active Development. The Status is indicated in brackets and is directly preceded by the Condition; i.e. Condition (Status), for example Obesity (Validated). Includes a Browse Index of available terms from which you may select.

Targetscape
A Yes/No field which searches targets for the presence of one or more associated Targetscapes. Targetscapes are images that map the molecular landscapes for a given condition with links to the specific target records for precedented targets. If a target is not precedented then there will not be an active link in the Targetscape, although you can search in Genomics to see a combined gene and protein record with associated gene-related studies. Yes and No are the only values permitted in this field. Type Y for yes; type N for no. If Yes, the associated Targetscapes appear as hyperlinks within each record; if No, then the Targetscape field is blank.

Note: The Targetscapes Quick Access Links found below the record count on left of the Targets & Pathways Advanced Search provide direct access to molecular landscapes related to a specific condition (either a broad group or one or more 'subgroups' can be selected).

Images & Pathways
A Yes/No field which searches targets for the presence of one or more associated images & pathways. Yes and No are the only values permitted in this field. Type Y for yes; type N for no. If Yes, the associated Images & Pathways appear as hyperlinks within each record; if No, then the Images &

Pathways field is blank.

Images & Pathways Title
A free text field which searches the title associated with any images & pathways. Type one or more words. Enclose adjacent words in double quotes. Operators: AND, OR, NOT, *. ?.

Available Since
A numeric field which searches the date the record was made available. Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

The table below summarizes the search fields available for Targets & Pathways:

Search Field	Field Type	Additional Details
Classification	Indexed Field	Browse (alphabetical/hierarchical)
Target Name – Name	Indexed Field	Browse (alphabetical)
Description	Free Text	Enclose adjacent words in double quotes. Operators: AND, OR, NOT, *, ?
GenBank ID	Indexed Field	Browse (alphabetical)
Entrez Gene ID	Indexed Field	Browse (alphabetical)
PDB ID	Indexed Field	Browse (alphabetical)
Swiss-Prot	Indexed Field	Browse (alphabetical)
EC Classification	Indexed Field	Browse (alphabetical)
Condition – Condition	Controlled Text	Browse (alphabetical/hierarchical)
Condition – Status	Controlled Text	Candidate or Validated
Targetscape	YES/NO	Yes and No are the only values; type Y for yes, N for no.

Search Field	Field Type	Additional Details
Images & Pathways	YES/NO	Yes and No are the only values; type Y for yes, N for no.
Images & Pathways Title	Free Text	Enclose adjacent words in double quotes. Operators: AND, OR, NOT, *, ?
Available Since	Numeric (date)	YYYYMMDD; From, From … To … ; no wildcards

GENOMICS

Found on the Genomics Advanced Search only. Includes the following choice of fields:

- Classification
- Gene Name
- Protein Name
- Gene/Protein Name
- EC Classification
- PDB ID
- Swiss-Prot
- GenBank ID
- Entrez Gene ID
- Condition
- Sequence
- Sequence Type
- Organism
- Gene Variants
  - Variation Type
  - Disease Association
  - Variation Name
  - Gene Variant Diseases
    - Condition
    - Effect
- Gene-Related Studies
  - Condition
  - Model
  - Study Type
  - Polymorphism (Y/N)
- Last Updated
- Available Since

Classification

An indexed field which searches the protein classification; available categories are: receptors, ion channels, transmitter-gated channels, carriers, cytokines, growth factors, hormones, neurotransmitters, neurotrophic factors, transcription factors, translation factors, adapter proteins, adhesion molecules, angiogenic factors, lipoproteins, structural proteins, mitochondrial tRNAs, other proteins, bacterial proteins, viral proteins, protozoal proteins, alga proteins, fungal proteins, yeast proteins, plant proteins, archaeal proteins, insect proteins, and other targets. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select. Examples: Dopamine D2 Receptor, IFN-gamma, Peptide Hormones, Neurotransmitters, C-Reactive Protein.

Gene Name

An indexed field which searches the gene name. Includes a Browse Index of available terms from which you may select. Examples: Interleukin-1 beta, Leucyl-tRNA synthetase 2, mitochondrial, 12S ribosomal RNA, tRNA isoleucine.

Protein Name

An indexed field which searches the protein name. Includes a Browse Index of available terms from which you may select. Examples: Cytochrome P-450 reductase, Oligopeptide Binding Protein, P-selectin, Atrial Natriuretic Peptide.

Gene/Protein Name

An indexed field which searches the gene/protein name. Includes a Browse Index of available terms from which you may select. Examples: L-arginine, P-selectin, R2 leukocyte antigen, V-CAM 1.

EC Classification

An indexed field which searches the EC Classification for a protein where that protein is an enzyme. The EC Classification (EC), according to the Enzyme Nomenclature (IUBMB) is based on six major biochemical reactions with enzymes denoted by a sequence of four numbers separated by periods (EC X.X.X.X) according to the chemical reactions they catalyze: EC 1.X.X.X – Oxidoreductases, EC 2.X.X.X – Transferases, EC 3.X.X.X – Hydrolases, EC 4.X.X.X – Lyases, EC 5.X.X.X – Isomerases, and EC 6.X.X.X – Ligases. The remaining three numbers represent a progressively finer classification of the enzyme. For more information on Enzyme Nomenclature, visit the NC-IUBMB Enzyme Nomenclature web page.

- EC 1 – Oxidoreductases catalyze oxidation/reduction reactions; transfer of H and O atoms or electrons from one substance to another. Example enzymes (trivial name): dehydrogenase, oxidase.
- EC 2 – Transferases catalyze the transfer of a functional group from one substance to another. The group may be methyl-, acyl-, amino- or a phosphate group. Example enzymes (trivial name): transaminase, kinase.
- EC 3 – Hydrolases catalyze the formation of two products from a substrate by hydrolysis. Example enzymes (trivial name): lipase, amylase, peptidase.
- EC 4 – Lyases catalyze the non-hydrolytic addition or removal of groups from substrates. C-C, C-N, C-O or C-S bonds may be cleaved. Example

enzymes (trivial name): decarboxylase.

- EC 5 – Isomerases catalyze intramolecule rearrangement, i.e. isomerisation changes within a single molecule. Example enzymes (trivial name): isomerise, mutase.
- EC 6 – Ligases catalyze the joining together of two molecules by synthesis of new C-O, C-S, C-N or C-C bonds with simultaneous breakdown of ATP. Example enzymes (trivial name): synthetase.

EC numbers do not specify enzymes per se, but instead represent enzyme-catalyzed reactions. If different enzymes (e.g. from different organisms) catalyze the same reaction, then they are allocated the same EC number. By contrast, Swiss-Prot/Uni-Prot identifiers uniquely specify a protein by its amino acid sequence.

PDB ID
An indexed field which searches the Protein Data Bank identification code for a protein. The PDB ID is the primary identifier by which entries can be retrieved from the RCSB Protein Data Bank. The PDB identification code consists of a single numeric digit followed by three alphanumeric characters. For more information on the Protein Data Bank, visit the RCSB Protein Data Bank website.

Includes a Browse Index of available terms from which you may select. Examples: 1A2K, 11GS, 6PAX.

Swiss-Prot
An indexed field which searches the Swiss-Prot code for a protein. Swiss-Prot is a curated protein sequence database that provides a high level of annotation (such as the description of protein function, domain structures, post-translational modifications, variants, etc.), a minimal level of redundancy, and high level of integration with other databases. For more information on Swiss Prot/UniProt, visit the Swiss Prot website.

Includes a Browse Index of available terms from which you may select. Examples: A1X283, P02533, Q00796.

GenBank ID
An indexed field which searches the GenBank identification code for a gene sequence. GenBank(R) is the NIH genetic sequence database, an annotated collection of all publicly available nucleotide sequences and their protein translations. GenBank is part of the International Nucleotide Sequence Database Collaboration, which is comprised of the DNA DataBank of Japan (DDBJ), the European Molecular Biology Laboratory (EMBL), and GenBank at the National Center for Biotechnology Information. For more information on GenBank, visit the GenBank website at NCBI.

Includes a Browse Index of available terms from which you may select. Examples: EU429475, W14812, NC_001416.

Entrez Gene ID

An indexed field which searches the Entrez Gene identification code for a gene sequence. Entrez Gene is a searchable database of genes, from RefSeq genomes. The NCBI Reference Sequences collection aims to provide a comprehensive, integrated, non-redundant, well-annotated set of sequences, including genomic DNA, transcripts, and proteins. For more information on Entrez Gene, visit the Entrez Gene web page at NCBI.

Includes a Browse Index of available terms from which you may select. Examples: Q30154, 10052, NM_001017995.

Condition

A controlled text field which searches the condition or type of disorder the gene/protein treats. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select. Examples: Chronic obstructive pumonary disease (COPD), Leukemia, acute myeloid, Crohn's disease, Hepatitis B.

Sequence

A free text field which searches the nucleotide sequence. Enter a sequence of bases. Eighteen bases are considered defining but up to 300 bases can be entered. Examples: ggatccattttgaaaaaccaggaag; MIHELLLALSGYPGSI.

Sequence Type

A controlled text field which searches the sequence type; available choices are: 5'-Promoter region, Antisense coding sequence, Artificial sequence, cDNA, Coding sequence, Coding sequence (mature protein), DNA fragment, Double-stranded DNA fragment, Double-stranded RNA fragment, Mixed backbone, RNA, Gene or Protein. Includes a Browse Index of available terms from which you may select.

Organism

An indexed field which searches the organism.

Gene Variants

There are four available choices for Gene Variants: Variation Type, Disease Association, Variation Name, and Gene Variant Disease.

Gene Variants – Variation Type

A controlled text field which searches the variation type of the gene variants. Includes a Browse Index of available terms from which you may select. Examples: Allelic loss; Epigenetic change, Gene duplication, Polymorphism/mutation.

Gene Variants – Disease Association

A controlled text field which searches the disease association of the gene variants. Includes a Browse Index of available terms from which you may select. Examples: Allele, Compound heterozygote, DNA, Genotype.

Gene Variants – Variation Name

An indexed field which searches the variation name of the gene variants. Includes a Browse Index of available terms from which you may select. Examples: (CAG)n, Dinucleotide repeat, p-Gly141Arg, SF-1.

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Gene Variants – Gene Variant Diseases
There are two available choices for Gene Variant Diseases: Condition and Effect.

Gene Variants – Gene Variant Diseases – Condition
An indexed field which searches the condition or type of disorder associated with gene variant diseases. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select. Examples: Chronic obstructive pumonary disease (COPD), Leukemia, acute myeloid, Crohn's disease, Hepatitis B.

Gene Variants – Gene Variant Diseases – Effect
A controlled text field which searches the effects of a bioactive compound on gene variant diseases. Includes a Browse Index of available terms from which you may select. Examples: Causative, Decreased risk, Good prognosis, Protective.

Gene-Related Studies
There are four available choices for Gene-Related Studies: Condition, Model, Study Type, and Polymorphism.

Gene-Related Studies – Condition
An indexed field which searches the condition or type of disorder associated with gene-related studies. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select. Examples: Chronic obstructive pumonary disease (COPD), Leukemia, acute myeloid, Crohn's disease, Hepatitis B.

Gene-Related Studies – Model
An indexed field which searches the model associated with gene-related studies. Includes a Browse Index of available terms from which you may select. Examples: Mast cells, human, Plasmodium falciparum, Transgenic mouse, Dendritic cells, human.

Gene-Related Studies – Study Type
A controlled text field which searches the study type associated with gene-related studies; Drugs and gene expression, Gene therapies, Molecular studies, Pharmacogenomics, Toxicogenomics.

Gene-Related Studies – Polymorphism (Y/N)
A Yes/No field which searches for the presence of gene-related studies on polymorphism. Yes and No are the only values permitted in this field. Type Y for yes; type N for no.

Last Updated
A numeric field which searches the date the record was last updated. Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

Available Since
A numeric field which searches the date the record was made available. Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

The table below summarizes the search fields available for Genomics:

Search Field	Field Type	Additional Details
Classification	Indexed Field	Browse (alphabetical/ hierarchical)
Gene Name	Indexed Field	Browse (alphabetical)
Protein Name	Indexed Field	Browse (alphabetical)
Gene/Protein Name	Indexed Field	Browse (alphabetical)
EC Classification	Indexed Field	Browse (alphabetical)
PDB ID	Indexed Field	Browse (alphabetical)
Swiss-Prot	Indexed Field	Browse (alphabetical)
GenBank ID	Indexed Field	Browse (alphabetical)
Entrez Gene ID	Indexed Field	Browse (alphabetical)
Condition	Controlled Text	Browse (alphabetical/ Hierarchical)
Sequence	Free Text	Enter a sequence of bases. Eighteen bases are considered defining but up to 300 bases can be entered.
Sequence Type	Controlled Text	Browse (alphabetical)
Organism	Indexed Field	Browse (alphabetical)

Search Field	Field Type	Additional Details
Gene Variants – Variation Type	Controlled Text	Browse (alphabetical)
Gene Variants – Disease Association	Controlled Text	Browse (alphabetical)
Gene Variants – Variation Name	Indexed Field	Browse (alphabetical)
Gene Variants – Gene Variant Diseases – Condition	Indexed Field	Browse (alphabetical/ hierarchical)
Gene Variants – Gene Variant Diseases – Effect	Controlled Text	Browse (alphabetical)
Gene-Related Studies – Condition	Indexed Field	Browse (alphabetical/ hierarchical)
Gene-Related Studies – Model	Indexed Field	Browse (alphabetical)
Gene-Related Studies – Study Type	Controlled Text	Browse (alphabetical)
Gene-Related Studies – Polymorphism (Y/N)	YES/NO	Yes and No are the only values; type Y for yes, N for no.

Search fields available for Genomics continued...

Search Field	Field Type	Additional Details
Last Updated	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards
Available Since	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards

BIOMARKER

Found on the Biomarkers Advanced Search only; the fields appear grouped as Biomarker or Biomarker Use. Includes the following choice of fields:

Biomarker
- Name
- Type
- Biological Process
- Description
- Product Modifier
- Mechanism Modifier
- Highest Validity
- Methods Papers
  - Type
  - Stage
  - Reference
- Review Type
- Review Title
- Last Update
- Available Since

Biomarker Use
- Use ID
- Indication
  - Condition
- Safety/Tox.
- Experimental Pathology
- Population
- Role
- Validity
- Parameter
- Technique
- Substrate
- Kit
  - Name
  - Organization
  - All Related Organizations
  - Regulatory Authority
  - Country
  - Status
  - Milestone
    - Country
    - Name
    - Date
- Genetic Variation
  - Gene Name (including synonyms)
  - Variation Type
- Correlates to...
- Product Name

- Mechanism of Action
- Product Category
- Therapeutic Group
- Authority

Biomarker Name
An indexed field which searches the most commonly used name or preferred name for the biomarker, including any synonyms and tracers. Includes a Browse Index of available terms from which you may select. Examples: HER2, BRCA2, T cell antigen ILA.

Type
A controlled text field which searches the biomarker type within an individual biomarker record; available choices are:

- **Anthropomorphic biomarkers** – are of the body shape/form, e.g. body mass index.
- **Biochemical biomarkers** – are metabolites and other biochemical entities, e.g. cholesterol and bilirubin.
- **Cellular biomarkers** – are whole cells, e.g. cancer cells identified by the Pap smear test.
- **Genomic biomarkers** – are variants in the DNA sequence and in the transcription level, e.g. HER2.
- **Physiological biomarkers** – are body processes, e.g. systolic blood pressure.
- **Proteomic biomarkers** – are variants in protein sequence, protein levels in a given tissue, proteins interactions and enzyme activities.
- **Structural (imaging) biomarkers** – are physical images, e.g. colorectal tumor margin (image obtained by magnetic resonance imaging, MRI), carotid intima media thickness.

Includes a Browse Index of available terms from which you may select.

Biological Process
A controlled text field which searches the biological processes biomarkers are involved in. An individual biomarker record may contain one or many processes. Includes a Browse Index of available terms from which you may select. Examples: angiogenesis, inflammation, blood coagulation, atherosclerosis.

Description
A free text field which searches the description of the biomarker. Type one or more words. Enclose adjacent words in double quotation marks. Operators: AND, OR, NOT, *. ?. Examples: hypertension; hypertens*, hypertension, "congestive heart failure".

Product Modifier
An indexed field which searches the product modifier e.g. drugs that modify the biomarker. A product modifier (launched drug) is cited in a biomarker record when measurement of the biomarker is specifically mentioned in a clinical guideline or in an FDA approval letter for the drug. Includes a Browse Index of available terms from which you may select. Examples: Selectin, Cetuximab, Ritalin.

Mechanism Modifier
A controlled text field which searches the modifier mechanism of the biomarker. A mechanism modifier is cited in a biomarker record when the mechanism has specific relevance to the biomarker, e.g. c-reactive protein inhibitors is the mechanism modifier for the c-reactive protein biomarker. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select. Examples: 5-HT3 Receptor Ligands, Drugs Acting on GABA(A) Receptors, VEGF Expression Enhancers.

Highest Validity
A controlled text field which searches the highest validity or lifecycle phase of a biomarker; available choices are:

- **Emerging** – First mention of biomarker use, usually from patents and press releases.
- **Experimental** – Reports from preclinical studies (laboratory and/or animal studies).
- **Early Studies in Humans** – The biomarker use has been studied in humans (clinical trials or observational studies). Studies with less than 500 individuals, the objective of which is to measure proof of concept and dose finding.
- **Late Studies in Humans** – The biomarker use has been studied in humans (clinical trials or observational studies) but has not yet been recommended by a scientific authority. Studies with more than 500 individuals, the objective of which is to measure efficacy and to establish the relationship found in early studies in humans.
- **Recommended/Approved** – Kit or measuring device/software is approved by the FDA or other regulatory authority, and/or the use of the biomarker

is described in clinical practice guidelines or consensus development statements have been issued by clinical societies of international standing.

Includes a Browse Index of available terms from which you may select.

Methods Papers
There are three available choices for Methods Papers: Type, Stage, and Reference.

Methods Papers – Type
A controlled text field which searches by the methods paper type. There are five available choices for Methods Papers – Type: Algorithm development, Contrast agent development, Reliability study, Technique development, Technique standardization.

Methods Papers – Stage
A controlled text field which searches by the methods paper stage. There are two available choices for Methods Papers – Stage: Clinical, and Preclinical.

Methods Papers – Reference
A free text field which searches by the reference title, and is limited to those articles indexed as a methods paper. Type one or more words. Enclose adjacent words in double quotation marks. Operators: AND, OR, NOT, *. ?. Examples: hypertension; hypertens*, hypertension and "congestive heart failure".

Review Type
A controlled text field which searches the review type of review papers associated with the biomarker. There are two available choices for Review Type: Review and Guidelines.

Review Title
A free text field which searches by the review title, and is limited to those articles indexed as a review. Type one or more words. Enclose adjacent words in double quotation marks. Operators: AND, OR, NOT, *. ?. Examples: hypertension; hypertens*, hypertension and "congestive heart failure".

Last Update
A numeric field which searches the date the record was last updated. Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

Available Since
A numeric field which searches the date the record was made available. Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

Use ID
A numeric field which searches the use ID. Type a number. Operators: OR, From, From ... To ...; no wildcards. Examples: 2000; From 2000; From 2000 to 20000; 2000 OR 20005.

Indication

There are three available choices for Indication: Condition, Safety/Tox., and Experimental Pathology.

Indication – Condition

A controlled text field which searches use indication where the type (class) is disease/condition, e.g. atherosclerosis. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select.

Indication – Safety/Tox.

A controlled text field which searches use indication where the type (class) is safety/tox, e.g. cardiotoxicity. Includes a Browse Index of available terms from which you may select.

Indication – Experimental Pathology

A controlled text field which searches use indication where the type (class) is experimental pathology, e.g. oxidative stress. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select.

Population

A controlled text field which searches use population, e.g. acute myocardial infarction. Includes a Browse Index of available terms from which you may select.

Role

A controlled text field which searches the roles that may be applied to a biomarker; available choices are:

- **Diagnosis** – identify or detect a disease.
- **Differential Diagnosis** – identify and distinguish between two or more diseases with similar signs and symptoms.
- **Disease Profiling** – provides information about the disease, but there is insufficient data to assign a clinical role. The data is often obtained from high throughput analyses, for example transcript profiling, and might be extrapolated to the processes that cause the disease.
- **Monitoring Disease Progress** – monitor the progress of a disease, usually for diseases for which there is no effective therapy.
- **Monitoring Treatment Efficacy** – identify signs of a change (usually beneficial) as a result of treatment. A biomarker used for monitoring treatment efficacy is usually measured before the treatment starts (baseline) and at stages throughout the treatment (follow up).
- **Monitoring Treatment Toxicity** – identify signs of adverse effects as a result of treatment. Measured at baseline and at stages throughout treatment.
- **Predicting Drug Resistance** – detect possible resistance to a therapy and thus to exclude that therapy from the possible therapies available to the patient.
- **Predicting Treatment Efficacy** – predict a probable beneficial outcome as a result of treatment.

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- **Predicting Treatment Toxicity** – predict a probable adverse effect as a result of treatment.
- **Prognosis** – predict the probable outcome of a disease, i.e. how a patient's disease will progress and his or her chances of recovery. The prediction is based on the usual course of the disease seen in similar patients without therapy.
- **Risk Stratification** – determine a person's risk of suffering a particular clinical event within a specified period of time.
- **Risk Factor** – describes the association between a biomarker and a disease on a basis of epidemiological evidence.
- **Screening** – sort a population into "healthy" and "non-healthy". Screening is an epidemiological process, though the same process may serve for diagnosis as well.
- **Selection for Therapy** – select a sub-group of patients suitable for a particular therapy.
- **Staging** – describes how far a disease has progressed in a patient. The stage at diagnosis is often a prognostic indicator of overall survival and can be used as a guide for subsequent therapy.
- **Toxicity Profiling** – provides information about the underlying cause of an adverse or toxic event, but there is insufficient data to assign a predictive or monitoring role. A biomarker use with "toxicity profiling" represents the birth of that use, often the first mention of the association between the biomarker and the adverse event and is always experimental. When new studies that focus on its predictive or monitoring role are added to our

database, the role will be changed and upgraded.

Includes a Browse Index of available terms from which you may select.

Validity

A controlled text field which searches the validities or lifecycle phases of a biomarker; available choices are:

- **Approved/Recommended** – Kit or measuring device/software is approved by the FDA or other regulatory authority, and/or the use of the biomarker is described in clinical practice guidelines or consensus development statements have been issued by clinical societies of international standing.
- **Late Studies in Humans** – The biomarker use has been studied in humans (clinical trials or observational studies) but has not yet been recommended by a scientific authority. Studies with more than 500 individuals, the objective of which is to measure efficacy and to establish the relationship found in early studies in humans.
- **Early Studies in Humans** – The biomarker use has been studied in humans (clinical trials or observational studies). Studies with less than 500 individuals, the objective of which is to measure proof of concept and dose finding.
- **Experimental** – Reports from preclinical studies (laboratory and/or animal studies).
- **Emerging** – First mention of biomarker use, usually from patents and press releases.
- **Discontinued** – For a biomarker use that is not "Recommended/

Approved" for which no data has been reported in 12 months.

Includes a Browse Index of available terms from which you may select.

Parameter
A controlled text field which searches parameters associated with the biomarker, e.g. Respiratory flow. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select.

Technique
A controlled text field which searches the technique used to measure the biomarker, e.g. FISH, CISH, EIA, ELISA, PCR. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select; options include Chemical Analytical Techniques, Cytological Techniques, Genetic Techniques, Molecular Probe Techniques, Physiological Techniques, Protein Techniques, and Imaging Methods.

Substrate
A controlled text field which searches the substrate used for the measurement technique, e.g. DNA, RNA, tissue, tumor, protein. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select.

Kit
There are seven available choices for Kit: Name, Organization, All Related Organizations, Regulatory Authority, Country, Status, and Milestone.

Kit – Name
An indexed field which searches which searches the name of the diagnostic kit, e.g. pharmDX. Includes a Browse Index of available terms from which you may select.

Kit – Organization
An indexed field which searches organizations that have developed diagnostic kits, e.g. Dako Denmark A/S, Bayer Healthcare AG, Genzyme Diagnostics. Includes a Browse Index of available terms from which you may select.

Kit – All Related Organizations
An indexed field which searches related organizations for the diagnostic kit, e.g. Siemens Medical Solutions. Includes a Browse Index of available terms from which you may select.

Kit – Regulatory Authority
An indexed field which searches the regulatory authority that has approved a diagnostic kit for measuring the biomarker, e.g. FDA. Includes a Browse Index of available terms from which you may select.

Kit – Country
A controlled text field which searches the country for the diagnostic kit, e.g. US. Includes a Browse Index of available terms from which you may select.

Kit – Status
A controlled text field which searches the development status of the diagnostic kit; Approved or Launched. Includes a Browse Index of available terms from

which you may select.

Kit – Milestone
There are three available choices for Kit – Milestone: Country, Name, and Date.

Kit – Milestone – Country
A controlled text field which searches the milestone country for the diagnostic kit, e.g. USA. Includes a Browse Index of available terms from which you may select.

Kit – Milestone – Name
A controlled text field which searches the milestone name for the diagnostic kit. Includes a Browse Index of available terms from which you may select.

Kit – Milestone – Date
A numeric field which searches the milestone date for the diagnostic kit. Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

Genetic Variation
There are two available choices for Genetic Variation: Gene Name and Variation Type.

Genetic Variation – Gene Name
An indexed field which searches gene names and synonyms of gene variants linked to a specific use, e.g. Interferon gamma, Interleukin 2 receptor, alpha chain. Includes a Browse Index of available terms from which you may select.

Genetic Variation – Variation Type
A controlled text field which searches the variation type of gene variants linked to a specific use; Allelic loss, Epigenetic change, Gene duplication, Polymorphism/mutation or Variable Number of Tandem Repeats.

- **Epigenetic change** – describes changes in the regulation of the expression of gene activity without alteration of the DNA sequence. For example, the hypermethylation status of the bone morphogenetic protein 6 gene promoter is prognostic in patients with diffuse large B-cell lymphoma.
- **Gene duplication** – describes a selective increase in the number of copies of a gene without a proportional increase in other genes. For example, duplication of the alpha-synuclein gene is a risk factor for Parkinson's Disease.
- **Polymorphism/mutation** – describes a common change in the genetic code. These changes include single nucleotide polymorphisms; mutations (any change in the DNA of a cell); deletions (loss of DNA from a chromosome); and insertions (insertion of DNA into a chromosome). For example, the 405G>C polymorphism in VEGFA is a risk factor for endometriosis.

Includes a Browse Index of available terms from which you may select.

Correlates to...
A controlled text field which searches the names of biomarkers indexed as Bmk-Bmk (biomarker to biomarker) correlations or of cognition tests indexed as Bmk-Cog (biomarker to cognition) correlations. Includes a Browse Index of

available terms from which you may select.

Product Name
An indexed field which searches drug names linked to a specific use, e.g. Mesalazine. Includes a Browse Index of available terms from which you may select.

Mechanism of Action
A controlled text field which searches against mechanisms of action linked to a specific use, e.g. 5HT Reuptake Inhibitors, Anti-HER2/neu/ErbB2, etc. When a biomarker has been used to indicate a response to therapy with drugs categorized by their mechanism of action, then the mechanism of action is linked to the use. Includes a Browse Index of available terms from which you may select.

Product Category
A controlled text field which searches product categories linked to a specific use, e.g. Antisense Therapy, Cytokines, etc. Includes a Browse Index of available terms from which you may select.

Therapeutic Group
A controlled text field which searches therapeutic groups linked to a specific use, e.g. Vasodilators, Thrombolytics, Disease-Modifying Anti-Rheumatic Drugs, etc. Includes a Browse Index of available terms from which you may select.

Authority
A controlled text field which searches the scientific society or similar authority that has recommended a biomarker use, e.g. European Group on Tumour Markers (EGTM), ASCO. Includes a Browse Index of available terms from which you may select.

The table below summarizes the search fields available for Biomarker:

Search Field	Field Type	Additional Details
Biomarker Name	Indexed Field	Browse (alphabetical)
Type	Controlled Text	Browse (alphabetical)
Biological Process	Controlled Text	Browse (alphabetical/ hierarchical)
Description	Free Text	Enclose adjacent words in double quotes. Operators: AND, OR, NOT, *, ?
Product Modifier	Indexed Field	Browse (alphabetical)
Mechanism Modifier	Controlled Text	Browse (alphabetical/ hierarchical)
Highest Validity	Controlled Text	Browse (alphabetical)
Methods Papers – Type	Controlled Text	Browse (alphabetical)
Methods Papers – Stage	Controlled Text	Clinical or Preclinical
Methods Papers – Reference	Free Text	Enclose adjacent words in double quotes. Operators: AND, OR, NOT, *, ?
Review Type	Controlled Text	Guidelines or Review

Search Field	Field Type	Additional Details
Review Title	Free Text	Enclose adjacent words in double quotes. Operators: AND, OR, NOT, *, ?
Last Update	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards
Available Since	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards
Use ID	Numeric	Operators; OR, From, From ... To... ; no wildcards
Indication – Condition	Controlled Text	Browse (alphabetical/ hierarchical)
Indication – Safety/Tox.	Controlled Text	Browse (alphabetical)
Indication – Experimental Pathology	Controlled Text	Browse (alphabetical/ hierarchical)
Population	Controlled Text	Browse (alphabetical)
Role	Controlled Text	Browse (alphabetical)
Validity	Controlled Text	Browse (alphabetical)
Parameter	Controlled Text	Browse (alphabetical/ hierarchical)

Search fields available for Biomarker continued...

Search Field	Field Type	Additional Details
Technique	Controlled Text	Browse (alphabetical/ hierarchical)
Substrate	Controlled Text	Browse (alphabetical/ hierarchical)
Kit – Name	Indexed Field	Browse (alphabetical)
Kit – Organization	Indexed Field	Kit Developers. Browse (alphabetical)
Kit – All Related Organizations	Indexed Field	Browse (alphabetical)
Kit – Regulatory Authority	Indexed Field	Browse (alphabetical)
Kit – Country	Controlled Text	Browse (alphabetical)
Kit – Status	Controlled Text	Browse (alphabetical)
Kit – Milestone – Country	Controlled Text	Browse (alphabetical)
Kit – Milestone – Name	Controlled Text	Approved or Launched
Milestone – Milestone Date	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards

Search Field	Field Type	Additional Details
Genetic Variation – Gene Name	Indexed Field	Browse (alphabetical)
Genetic Variation – Variation Type	Controlled Text	Browse (alphabetical)
Correlates to...	Controlled Text	Browse (alphabetical)
Product Name	Indexed Field	Browse (alphabetical)
Mechanism of Action	Controlled Text	Browse (alphabetical)
Product Category	Controlled Text	Browse (alphabetical)
Therapeutic Group	Controlled Text	Browse (alphabetical)
Authority	Controlled Text	Browse (alphabetical)

ORGANIC SYNTHESIS

Found on the Organic Synthesis Advanced Search only. Includes the following choice of fields:

- Synthesis Text
- Drug (End Product) Name
- End Product Entry Number
- Scheme Number
- Available Since
- Intermediate
  - Number
  - Chemical Name
  - Standard InChI
  - Standard InChIKey
  - CAS Registry No.
  - Molecular Formula
  - Molecular Weight
  - Supplier
- Reagent
  - Number
  - Chemical Name
  - Standard InChI
  - Standard InChIKey
  - CAS Registry No.
  - Molecular Formula
  - Molecular Weight
  - Supplier
  - Representation

The Organic Synthesis section of search fields has the option to display Schemes or Intermediates or Reagents:

- Choose to display Schemes or Intermediates or Reagents; initially, Schemes is selected.

(For Intermediate sub-fields, available choices are Schemes or Intermediates; for Reagent sub-fields, available choices are Schemes or Reagents.)

Synthesis Text

A free text field which searches the synthesis text. Type one or more words. Enclose adjacent words in double quotation marks. Operators: AND, OR, NOT, *. ?. Examples: hypertension; hypertens*, hypertension and ''congestive heart failure''.

Drug (End Product) Name

An indexed field which searches the drug (end product) name. Includes a Browse Index of available terms from which you may select. Examples: Azulfidine, C reactive protein, R(+)-Bisoprolol.

End Product Entry Number

A numeric field which searches the end product entry number.

Scheme Number

A numeric field which searches the scheme number. Type a 6-digit number. Operators: OR, From, From ... To ...; no wildcards. Examples: 176436; From 176436; From 176436 to 178099; 176436 OR 178099.

Available Since

A numeric field which searches the date the record was made available. Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

Intermediate

There are eight available choices for Intermediate: Number, Chemical Name, Standard InChI, Standard InChIKey, CAS Registry No., Molecular Formula, Molecular Weight, and Supplier.

Intermediate – Number

A numeric field which searches the intermediate number. Type an Intermediate Number (5 or 6 digits). Operators: OR, From, From ... To ...; no wildcards. Examples: 10001; 010001; From 10001; From 10001 to 10003; 10001 OR 10003.

Intermediate – Chemical Name

A free text field which searches the chemical name of an intermediate. Type a fragment of a chemical name. Operators: AND, OR, NOT, *, ?. Examples: imidazoline; imidazolin*; imidazoline AND *chloro*.

Intermediate – Standard InChI

A free text field which searches the standard InChI of an intermediate. The International Chemical Identifier (InChI) is a non-proprietary identifier for chemical substances that can be used in printed and electronic data sources; InChI was developed in cooperation of IUPAC and NIST and is the newest way of describing chemical structures in text. Type a fragment of a Standard InChI. Operators: AND, OR, *, ?. Examples: 1S/C47H51NO14*; *38,24-58-33)62-27*.

Intermediate – Standard InChIKey

A free text field which searches the standard InChIKey of an intermediate. InChIKey is a fixed-length format derived directly from InChI. The 27 characters long InChIKey is made of three parts connected by hyphens. The first part is 14 characters long and is based on the connectivity and proton layers of an InChI

string. The second part contains 9 characters that are related to all other InChI layers (isotopes, stereochemistry, etc.) and also contains the version of InChI and its standard/non-standard property in the last two characters. The third part is one letter, describing the (de)protonation layer of the original InChI. Type a Standard InChIKey or a fragment of a Standard InChIKey. Operators: AND, OR, *, ?. Examples: RCINICONZNJXQF-MZXODVADSA-N; RCI*.

Intermediate – CAS Registry No.
A numeric field which searches the CAS Registry Number, a sequentially assigned accession number from the CAS Registry – the world's largest substance database. The CAS Registry Number (RN) is made of three parts connected by hyphens and has the format: 123456-78-9. The first part can be from two to seven digits long. The second part contains 2 digits. The third part is a single check-digit. The CAS RN has no chemical or structural meaning in itself. It is simply an identifier for a specific substance that CAS has registered during the process of indexing the literature or added from another source. The shorter the first part, the older the registration and therefore the more common (and probably better described) the compound is. Type a CAS Registry Number or part thereof. Operators: OR, NOT, *. Examples: 138402-11-6; 138402*.

Intermediate – Molecular Formula
A free text field which searches the molecular formula of an intermediate. Type a molecular formula or part thereof. Operators: OR, NOT; * (on both the right and the left). Examples: C25H28*; C25H28N6O.

Intermediate – Molecular Weight
A numeric field which searches the molecular weight of an intermediate. Type a number. Operators: From, From ... To ...; no wildcards. Examples: From 10000; From 451 to 452.

Intermediate – Supplier
An indexed field which searches the supplier of an intermediate. Includes a Browse Index of available terms from which you may select. Examples: Daiichi Pure Chemicals Co. Ltd, Bayer Corporation, Pharmacia & Upjohn Company.

Reagent
There are nine available choices for Reagent: Number, Chemical Name, Standard InChI, Standard InChIKey, CAS Registry No., Molecular Formula, Molecular Weight, Supplier, and Representation.

Reagent – Number
A numeric field which searches the reagent number. Type a Reagent Number (1-6 digits). Operators: OR, From, From ... To ...; no wildcards. Examples: 99; 000099; From 2045; From 75 to 110; 75 OR 76.

Reagent – Chemical Name
A free text field which searches the chemical name of a reagent. Type a fragment of a chemical name. Operators: AND, OR, NOT, *, ?. Examples: imidazoline; imidazolin*; imidazoline AND *chloro*; monoclonal; interferon; gamma.

Reagent – Standard InChI
A free text field which searches the standard InChI. The International Chemical Identifier (InChI) is a non-proprietary identifier for chemical substances that can be used in printed and electronic data sources; InChI was developed in cooperation of IUPAC and NIST and is the newest way of describing chemical structures in text. Type a fragment of a Standard InChI. Operators: AND, OR, *, ?. Examples: 1S/C47H51NO14*; *38,24-58-33)62-27*.

Reagent – Standard InChIKey
A free text field which searches the standard InChIKey. InChIKey is a fixed-length format derived directly from InChI. The 27 characters long InChIKey is made of three parts connected by hyphens. The first part is 14 characters long and is based on the connectivity and proton layers of an InChI string. The second part contains 9 characters that are related to all other InChI layers (isotopes, stereochemistry, etc.) and also contains the version of InChI and its standard/non-standard property in the last two characters. The third part is one letter, describing the (de)protonation layer of the original InChI. Type a Standard InChIKey or a fragment of a Standard InChIKey. Operators: AND, OR, *, ?. Examples: RCINICONZNJXQF-MZXODVADSA-N; RCI*.

Reagent – CAS Registry No.
A numeric field which searches the CAS Registry Number of a reagent, a sequentially assigned accession number from the CAS Registry – the world's largest substance database. The CAS Registry Number (RN) is made of three parts connected by hyphens and has the format: 123456-78-9. The first part

can be from two to seven digits long. The second part contains 2 digits. The third part is a single check-digit. The CAS RN has no chemical or structural meaning in itself. It is simply an identifier for a specific substance that CAS has registered during the process of indexing the literature or added from another source. The shorter the first part, the older the registration and therefore the more common (and probably better described) the compound is. Type a CAS Registry Number or part thereof. Operators: OR, NOT, *. Examples: 138402-11-6; 138402*.

Reagent – Molecular Formula
A free text field which searches the molecular formula of a reagent. Type a molecular formula or part thereof. Operators: OR, NOT; * (on both the right and the left). Examples: C25H28*; C25H28N6O.

Reagent – Molecular Weight
A numeric field which searches the molecular weight of a reagent. Operators: From, From ... To ...; no wildcards. Examples: From 10000; From 451 to 452.

Reagent – Supplier
An indexed field which searches the supplier of a reagent. Includes a Browse Index of available terms from which you may select. Examples: Daiichi Pure Chemicals Co. Ltd, Bayer Corporation, Pharmacia & Upjohn Company.

Reagent – Representation
A free text field which searches the synonyms of a reagent. Type a synonym or part thereof. Operators: OR, NOT; * (on both the right and the left). Examples:

Bu4NF; *Bu4N*.

The table below summarizes the search fields available for Organic Synthesis:

Search Field	Field Type	Additional Details
Synthesis Text	Free Text	Enclose adjacent words in double quotes. Operators: AND, OR, NOT, *, ?
Drug (End Product) Name	Indexed Field	Browse (alphabetical)
End Product Entry Number	Numeric	6-digit number; operators: OR, From, From ... To ... ; no wildcards
Scheme Number	Numeric	6-digit end product entry number, hyphen, 2-digit number, hyphen, alphabetic character; operators: AND, OR, *, ?
Available Since	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards
Intermediate – Number	Numeric	5 or 6-digit number; operators: OR, From, From ... To ... ; no wildcards
Intermediate – Chemical Name	Free Text	Chemical name or fragment; operators, AND, OR, NOT, *, ?

Search fields available for Organic Synthesis continued...

Search Field	Field Type	Additional Details
Intermediate – Standard InChl	Free Text	Standard InChl or fragment; operators, AND, OR, *, ?
Intermediate – Standard InChlKey	Free Text	Standard InChlKey or fragment; operators, AND, OR, *, ?
Intermediate – CAS Registry No.	Numeric	CAS Registry Number or part thereof; operators, OR, NOT, *
Intermediate – Molecular Formula	Free Text	Molecular Formula or part thereof; operators, OR, NOT, * (on both the right and left)
Intermediate – Molecular Weight	Numeric	Operators: From, From ... To ... ; no wildcards
Intermediate – Supplier	Indexed Field	Browse (alphabetical)
Reagent – Number	Numeric	1-6 digit number; operators: OR, From, From ... To ...; no wildcards
Reagent – Chemical Name	Free Text	Chemical name or fragment; operators, AND, OR, NOT, *, ?

Search Field	Field Type	Additional Details
Reagent – Standard InChl	Free Text	Standard InChl or fragment; operators, AND, OR, *, ?
Reagent – Standard InChlKey	Free Text	Standard InChlKey or fragment; operators, AND, OR, *, ?
Reagent – CAS Registry No.	Numeric	CAS Registry Number or part thereof; operators, OR, NOT, *
Reagent – Molecular Formula	Free Text	Molecular Formula or part thereof; operators, OR, NOT, * (on both the right and left)
Reagent – Molecular Weight	Numeric	Operators: From, From ... To ... ; no wildcards
Reagent – Supplier	Indexed Field	Browse (alphabetical)
Reagent – Representation	Free Text	Synonym or part thereof; operators: OR, NOT, * (on both the right and left)

EXPERIMENTAL PHARMACOLOGY

Found on the Experimental Pharmacology Advanced Search only. Includes the following choice of fields:

- Pharmacological Activity
- Parameter
- Unit
- Method
- Material
- Available Since

The Experimental Pharmacology section of search fields has the option to Include Literature Results and/or Include Patent Results:

- Choose to Include Literature Results and/or Include Patent Results; initially, both options are selected.

Display ⊙ Schemes ○ Intermediates ○ Reagents

Pharmacological Activity
A controlled text field which searches pharmacological activity, e.g. Cytotoxicity, Phosphodiesterase IV, inhibition. Includes a Browse Index of available terms from which you may select.

Parameter
A controlled text field which searches the pharmacological parameter, e.g. IC50, Kd, pKa. Includes a Browse Index of available terms from which you may select.

Unit
A controlled text field which searches the pharmacological units of measure, e.g. g/kg i.p. q.i.d., mol/kg. Includes a Browse Index of available terms from which you may select.

Method
A controlled text field which searches the pharmacological method employed, e.g. 3T3 cells, 12-HETE formation assay. Includes a Browse Index of available terms from which you may select.

Material
A controlled text field which searches the pharmacological material used, e.g. 3T3 mouse embryonic fibroblasts, Macrophage cells (bone marrow-derived), Humans. Includes a Browse Index of available terms from which you may select.

Available Since

A numeric field which searches the date the record was made available. Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

The table below summarizes the search fields available for Experimental Pharmacology:

Search Field	Field Type	Additional Details
Pharmacological Activity	Controlled Text	Browse (alphabetical)
Parameter	Controlled Text	Browse (alphabetical)
Unit	Controlled Text	Browse (alphabetical)
Method	Controlled Text	Browse (alphabetical)
Material	Controlled Text	Browse (alphabetical)
Available Since	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards

PHARMACOKINETICS/METABOLISM

Found on the Pharmacokinetics/Metabolism Advanced Search only. Includes the following choice of fields:

- Model
- Condition
- Administered Product
  – Drug Name
  – Formulation
  – Administration Route
  – Interacting Agent
- Measured Product
  – Drug Name
  – Compartment
  – Measured As
  – Parameter
- Available Since

Model
A controlled text field which searches the model used, e.g. ABCB1 (homozygous), CYP3A5, Marmosets. Includes a Browse Index of available terms from which you may select.

Condition
A controlled text field which searches the condition or type of disorder the bioactive compound treats. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select. Examples: Chronic obstructive pumonary disease (COPD), Leukemia, acute myeloid, Crohn's disease, Hepatitis B.

Administered Product
There are four available choices for Administered Product: Drug Name, Formulation, Administration Route, and Interacting Agent.

Administered Product – Drug Name
An indexed field which searches the drug name of the administered product, e.g. Celecoxib, Simvastatin, Ramapril. Includes a Browse Index of available terms from which you may select.

Administered Product – Formulation
A controlled text field which searches the formulation associated with the administered product, e.g. Capsules (controlled-release), Nanoparticles, Syrup. Includes a Browse Index of available terms from which you may select.

Administered Product – Administration Route
A controlled text field which searches the route of administration associated with the administered product, e.g. oral, intravenous, epidural. Includes a Browse Index of available terms from which you may select.

Administered Product – Interacting Agent
A controlled text field which searches any interacting agents associated with the administered product, e.g. Corticosteroids, Hormone replacement therapy, Tyrosine kinase inhibitors. Includes a Browse Index of available terms from which you may select.

Measured Product
There are four available choices for Measured Product: Drug Name, Compartment, Measured As, and Parameter.

Measured Product – Drug Name
An indexed field which searches the drug name of the measured product, e.g. (R)-Citalopram, Gabapentin, Penciclovir. Includes a Browse Index of available terms from which you may select.

Measured Product – Compartment
A controlled text field which searches the compartment of the measured product, e.g. Blood, Pituitary gland, Retina/choroid. Includes a Browse Index of available terms from which you may select.

Measured Product – Measured As
A controlled text field which searches the assay method employed to determine the measured product, e.g. HPLC, Gel electrophoresis, Mass spectrometry. Includes a Browse Index of available terms from which you may select.

Measured Product – Parameter
A controlled text field which searches pharmacokinetic/metabolic parameter, e.g AUC(0-50), Cmax, t1/2alpha. Includes a Browse Index of available terms from which you may select.

Available Since
A numeric field which searches the date the record was made available. Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

The table below summarizes the search fields available for Pharmacokinetics/ Metabolism:

Search Field	Field Type	Additional Details
Model	Controlled Text	Browse (alphabetical)
Condition	Controlled Text	Browse (alphabetical/ hierarchical)
Administered Product – Drug Name	Indexed Field	Browse (alphabetical)
Administered Product – Formulation	Controlled Text	Browse (alphabetical)
Administered Product – Administration Route	Controlled Text	Browse (alphabetical)
Administered Product – Interacting Agent	Controlled Text	Browse (alphabetical)
Measured Product – Compartment	Indexed Text	Browse (alphabetical)
Measured Product – Measured As	Controlled Text	Browse (alphabetical)

Search Field	Field Type	Additional Details
Measured Product – Parameter	Controlled Text	Browse (alphabetical)
Available Since	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards

CLINICAL STUDIES

Found on the Clinical Studies Advanced Search only. Includes the following choice of fields:

- Condition
- Study Design
- Study
- Intervention Type
- Population No.
- Journal or Congress
- Available Since

Condition

A controlled text field which searches the condition or type of disorder the bioactive compound treats. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select. Examples: Chronic obstructive pumonary disease (COPD), Leukemia, acute myeloid, Crohn's disease, Hepatitis B.

Study Design

A controlled text field which searches the study design, e.g. Double-blind, Open, Crossover, Multicenter. Includes a Browse Index of available terms from which you may select.

Study

A free text field which searches the study title. Type one or more words. Enclose adjacent words in double quotation marks. Operators: AND, OR, NOT, *. ?. Examples: hypertension; hypertens*, hypertension and "congestive heart failure".

Intervention Type

A controlled text field which searches the intervention type, e.g. Drug therapy, Prevention, Psychotherapy. Includes a Browse Index of available terms from which you may select.

Population No.

A numeric field which searches the population number. Type a number. Operators: From, From ... To ...; no wildcards. Examples: From 10000; From

451 to 452.

Journal or Congress

A Yes/No field which searches for studies where the source is Journal or Congress. Yes and No are the only values permitted in this field. Type Y for yes; type N for no.

Available Since

A numeric field which searches the date the record was made available. Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

The table below summarizes the search fields available for Clinical Studies:

Search Field	Field Type	Additional Details
Condition	Controlled Text	Browse (alphabetical/ hierarchical)
Study Design	Controlled Text	Browse (alphabetical)
Study	Free Text	Enclose adjacent words in double quotes. Operators: AND, OR, NOT, *, ?
Intervention Type	Controlled Text	Browse (alphabetical)
Population No.	Numeric	Operators: From, From ... To ... ; no wildcards
Journal or Congress	YES/NO	Yes and No are the only values; type Y for yes, N for no.
Available Since	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards

DISEASE BRIEFINGS

Found on the Disease Briefings Advanced Search only. Includes the following choice of fields:

- Disease Briefing
- Text
- Available Since
- Last Updated

Disease Briefing
A controlled text field which searches the disease briefing, e.g. Asthma, Multiple Sclerosis, Diabetes.

Text
A free text field which searches the Disease Briefings text. Type one or more words. Enclose adjacent words in double quotation marks. Operators: AND, OR, NOT, *, ?. Examples: hypertension; hypertens*, hypertension and "congestive heart failure".

Available Since
A numeric field which searches the date the record was last updated. Format is YYYYMMDD; operators are: From, From ... To ...; use of wildcards is not permitted. Examples: 19971201; From 19980101; From 19980101 to 19980131.

Last Updated
A numeric field which searches the date the record was made available. Format is YYYYMMDD; operators are: From, From ... To ...; use of wildcards is not permitted. Examples: 19971201; From 19980101; From 19980101 to 19980131.

The table below summarizes the search fields available for Disease Briefings:

Search Field	Field Type	Additional Details
Disease Briefing	Controlled Text	Browse (alphabetical)
Text	Free Text	Enclose adjacent words in double quotes. Operators: AND, OR, NOT, *, ?
Available Since	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards
Last Updated	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards

COMPANIES & RESEARCH INSTITUTIONS

Found on the Companies & Research Institutions Advanced Search only. Includes the following choice of fields:

- Organization Name
- Organization (+ Related Orgs.)
- Headquarters (Country)
- Main Activity
- Product Economic Data
  – Product Annual Sales
  – Drug Name
  – Year
  – Geographic Area
- Company Economic Data
  – Number of Employees
  – R&D (% of Sales)
  – Total Sales
  – Total Revenues
  – Total Sales/Revenues
  – Year
- Last Updated
- Available Since

Organization Name

An indexed field which searches the organization(s) – the names of companies, institutes, universities and other entities related to the product. Includes a Browse Index of available terms from which you may select. Examples: Bayer, GlaxoSmithKline, Indiana State University, King's College London.

Organization (+ Related Orgs.)

An indexed field which searches the organization plus any related organization(s). For example, a search for Roche will also retrieve Genentech, Chugai, etc. Includes a Browse Index of available terms from which you may select. Examples: Daiichi Sankyo, Genentech, Oklahoma State University, Sanofi-Aventis.

Headquarters (Country)

A controlled text field which searches the country of the organization's headquarters, e.g. India, Japan, United States. Includes a Browse Index of available terms from which you may select.

Main Activity

A controlled text field which searches the main activity of the organization, e.g. Pharmaceuticals, Generics, Nanotechnology. Includes a Browse Index of available terms from which you may select.

Product Economic Data

There are four available choices for Product Economic Data: Product Annual Sales, Drug Name, Year, and Geographic Area.

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Product Economic Data – Product Annual Sales
A numeric field which searches product annual sales within the product economic data. Type a number. Figures are in millions (M; e.g., a search on "From 1 to 2" means from 1 million to 2 million). Operators: From, From … To …; no wildcards. Examples: From 2300; From 2300 to 3000.

Product Economic Data – Drug Name
An indexed field which searches the drug name within the product economic data, e.g. (S)-Citalopram, Ibuprofen, Naproxen. Includes a Browse Index of available terms from which you may select.

Product Economic Data – Year
A numeric field which searches the year within the product economic data. Type a year in YYYY format. Operators: OR, From, From … To …; no wildcards. Examples: 1999; From 1999; From 1999 to 2000.

Product Economic Data – Geographic Area
A controlled text field which searches the geographic area within the product economic data, e.g. Asia, Canada, Worldwide. Includes a Browse Index of available terms from which you may select.

Company Economic Data
There are six available choices for Company Economic Data: Number of Employees, R&D (% of Sales), Total Sales, Total Revenues, Total Sales/Revenues, and Year.

Company Economic Data – Number of Employees
A numeric field which searches the number of employees within the company economic data. Type a number. Operators: From, From … To …; no wildcards. Examples: From 100; From 100 to 200.

Company Economic Data – R&D (% of Sales)
A numeric field which searches R&D (% of Sales) within the company economic data. Type a number between 0 and 100. Operators: From, From … To …; no wildcards. Examples: From 10; From 80 to 100.

Company Economic Data – Total Sales
A numeric field which searches total sales within the company economic data. Type a number. Figures are in millions (M; e.g., a search on "From 1 to 2" means from 1 million to 2 million). Operators: From, From … To …; no wildcards. Examples: From 2300; From 2300 to 3000.

Company Economic Data – Total Revenues
A numeric field which searches total revenues within the company economic data. Type a number. Figures are in millions (M; e.g., a search on "From 1 to 2" means from 1 million to 2 million). Operators: From, From … To …; no wildcards. Examples: From 2300; From 2300 to 3000.

Company Economic Data – Total Sales/Revenues
A numeric field which searches total sales/revenues within the company economic data. Type a number. Figures are in millions (M; e.g., a search on "From 1 to 2" means from 1 million to 2 million). Operators: From, From … To

...; no wildcards. Examples: From 2300; From 2300 to 3000.

Company Economic Data – Year
A numeric field which searches the year within the company economic data. Type a year in YYYY format. Operators: OR, From, From ... To ...; no wildcards. Examples: 1999; From 1999; From 1999 to 2000.

Last Updated
A numeric field which searches the date the record was last updated. Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

Available Since
A numeric field which searches the date the record was made available. Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

The table below summarizes the search fields available for Companies & Research Institutions:

Search Field	Field Type	Additional Details
Organization Name	Indexed Field	Browse (alphabetical)
Organization (+ Related Orgs.)	Indexed Field	Browse (alphabetical)
Headquarters (Country)	Controlled Text	Browse (alphabetical)
Main Activity	Controlled Text	Browse (alphabetical)
Product Economic Data – Product Annual Sales	Numeric	Figures in millions (M; i.e. "From 1 to 2" means from 1 to 2 million); operators: From, From ... To ... ; no wildcards
Product Economic Data – Drug Name	Indexed Field	Browse (alphabetical)
Product Economic Data – Year	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards
Product Economic Data – Geographic Area	Controlled Text	Browse (alphabetical)

Search fields available for Companies & Research Institutions continued...

Search Field	Field Type	Additional Details
Company Economic Data – Number of Employees	Numeric	Operators; From, From ... To ... ; no wildcards
Company Economic Data – R&D (% of Sales)	Numeric	Number between 0 and 100; operators; From, From ... To ... ; no wildcards
Company Economic Data – Total Sales	Numeric	Figures in millions (M; i.e. "From 1 to 2" means from 1 to 2 million); operators: From, From ... To ... ; no wildcards
Company Economic Data – Total Revenues	Numeric	Figures in millions (M; i.e. "From 1 to 2" means from 1 to 2 million); operators: From, From ... To ... ; no wildcards
Company Economic Data – Total Sales/Revenues	Numeric	Figures in millions (M; i.e. "From 1 to 2" means from 1 to 2 million); operators: From, From ... To ... ; no wildcards

Search Field	Field Type	Additional Details
Company Economic Data – Year	Numeric (date)	YYYY; OR, From, From ... To...; no wildcards
Last Updated	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards
Available Since	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards

LITERATURE

Found on the Drugs & Biologics, Targets & Pathways, Genomics, Biomarkers, Organic Synthesis, Experimental Pharmacology, Pharmacokinetics/ Metabolism, Clinical Studies, and Literature Advanced Search. Includes the following choice of fields:

- Title
- Text
- Title/Text
- Author
- Source
- Year
- Volume
- Issue/Number
- News Date
- Congress
  - Source
  - Year
  - Congress Edition
  - City
  - Country
- Last Updated
- Available Since

Title
A free text field which searches the title associated with the reference. Type one or more words. Enclose adjacent words in double quotation marks. Operators: AND, OR, NOT, *. ?. Examples: hypertension; hypertens*, hypertension and "congestive heart failure".

Text
A free text field which searches any text associated with the reference. Type one or more words. Enclose adjacent words in double quotation marks. Operators: AND, OR, NOT, *. ?. Examples: hypertension; hypertens*, hypertension and "congestive heart failure".

Title/Text
A free text field which searches the title/text associated with the reference. Type one or more words. Enclose adjacent words in double quotation marks. Operators: AND, OR, NOT, *. ?. Examples: hypertension; hypertens*, hypertension and "congestive heart failure".

Author
An indexed field which searches the author(s) associated with the reference, e.g. Aaberg, T.M., (G)SMART Study Grp. Includes a Browse Index of available terms from which you may select.

Source
An indexed field which searches the source of the reference; available choices include periodic publications, congresses, company communications, and

books. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select.

Year
A numeric field which searches the year of the reference. Type a year in YYYY format. Operators: OR, From, From … To …; no wildcards. Examples: 1999; From 1999; From 1999 to 2000.

Volume
A numeric field which searches the volume of the reference. Type a number.

Operators: OR, NOT; *. Examples: 110; 110*.

Issue/Number
A numeric field which searches the issue/number of the reference. Type a number. Operators: OR, NOT; *. Examples: 110; 110*.

News Date
A numeric field which searches the date associated with a news story. Type a date in YYYYMMDD format. Operators: From, From … To …; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

Congress
There are five available choices for Congress: Source, Year, Congress Edition, City, and Country.

Congress – Source
An indexed field which searches the source of the congress, e.g. ACS Natl

Meet. Eur Pept Symp, Life Sci Meet. Includes a Browse Index of available terms from which you may select.

Congress – Year
A numeric field which searches the year of the congress. Type a year in YYYY format. Operators: OR, From, From … To …; no wildcards. Examples: 1999; From 1999; From 1999 to 2000.

Congress – Congress Edition
A numeric field which searches the edition of the congress. Type an ordinal number. Examples: 1st, 2nd, 3rd, 4th, 11th, 12th, 21st, 32nd, 43rd, 54th, 212th.

Congress – City
An indexed field which searches the city location of the congress, e.g. Kansas City, Nagoya, Paris. Includes a Browse Index of available terms from which you may select.

Congress – Country
An indexed field which searches the country location of the congress, e.g. China, Finland, Japan. Includes a Browse Index of available terms from which you may select.

Last Updated
A numeric field which searches the date the record was last updated. Format is YYYYMMDD; operators: From, From … To …; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

Available Since

A numeric field which searches the date the record was made available.
Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples:
19971201; From 19980101; From 19980101 to 19980131.

The table below summarizes the search fields available for Literature:

Search Field	Field Type	Additional Details
Title	Free Text	Enclose adjacent words in double quotes. Operators: AND, OR, NOT, *, ?
Text	Free Text	Enclose adjacent words in double quotes. Operators: AND, OR, NOT, *, ?
Title/Text	Free Text	Enclose adjacent words in double quotes. Operators: AND, OR, NOT, *, ?
Author	Indexed Field	Browse (alphabetical)
Source	Indexed Field	Browse (alphabetical/ hierarchical)
Year	Numeric (date)	YYYY; OR, From, From ... To... ; no wildcards
Volume	Numeric	Operators: OR, NOT, *
Issue/Number	Numeric	Operators: OR, NOT, *
News Date	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards

Search Field	Field Type	Additional Details
Congress – Source	Indexed Field	Browse (alphabetical)
Congress – Year	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards
Congress – Congress Edition	Numeric	Ordinal number; 1st, 2nd, 3rd, 4th, 11th, 12th, 43rd, 212th, etc
Congress – City	Indexed Field	Browse (alphabetical)
Congress – Country	Indexed Field	Browse (alphabetical)
Last Updated	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards
Available Since	Numeric (date)	YYYYMMDD; From, From ... To ... ; no wildcards

PATENT

Found on the Drugs & Biologics, Targets & Pathways, Genomics, Biomarkers, Organic Synthesis, Experimental Pharmacology, Companies & Research Institutions, and Patents Advanced Search. Includes the following choice of fields:

- Title
- Integrity Abstract
- Original Abstract
- Title/Abstracts
- Condition
- Subject Matter
- Applicant Data
    - Applicant Name
    - Applicant Name (+ All Related)
    - Country
    - State
    - Research Institution (Y/N)
- Inventor
- Patent
    - Patent Number
    - Publication Date
    - Expiration Date
    - Basic Patent (Y/N)
- Priority
    - Priority Data
    - Priority Date
- Last Updated
- Available Since

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Title

A free text field which searches the title associated with the patent. Type one or more words. Enclose adjacent words in double quotation marks. Operators: AND, OR, NOT, *. ?. Examples: hypertension; hypertens*, hypertension and "congestive heart failure".

Integrity Abstract

A free text field which searches the Integrity abstract. Type one or more words. Enclose adjacent words in double quotation marks. Operators: AND, OR, NOT, *. ?. Examples: hypertension; hypertens*, hypertension and "congestive heart failure".

Original Abstract

A free text field which searches the original abstract. Type one or more words. Enclose adjacent words in double quotation marks. Operators: AND, OR, NOT, *. ?. Examples: hypertension; hypertens*, hypertension and "congestive heart failure".

Title/Abstracts

A free text field which searches the title/abstracts. Type one or more words. Enclose adjacent words in double quotation marks. Operators: AND, OR, NOT, *. ?. Examples: hypertension; hypertens*, hypertension and "congestive heart failure".

Condition

A controlled text field which searches the condition or type of disorder the bioactive compound treats. Includes a Browse Index of available terms (with both Alphabetical and Hierarchical display) from which you may select. Examples: Chronic obstructive pumonary disease (COPD), Leukemia, acute myeloid, Crohn's disease, Hepatitis B.

Subject Matter

A controlled text field which searches the subject matter of the patent. Subject Matter is comprehensively populated since Jan 2005; therefore the back file may not have content for this field. Includes a Browse Index of available terms from which you may select.

Applicant Data

There are five available choices for Applicant Data: Applicant Name, Applicant Name (+ All Related), Country, State, and Research Institution.

Applicant Data – Applicant Name

An indexed field which searches applicant name within the applicant data. Includes a Browse Index of available terms from which you may select.

Applicant Data – Applicant Name (+ All Related)

An indexed field which searches applicant name (+ all related) within the applicant data. Includes a Browse Index of available terms from which you may select.

Applicant Data – Country

A controlled text field which searches country within the applicant data. Includes a Browse Index of available terms from which you may select.

Applicant Data – State
A controlled text field which searches state within the applicant data. Includes a Browse Index of available terms from which you may select.

Applicant Data – Research Institution (Y/N)
A Yes/No field which searches for the presence of a research institution within the applicant data. Yes and No are the only values permitted in this field. Type Y for yes; type N for no.

Inventor
An indexed field which searches inventors(s) associated with the patent, e.g. O'Brien, B., Waldeck, C.B. Includes a Browse Index of available terms from which you may select.

Patent
There are four available choices for Patent: Patent Number, Publication Date, Expiration Date, and Basic Patent.

Patent – Patent Number
A numeric field which searches the patent number. Type a patent number in the following format: two-letter country/source code, space, patent number. Operators: AND, OR, *, ?. Examples: EP 0726072; WO 2006004226, WO 2005*.

Patent – Publication Date
A numeric field which searches the date the patent was published. Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples:

19971201; From 19980101; From 19980101 to 19980131.

Patent – Expiration Date
A numeric field which searches the date the patent expires. Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

Patent – Basic Patent (Y/N)
A Yes/No field which searches for the presence of a basic patent. Yes and No are the only values permitted in this field. Type Y for yes; type N for no.

Priority
There are two available choices for Priority: Priority Data and Priority Date

Priority – Priority Data
A numeric field which searches the priority data. Format: four-digit year, space, two-letter country/source code, space, priority number. Operators: AND, OR, *, ?. Examples: 2004 US 773678, 2004 EP *

Priority – Priority Date
A numeric field which searches the priority date. Format is YYYYMMDD; operators are: From, From ... To ...; no wildcards. Examples: 19971201; From 19980101; From 19980101 to 19980131.

Last Updated
A numeric field which searches the date the record was last updated. Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples:

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19971201; From 19980101; From 19980101 to 19980131.

Available Since
A numeric field which searches the date the record was made available.
Format is YYYYMMDD; operators: From, From ... To ...; no wildcards. Examples:
19971201; From 19980101; From 19980101 to 19980131.

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USER GUIDE - VIEWING AND MANAGING RESULTS

RELEASE 10.1

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VIEWING AND MANAGING RESULTS

When your search strategy is complete on screen, click Start. Whenever you perform a search in *Thomson Reuters Integrity*^{SM}, or navigate through to results lists from the quick access links on the Integrity Home Page or on the left hand side of the Knowledge Area pages, the results are displayed in a table, list or record format, depending on the Knowledge Area chosen for your search and the number of records retrieved.To begin searching *Integrity*.

THE RESULTS SCREEN
The results screen is designed to enable you to manipulate and manage your search results; you can select alternative display formats and process results further using the options available via the screen menus (Options and Filter by Statistics).

- Display menu options (i.e. how your results look) include alternate display formats; e.g. Full Records, Product List with Structures, Display Milestones, Gateways to Development Status, Structure Activity, and Patent List with Structure.
- Process menu options (i.e. what you can do with your results) include Save Query, Keep me Posted, Export Center, Integrity Reports, References, Patents, All Related Information via Quick Search, and Printer Friendly Format.

Note: The display formats available depend on the Knowledge Area in which the results are found. Drugs & Biologics, for example, has Product List, Product
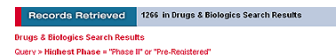
List with Structures, Full Records, Gateways to Development Status List, and Milestones List while the Literature Knowledge Area has a References List and References with Associated Text List.

- From any Knowledge Area, open the Options menu to view the full selection of display formats and to select the display format of choice.

The 'All Related Information via Quick Search' option found under the Options menu provides you with a summary of all of the Related Information links for the entire set of products displayed on screen.

- See how many records are related to the original results in each Knowledge Area and move to those records simply by clicking on the bar for the Knowledge Area of choice.

Number of Results

| Records Retrieved | 1266 in Drugs & Biologics Search Results |

Drugs & Biologics Search Results
Query » Highest Phase = "Phase II" or "Pre-Registered"

The number of results is displayed at the top of the page, together with the Knowledge Area in which the results are found. The search query is displayed below the number of records retrieved. All terms entered are preserved. For example: Query > Highest Phase = ''Phase III'' or ''Pre-Registered'' or ''Recommended Approval'' or ''Registered''

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Navigation

Depending on the display format, up to 20 results (25 in Biomarkers) may be included per page.

- Use the First, Previous, Next, Last and page number links at the top right (and at the bottom right) of the results screen to navigate forward and back through the results pages or to display to a particular page directly.
- For any results of interest, click the product or reference links in the table or list to view the individual records.
- Almost all records in *Integrity* have related records in other Knowledge Areas. Links to these related records are found at the bottom of the full records; click on the links to view associated records in other Knowledge Areas.

Selecting Records

You can check or clear records within the results list to create a subset to be displayed, filtered, or processed further using actions such as print and export.

- Use the check boxes associated with each record to check or clear

individual records.
- Use the **Check/Reset** buttons at the bottom of the results list to select multiple records; choose from Check All This Page, Check All Results, Reset All This Page, and Reset All Results.

Sorting Results

You can change the sort order of your results by clicking on the column headings in the table where available.

To display your results sorted in a different order:

- Click an underlined column heading in the results table to sort results based on the content of the column. Columns with text data are sorted in ascending alphabetical order; columns with numeric data are sorted in ascending numeric order. Please note that columns without underlined headings cannot be used to sort data.

Filter by Statistics

Integrity includes a Filter by Statistics feature that allows ranking and graphical representation of your search results. Charts are Knowledge Area specific and offer the option to refine the search or view the results grouped under the same criteria:

- **Drugs & Biologics** – Development Status, Organization, Major Therapeutic

Groups, Therapeutic Group, Major Condition Groups, Condition, Mechanistic Scope (includes Molecular Mechanisms and Cellular Mechanisms), Major Product Categories, Product Category, Launch Year, Therapeutic Impact and Organization (3D chart), Target, Under Active Development/No Development Reported, Condition and Phase (3D Chart), Filter Only Lead Compounds, Natural Source Categories, Natural Source Scientific Name, Prescription/Indication Type, Administration Route.

- **Targets & Pathways** – Target Condition, Target Mechanisms of Action, Target Type.
- **Genomics** – Condition, Organism, Genes Variation Type, Variant Condition.
- **Biomarkers** – Indication, Condition, Role, Population, Validity, Type, Biological Process, Technique, Substrate, Scientific Authority, Organization, Kit, Country + Country Group, Regulatory Authority.
- **Organic Synthesis** – Drug Name, Development Status, Organization, Major Therapeutic Group, Therapeutic Group, Major Condition, Condition, Mechanistic Scope (includes Molecular Mechanisms and Cellular Mechanisms), Under Active Development/No Development Reported, Natural Product Y/N.
- **Experimental Pharmacology** – Pharmacological Activity, Parameter, Material, Method, Reference Type, Product in Studies, Drug Mechanism of Action.
- **Pharmacokinetics/Metabolism** – Administered Product, Measured Product, Formulation, Administration Route, Model, Measured Compartment, Parameter, Study Condition, Analytical Method, Interacting

Agents, Studies in Humans/Studies in Animals.
- **Clinical Studies** – Study Design, Population Number, Study Condition, Product in Studies, Intervention Type, Reference Publication Year.
- **Disease Briefings** – the Filter by Statistics feature is not applicable to content derived from the Disease Briefings Knowledge Area.
- **Companies & Research Institutions** – Associated Patents by Applicant/Assignee, Organization Total Sales by Year (3D chart), Organization Total Sales by Condition (3D chart), Pipeline List by Year.
- **Literature** – Source, Publication Year, Product Citation.
- **Patents** – Applicant/Assignee, Inventor, Priority Date, Applicant Country, Applicant State or Province (U.S. + Canada), Basic Patent Publication Year, Expiration Date, Subject Matter, Condition, Compound Mechanism of Action.

A visual representation of the results is presented in a bar chart (you can change to another display format from the Filter by Statistics chart page), allowing you to view a breakdown by the selected criteria and select subsets of data, export the chart results, or take a screen capture of the chart. Rollover the chart bars to reveal the exact number of results represented by each bar. Use the check boxes to the left of the bars and click View Subset to refine and navigate to a subset of results.

To display your results filtered by statistics:

1. Choose a **Filter by Statistics** option from those available to the Knowledge Area (see above).

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2. The Chart Results Page opens with the query results ranked by the selected criterion and presented as a chart. The criterion the content is ranked by and the query string that generated the results are displayed (where available).

3. Choose a Display Option: [icon] **Bar Chart**, [icon] **Column Chart**, or [icon] **Pie Chart**; click these buttons at any point to alternate between display types.

   - Bar Chart (default display option) – horizontal display (with scroll bars to scroll up and down for large sets of data).
   - Column Chart – vertical display (with scroll bars to scroll left and right for large sets of data).
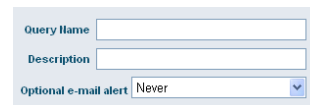   - Pie Chart.

   In three-dimensional charts (e.g. Therapeutic Impact by Organization, Condition and Phase, etc), click the 'eye' icon next to one or more rows to eliminate them from the display to better view nearby information.

4. Move your mouse pointer over a chart bar, column or pie segment to reveal the precise number of records for a particular category of information.

5. Click a chart bar, column or pie segment to display the corresponding subset results list of records.

6. Bar and column charts only. Use the check boxes to select individual chart bars or columns; alternatively, click **Check All** [icon] to select the entire chart content. Click **View Subset(s)** to display a results list containing all records from the original query indexed with the selected criteria.

7. Process your results further using the Export Options (Export to Excel and Print Chart) or use the Snapshot Tool to take a screen capture of the chart. Use Export to Excel to export the content of the filtered results set to MS Excel; specifically, this exports the ranked categories and the number of records in each of those categories into an Excel table.

8. Click **Help** to view the latest context Help on Integrity Statistics Charts.

SAVE QUERY AND EXPORT OPTIONS

Save Query

- **Save Query** – save the query that generated the Integrity results list on display.
- **Keep me Posted** – receive e-mail notification when changes occur to a record or set of records.

Your saved queries and keep me posted alerts appear listed and can be accessed via the Query Manager/Alert Center, where you can also modify or delete them.

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Export Options

Export your results using the Export Options:

- **Export Center** – access the Export Center, which displays in a pop-up; export your results to a spreadsheet (MS Excel), in word processor (MS Word) format, to BizInt or in SDFile format.
- **Printer Friendly Format** – generates a printer friendly version of the current results list in a pop-up window. Click on the print icon within the pop-up window to print out the content.
- **Integrity Report** – provides a formatted export of the document, which is generated 'off line'. This option appears listed whenever it is possible to generate a suitable *Integrity* report.

Export Center

The Export Center allows you to export selected data from *Integrity* for use in other applications. Up to 100 records can be exported at a time, either as full pages of records or as selected records (i.e. a subset selection defined using the record check boxes).

To export content from *Integrity*:

1. Select one or more records from your results to create a subset of records

for export:
- Use the check boxes associated with each record to check or clear individual records.
- Use the **Check/Reset** buttons at the bottom of the results list to select multiple records; choose from Check All This Page, Check All Results, Reset All This Page, and Reset All Results.

Note: If you do not select a subset of records first, the entire results set will be exported by default.

2. Choose **Export Center** from the Options menu.

The *Integrity* Export Center displays in a pop-up window.

3. Select the desired export format from the Export type menu; available choices are Knowledge Area specific and may include Microsoft® Excel, Word, BizInt, Endnote, Reference Manager, Refworks, SDFile and RDFile formats:
- **Excel** – export the results as an MS Excel spreadsheet.
- **Word** – export the results as an MS Word document.
- **BizInt** – export the results as a BizInt Smart chart. There are two types of chart in *Integrity*:
  - BizInt Smart Charts for Drug Pipeline from the Drugs & Biologics Knowledge Area.

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–   BizInt Smart Charts for Patents from the Patents Knowledge Area.

The *Integrity* fields are exported to the relevant fields in the BizInt charts where they can be combined with information from other sources.

BizInt is software that manages and stores pipeline information; it allows you to search and import references from online databases and CD-ROMs. BizInt also creates charts and formats records for scientific and business use.

*   **Endnote** – export the results to Endnote.
    EndNote is software that manages and stores bibliographic information; it allows you to search and import references from online databases and catalogs. EndNote also creates manuscripts and formats bibliographies for research papers.
*   **Reference Manager** – export the results to Reference Manager.
    Reference Manager is software for publishing and managing bibliographies; it offers network features with simultaneous read/write access to databases.
*   **Refworks** – export the results to RefWorks.
    Refworks is a web-based bibliographic software and database manager; it allows you to create your own personal database by importing references from text files or online databases and other various sources.
*   **SDFile** – exports the results as a Structure-data file.
*   **RDFile** – exports the results as a Reaction-data file. Similar to SDfiles

in concept, the RDFile is a more general format that can include reactions as well as molecules.

Note: Chemical structures can be exported from the Drugs & Biologics Knowledge Area in SDFile format for use in chemical structure database management programs such as CS ChemFinder™ and Symyx MDL ISIS™. They can be exported from the Patents and Experimental Pharmacology Knowledge Areas in RDFile format. Finally, they can also be exported in MS Word and Excel formats as images.

With RDFiles multiple records are associated to the same structure, whereas in an SDFile it is just the structure with its data.

4. Select the content you wish to export for each record:

    *   Use the check boxes associated with each field to check or clear individual fields.
    *   Use the **Check all/Reset all** buttons at the bottom of the field selection to check or clear all fields.

Initially, all content fields are selected by default. Available choices are Knowledge Area and display specific:

*   **Drugs & Biologics** – Entry Number, CAS Registry No., Molecular Formula, Molecular Weight, Highest Phase, Under Active Development, Chemical Name/Description, Code Name (CD), Generic Name (GN), Brand Name (BN), Drug Name (CN, GN, BN), Molecular Mechanism,

Cellular Mechanism, Product Category, Therapeutic Group, Prescription/Indication Type, Mechanism of Action, Organization, Natural Source, Condition, Development Status, Milestones Table, Product Summary, Related Basic Patent, Link to Integrity, Structure Image.

- **Targets & Pathways** – Target Name, Type, Function/Description, Links, Conditions, Related Names.
- **Genomics** – Gene Symbol, Gene Name, Synonyms, Sequence, Condition, Gene Description, Organism, Links, Protein Name, Protein Synonym, Protein Links, Protein Sequence, Gene Variation, Genomic Base Studies.
- **Biomarkers** – Name, Biological Process, Organization, Environmental Modifier, Highest Validity, Indication, Role, Technique, Scientific Authority, Milestone, Last Updated, Synonyms, Type, Description, Product Modifier, Mechanism Modifier, Methods Papers, Population, Validity, Substrate, Kit Development Status, Available Since.
- **Organic Synthesis** – Scheme Number, End Product, Intermediate Chemical Names, Reagent Chemical Names, Reagent Representations, Patents, References, Synthesis Text, Synthesis Scheme.
- **Experimental Pharmacology** – Entry Number, Drug Name, Mechanism of Action, Pharmacological Activity, Parameter, Material, Method, Operator, Means, Var, Min Value, Max Value, String Value, Unit, Source, Structure Image.
- **Pharmacokinetics/Metabolism** – Administered Products, Measured Product, Model, Parameter, String Value, Condition, Measured As, Min Value, Range, Max Value, Units, Reference, Compartment, Interacting Agent.
- **Clinical Studies** – Study, Condition, Design, Therapeutic Group, Treatment, Pop. No., Conclusions/Objectives, Reference.
- **Companies & Research Institutions** – Company Name, Website, Year, Annual Sales (M).
- **Literature** – Author (with an option for Primary Author), Title, Citation (with options for Abbreviated Journal, Volume, Issue, Page Numbers, Publication Year), Abstract, Document Type.
- **Patents** – Title, Applicant, Inventor, Patent Number, Publication Date, Priority Data, Priority Date, Expiration Date, Subject Matter, Condition, Integrity Abstract, Original Abstract, Link to Integrity Patent Record Related Lead Compounds, Main Name, Entry Number, Structure Image.

Export is not available for content from the Disease Briefings Knowledge Area.

5. Optional. Enter the page numbers for the pages that contain the records to be exported. Use commas and hyphens to indicate multiple pages and page ranges. For example, entering 1,3-5,14 without using record checkboxes exports the first 100 records from pages 1, 3, 4, 5 and 14. Leaving the box blank exports the first 100 records starting at page 1. Using record checkboxes and entering pages 25-75 exports the first 100

records checked within pages 25 to 75 (inclusive).

6. Click **Export** to initiate the process (exports the selected content in the format of your choice); click **Close** to close the *Integrity* Export Center pop-up window without exporting.

Important: Please note that use of any exported data is subject to the *Thomson Reuters Integrity*[SM] Terms of Use.

EXPORT FORMATS AVAILABILITY

The table below summarizes which export formats are available for each of the knowledge areas.

Knowledge Area	Excel	Word	BizInt	EndNote	Ref Manager	Refworks	SDFile	RDFile
Drugs & Biologics	Yes	Yes	Yes	No	No	No	Yes	No
Targets & Pathways	Yes	Yes	No	No	No	No	No	No
Genomics	Yes	Yes	No	No	No	No	No	No
Biomarkers	Yes	Yes	No	No	No	No	No	No
Organic Synthesis	Yes	Yes	No	No	No	No	No	No
Experimental Pharmacology	Yes	Yes	No	No	No	No	No	Yes
Pharmacokinetics/ Metabolism	Yes	Yes	No	No	No	No	No	No
Clinical Studies	Yes	Yes	No	No	No	No	No	No
Disease Briefings	No	No	No	No	No	No	No	No
Companies & Research Institutions	Yes	Yes	No	No	No	No	No	No
Literature	Yes	Yes	No	Yes	Yes	Yes	No	No
Patents	Yes	Yes	Yes	No	No	No	No	Yes

PRINTER FRIENDLY FORMAT

The Printer Friendly Format allows you to generate a printer friendly version of your current results list or individual records. All Knowledge Areas and all display formats have the option to display the results in a Printer Friendly Format.

To print results from *Integrity* in a report format:

1. Select one or more records from your results to create a subset of records for printing:
   * Use the check boxes associated with each record to check or clear individual records.
   * Use the **Check/Reset** buttons at the bottom of the results list to select multiple records; choose from Check All This Page, Check All Results, Reset All This Page, and Reset All Results.

Note: If you do not select a subset of records first, the entire results set will be exported by default.

To print the content of an individual record, click the product or reference link in the table or list to display the record.

2. Choose **Printer Friendly Format** from the Options menu.

Integrity displays the selected content in a pop-up window, formatted ready

for print.

3. Click **Print** 🖨 to initiate the process (prints the selected content in printer friendly format).

In the Disease Briefings Knowledge Area, click on the Printer Friendly Format icon at the top right of each page to be printed – this prints only the page currently on display. Alternatively, choose the Print Full Document option at the bottom of the Disease Briefings Chapters menu to display all sections, formatted ready for print.

Disease Briefings are dynamic executive summaries on the current status and future trends in drug therapy for specific diseases. These include background information on the disease, compounds currently used to treat it and those under study for this condition, as well as links to related information and sites.

INTEGRITY REPORTS

Selected reports that combine information from different Knowledge Areas are available, in Microsoft® Word format, via Integrity Reports. There are currently 11 different types of Reports available in *Integrity*:

Product Report – product information including recent updates, development status, milestones plus a table with the number of associated records in other Knowledge Areas for the compounds selected

Sales and Intellectual Property Report – combined product, sales and patent information for the compounds selected

Chemistry Report – product information and synthesis schemes for the compounds selected

Target Pipeline Report – basic target information with a table of related products

Organic Synthesis Report – synthesis schemes with end product, intermediate and reagent information

Experimental Pharmacology Report – table of experimental pharmacology data combined with product information for the associated compounds

Pharmacokinetics Report – table of PK data combined with product information for the associated compounds

Clinical Studies Report – clinical trial information combined with product

information for the associated compounds

Company Report – company information plus a table with the number of associated records in other Knowledge Areas for the organizations selected

Literature Report – full citation with related information from other Knowledge Areas (e.g., PK data, synthesis schemes) for the reference(s) selected

Patent Report with related information – patent information combined with information from associated product, experimental pharmacology, organic synthesis, targets, genomics and/or biomarkers records for the patent(s) selected

The Integrity Reports export appears listed in the Options menu whenever it is possible to generate a suitable report.

To generate a report from *Integrity*:

1. Select one or more records from your results to create a subset of records for report export:

   • Use the check boxes associated with each record to check or clear individual records.
   • Use the **Check/Reset** buttons at the bottom of the results list to select multiple records; choose from Check All This Page, Check All Results, Reset All This Page, and Reset All Results.
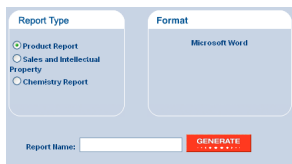
Note: If you do not select a subset of records first, the entire results set will be exported by default.

To generate a report from the content of an individual record, click the product or reference link in the table or list to display the individual record.

2. Choose **Integrity Reports** from the Options menu.

The Integrity Reports export options display in a pop-up window.

3. Choose a Report Type (options vary according to Knowledge Area):

    - **Drugs & Biologics** – Product Report, Sales and Intellectual Property, Chemistry Report
    - **Targets & Pathways** – Pipeline Report
    - **Biomarkers** – Biomarker Full Record, Biomarker References, Biomarker Genomics, Biomarker Companies
    - **Organic Synthesis** – Organic Synthesis Report

    - **Experimental Pharmacology** – Experimental Pharmacology Report
    - **Pharmacokinetics/Metabolism** – Pharmacokinetics Report
    - **Clinical Studies** – Clinical Studies Report
    - **Companies & Research Institutions** – Companies Report
    - **Literature** – Literature Report
    - **Patents Report** – Patents Report with Related Information

    The report export will be created in Microsoft® Word format. Reports are not available for content from the Genomics or Disease Briefings Knowledge Areas.

4. Enter a **Name** for the report to be saved as.

5. Click **Generate** to initiate the process (generates a report from the selected content).

    Reports are generated 'off line', and this may take some time, depending on the type of report and number of records selected.

6. Any reports you create appear listed and can be accessed via Reports (on the Integrity toolbar), where you can view the progress of a report as it is generated, download the report when it is available (opens in MS Word) and delete any reports that are no longer required.

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THOMSON REUTERS

THOMSON REUTERS INTEGRITY℠
USER GUIDE - QUERY MANAGER AND ALERT CENTER

RELEASE 10.1

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CONTENTS

QUERY MANAGER AND ALERT CENTER

The Query Manager/Alert Center allows you to view and manage your Saved Queries, Keep me Posted alerts, Controlled Vocabulary tracking and Session History.

- The **Query Manager** utility allows you to save search strategies as 'saved queries' and then re-run them in a future session. An unlimited number of queries can be saved, including queries that utilize structure searching.
- The **Alert Center** utility allows you to set up searches to be run automatically at daily, weekly and monthly intervals with notification via e-mail of new and updated information added to Integrity. It is also possible to set up an alert even if the original query did not give results.

The Query Manager/Alert Center also includes a Session History feature that tracks queries run in Integrity during the last 24 hours.
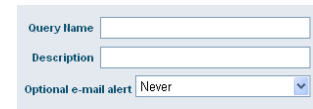
There are three types of alert: Saved Query, Keep Me Posted and Controlled Vocabulary. When new or updated results are detected in *Integrity*, you will receive notification by e-mail. Clicking a 'Follow This Link' hyperlink in the e-mail launches your browser, goes to *Integrity*, requests you to login and then displays results.

SAVED QUERY ALERTS
You can set up Saved Query Alerts to detect new records in *Integrity* (i.e., to track results that would be included if the search with the same criteria were

re-run). Saved Query Alerts can be set from the results display using the Options menu after a search is run.

1. Perform a search in Integrity, using either the Quick Search facility or Advanced Search within any of the Knowledge Areas.
2. With your results on display, choose **Save Query** from the Options menu.
3. In the Save Query pop up:

- **Query Name** – Enter a name for your query
- **Description** – Enter a description for your saved query (120 characters maximum)
- **Optional e-mail alert** – Specify the frequency with which the Saved Query Alert is run: choose to receive e-mail alerts notifying you of any new records added to *Integrity* (and which match your search criteria) Daily, Weekly (sent Saturday), Every 4 weeks (sent Sunday) or Never. The default is 'Never' in which case an alert is not set.

The Alert Set indicator within Query Manager/Alert Center indicates whether or not an alert is set:

◉ – Indicates a saved query for which an alert is set.
◯ – Indicates a saved query for which no alert is set.

4. Click **Save Query** to save the query and optionally set an e-mail alert, or click **Cancel** to close the Save Query pop up without saving.
    • The query is saved to your user account and can be accessed via the Saved Queries tab within the Query Manager/Alert Center; from here you can re-run (Execute) the Saved Query, delete it, copy it back into the search form (Edit) and modify existing or add additional search criteria and view the details.
    • Select **View Details** from the options menu for the query – the Saved Query Alert pop up opens; from here you can see the results obtained (number of records) when the query was created and when it was last performed, edit the query name or description and specify the e-mail alert frequency. Click **Apply changes** to save the current settings for query name, description, and e-mail alert frequency, or click **Cancel** to close the pop up without saving.

5. When you receive an e-mail alert notification, click the 'Follow this link' text to access the results, optionally via the *Integrity* login screen (if you are not currently logged in).
    • The e-mail notification contains two hyperlinks; click on the first link to display only new records, or click the second link to re-rerun the query and display all matching results.

You can also save queries and set up Alerts for information that has not yet entered Integrity, such as for forthcoming congresses. To do this, run your search, and then click **Save Query** when the 'No Results Found' (0 results) message appears.

ACCESSING SAVED QUERIES/SAVED QUERY ALERTS

Your saved queries appear listed and can be accessed via the Query Manager/ Alerts Center, Saved Queries tab – where you can also re-run, modify or delete them.

1. On the **Navigation Bar**, click **Query Manager/Alert Center**.
2. Select the **Saved Queries** tab to view details of your saved queries. For each entry the Alert Set indicator, Query Name, Description, Knowledge Area and Last Performed (date the query/alert was last run) are shown.
    • The Saved Queries tab is limited to showing 10 queries per page. If

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there are more than 10 then the queries list is separated into multiple pages that you can navigate between using the paging number links at the top or bottom of the display.
- Use the Filter feature at the top right of the display to filter the content; enter the desired text and click **Go**. Click **View All** to return to the full display.
3. Optional. Select **Execute**, **Delete**, **Edit**, or **View Details** from the Options menu for the desired query.
   - **Execute** – re-run the saved query to generate a new results list.
   - **Delete** – remove the saved query/alert from your user account.
   - **Edit** – copy the saved query back into the search form to modify existing or add additional search criteria (you can then re-run or save it).
   - **View Details** – display the Saved Query Alert pop up; from here you can see the results obtained (number of records) when the query was created and when it was last performed, edit the query name or description and specify the e-mail alert frequency (and whether an alert is set). Click **Apply changes** to save the current settings for query name, description and e-mail alert frequency, or click **Cancel** to close the pop up without saving.

KEEP ME POSTED ALERTS
You can set up Keep Me Posted Alerts to detect any changed or updated records in *Integrity* (i.e., to receive notification of updates to existing records). Keep Me Posted Alerts can be set from a results display at any point in time, by selecting records and using the Options menu.

1. Perform a search in *Integrity*, using either the Quick Search facility or Advanced Search within any of the Knowledge Areas; alternatively, display a results list using the quick links provided on the *Integrity* Home page.
2. Select one or more records from your results for which you wish changes to be monitored:
   - Use the check boxes associated with each record to check or clear individual records.
   - Use the **Check/Reset** buttons at the bottom of the results list to select multiple records; choose from Check All This Page, Check All Results, Reset All This Page, and Reset All Results.

CHECK ALL THIS PAGE	RESET ALL THIS PAGE
CHECK ALL RESULTS	RESET ALL RESULTS

3. With your results on display, choose **Keep Me Posted** from the Options menu.

4. In the Keep Me Posted pop up:

- **Alert Name** – Enter a name for your saved alert.
- **Description** – Enter a description for your saved Alert (120 characters maximum).
- **Changes Monitored** – Use the check boxes to select one or more criteria to monitor for changes. Available options are Knowledge Area specific:
  Drugs & Biologics – Updated Highest Phase Field, Updated 'Under Active Development' Flag, New CAS Registry Number, New Mechanism of Action, New Condition, Development Status Table Newly Available, New Milestone, New Related Reference, New/Updated Structure, New Chemical Name, New Product Name, New Therapeutic Group, New Organization, Milestone History Newly Available, New Related Patent Family.

Targets & Pathways – New Related Product, Updated Validity, New Landscape, New Condition, New signalling Pathways.
Genomics – New in Targets & Pathways, New Gene Study, New Related Literature, Updated Symbol, New Genetic Variant, New Conditions, New Related Patents
Biomarkers – New Name, New Related Reference, New Related Patent, New Related Target, New Related Organization, New Environmental Modifier, New Scientific Authority, New Review, New Use, New Related Biomarker, New Related Product, New Related Gene, New Product Modifier, New Mechanism Modifier, New Methods Paper, Highest Validity Change
Literature – New Text, New Related Target, New Related Product
Patents – New Prous Science Abstract, New Condition, New Related Target, New Equivalent Patent, New Related Product, New/Updated Subject Matter

Keep Me Posted Alerts are not available for content from the Organic Synthesis, Experimental Pharmacology, Pharmacokinetics/Metabolism, Clinical Studies or Companies & Research Institutions Knowledge Areas.

- **Optional e-mail alert** – Specify the frequency with which the Keep Me Posted Alert is run: choose to receive e-mail alerts notifying you of any new records added to *Integrity* (and which match your search criteria) Daily, Weekly (sent Saturday), Every 4 weeks (sent Sunday) or Never.

The default is 'Never' in which case an alert is not set.
The Alert Set indicator within Query Manager/Alert Center indicates whether or not an alert is set:

◉ – Indicates a saved query for which an alert is set.
○ – Indicates a saved query for which no alert is set.

5. Click **Create Alert** to save the query and optionally set an e-mail alert, or click **Cancel** to close the Keep Me Posted pop up without saving.
   • The query string (record identifiers and criteria to be monitored) is saved to your user account and can be accessed via the Keep Me Posted tab within the Query Manager/Alert Center; from here you can display the set of records on which the Alert is established (Execute), delete it and view the details.
   • Select **View Details** from the options menu for the alert – the Keep Me Posted pop up opens; from here you can see the Knowledge Area and the records monitored, when the Alert was created and when it was last performed, edit the Alert name or description, specify the changes monitored and the e-mail alert frequency. Click **Apply changes** to save the current settings for Alert name, description and e-mail alert frequency, or click **Cancel** to close the pop up without saving.

6. When you receive an e-mail alert notification, click the 'Follow this link' text to access the results, optionally via the *Integrity* login screen (if you are not currently logged in).
   • The e-mail notification contains two hyperlinks; click on the first link to display only new records, or click the second link to re-rerun the query and display all matching results.

ACCESSING KEEP ME POSTED ALERTS

Your Keep Me Posted Alerts appear listed and can be accessed via the Query Manager/Alerts Center, Keep Me Posted tab – where you can also re-run, modify or delete them.

1. On the **Navigation Bar**, click **Query Manager/Alert Center**.
2. Select the **Keep Me Posted** tab to view details of your Keep Me Posted Alerts. For each entry the Alert Set indicator, Query Name, Description, Knowledge Area and Last Performed (date the alert was last run) are shown.

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3. Optional. Select **Execute**, **Delete**, or **View Details** from the options menu for the desired alert.
   - **Execute** – display the set of records on which the Alert was established.
   - **Delete** – remove the Keep Me Posted Alert from your user account.
   - **View Details** – display the Keep Me Posted Alert pop up; from here you can see the Knowledge Area and the records monitored, when the Alert was created and when it was last performed, edit the Alert name or description, specify the changes monitored and the e-mail alert frequency (and whether an alert is set). Click **Apply changes** to save the current settings for Alert name, description and e-mail alert frequency, or click **Cancel** to close the pop up without saving.

CONTROLLED VOCABULARY ALERTS

You can set up Controlled Vocabulary Alerts to detect new controlled vocabulary terms for certain fields in *Integrity* (i.e., to receive notification of new mechanisms, therapeutic groups, conditions, organizations/applicants, sources (natural products), pharmacological activities and product categories appearing in the Browse Indexes). Controlled Vocabulary Alerts can be set up in Query Manager/Alert Center.

1. On the **Navigation bar**, click **Query Manager/Alert Center**.
2. Select the Controlled Vocabulary tab to view details of your Controlled Vocabulary Alerts.
3. Use the check boxes to select one or more criteria to monitor for new vocabulary. Available options include: Mechanism of Action, Therapeutic Group, Condition, Organization/Applicant, Source (Natural products), Pharmacological Activity, Product Category.

   - **Optional e-mail alert** – Specify the frequency with which the Controlled Vocabulary Alert is run: choose to receive e-mail alerts notifying you of any new vocabulary added to *Integrity* (and which match your selected criteria) Daily, Weekly (sent Saturday), Every 4 weeks (sent Sunday) or Never. The default is 'Never' in which case an alert is not set.

   The Alert Set check boxes within Query Manager/Alert Center indicate whether or not an alert is set for a Controlled Vocabulary Field; initially, none of the check boxes are selected. The e-mail alert frequency applies to all of the fields selected.

4. Click **Apply changes** to save the current settings for each of the Controlled Vocabulary Fields, together with the e-mail alert frequency (if set), or click **Cancel** to reset the tab settings to the default values and start afresh.
5. When you receive an e-mail alert notification, the type of change (e.g., Mechanism of Action) and a description of what has been added are included.

SESSION HISTORY

Searches conducted during the current session and past 24 hours appear listed and can be accessed via the Session History. The Session History is available both within the Query Manager/Alert Center and as a tab on the Advanced Search. Use the Session History to retrace queries submitted and review results obtained during the past 24 hours, or to save a query not saved when it was created. You can also set up an Alert when saving the query.

1. Each time you perform a search in *Integrity*, using either the Quick Search facility or Advanced Search within any of the Knowledge Areas, the search query appears as an entry within the Session History (new entries are added from the top); queries remain available to you within the Session History for a period of 24 hours, after which they are aged off.
   • **Query Manager/Alert Center** – includes all search queries submitted during the past 24 hours, from Quick Search or Advanced Search within any of the Knowledge Areas.
   • **Advanced Search** – includes search queries submitted during the past 24 hours for the specific Knowledge Area only.

2. Use the Session History to review results from an earlier query or to save a query not saved when it was first run. You can also set up an Alert when saving the query, if desired.

   Note: If a period of 24 hours or more has elapsed since your last login, the Session History will be cleared and appear completely empty. It is therefore strongly recommended that you save any queries you may require at a later date during the current session in order to prevent accidental loss of search strategies that might be of use to you. Any queries you save can be deleted at any point if they are no longer required, using the options menu on the Saved Queries tab.

3. Optional. Select **Save Query** from the options menu for the desired query/ search strategy.

4. In the Save Query pop up:

   • **Query Name** – Enter a name for your saved query.
   • **Description** – Enter a description for your saved query (120 characters maximum)
   • **Optional e-mail alert** – Specify the frequency with which the Saved Query Alert is run: choose to receive e-mail alerts notifying you of any new records added to *Integrity* (and which match your search criteria) Daily, Weekly (sent Saturday), Every 4 weeks (sent Sunday) or Never. The default is 'Never' in which case an alert is not set.

   (Please note that e-mail Alerts cannot be set for queries generated from Quick Search; they can only be set for queries generated from Advanced Search within the Knowledge Areas.)

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The Alert Set indicator within Query Manager/Alert Center indicates whether or not an alert is set.

◉ – Indicates a saved query for which an alert is set.
◯ – Indicates a saved query for which no alert is set.

5. Click **Save Query** to save the query and optionally set an e-mail alert, or click **Cancel** to close the Save Query pop up without saving.
   • The query string (record identifiers and criteria to be monitored) is saved to your user account and can be accessed via the Saved Queries tab within the Query Manager/Alert Center; from here you can display the set of records on which the Alert is established (Execute), delete it and view the details.
   • Select **View Details** from the options menu for the alert – the Saved Queries Alert pop up opens; from here you can see the Knowledge Area and the records monitored, when the Alert was created and when it was last performed, edit the Alert name or description, specify the changes monitored and the e-mail alert frequency. Click **Apply changes** to save the current settings for Alert name, description and e-mail alert frequency, or click **Cancel** to close the pop up without saving.

6. When you receive an e-mail alert notification, click the 'Follow this link' text to access the results, optionally via the Integrity login screen (if you are not currently logged in).
   • The e-mail notification contains two hyperlinks; click on the first link to display only new records, or click the second link to re-rerun the query and display all matching results.

ACCESSING PREVIOUS SEARCHES VIA SESSION HISTORY

Your searches conducted during the current session and past 24 hours appear listed and can be accessed via the Query Manager/Alerts Center (or Advanced Search), Session History tab – where you can also re-run, modify or save them.

1. On the **Navigation bar**, click **Query Manager/Alert Center**.
2. Select the Session History tab to view details of queries run in *Integrity* during the last 24 hours. For each entry the Knowledge Area, Query Conditions, Last Performed (date the query was last run), and Results are shown.
   • The Session History tab is limited to showing 10 queries per page. If

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there are more than 10 then the queries list is separated into multiple pages that you can navigate between using the paging number links at the top or bottom of the display.

3. Optional. Select **Re-execute**, **Edit**, or **Save Query** from the options menu for the desired query.
   - **Re-execute** – re-run a previous search query to generate a new results list.
   - **Edit** – copy a previous search strategy back into the search form to modify existing or add additional search criteria (you can then re-run or save it).
   - **Save Query** – save a previous query for future use and (optionally) set the search as an e-mail alert. (e-mail Alerts cannot be set for queries generated from Quick Search; they can only be set for queries generated from Advanced Search within the Knowledge Areas.)

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USER GUIDE - INTEGRITY REPORTS

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INTEGRITY REPORTS

Selected reports that combine information from different Knowledge Areas are available, in Microsoft® Word Format, via Integrity Reports. There are currently 11 different types of Reports available in *Integrity*:

Product Report – product information including recent updates, development status, milestones plus a table with the number of associated records in other Knowledge Areas for the compounds selected.

Sales & Intellectual Property Report – combined product, sales and patent information for the compounds selected.

Chemistry Report – product information and synthesis schemes for the compounds selected.

Target Pipeline Report – basic target information with a table of related products.

Organic Synthesis Report – synthesis schemes with end product, intermediate and reagent information.

Experimental Pharmacology Report – table of experimental pharmacology data combined with product information for the associated products.

Pharmacokinetics Report – table of PK data combined with product information for the associated compounds.

Clinical Studies Report – clinical trial information combined with product information for the associated compounds.

Company Report – company information plus a table with the number of associated records in other Knowledge Areas for the organizations selected.

Literature Report – full citation with related information from other Knowledge Areas (e.g., PK data, synthesis schemes) for the reference(s) selected.

Patent Report with related information – patent information combined with information from associated product, experimental pharmacology, organic synthesis, targets, genomics and/or biomarkers records for the patent(s) selected.

The Integrity Reports export appears listed in the Options menu whenever it is possible to generate a suitable report.

SAVED REPORTS
Reports generated in *Integrity* appear listed and can be accessed via the Reports screen. This includes updates on the progress of any reports that are currently being generated and access to completed reports for download.

1. Perform a search in *Integrity*, using either the Quick Search facility or Advanced Search within any of the Knowledge Areas; alternatively, display a results list using the Gateways to Clinical Trials Quick Link on the *Integrity* Home page.
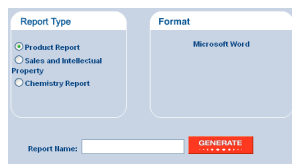
2. With your results on display, select one or more records from your results to create a subset of records for export:
    *   Use the check boxes associated with each record to check or clear individual records.
    *   Use the **Check/Reset** buttons at the bottom of the results list to select multiple records; choose from Check All This Page, Check All Results, Reset All This Page, and Reset All Results.

Note: If you do not select a subset of records first, the entire results set will be exported by default.

To generate a report from the content of an individual record, click the product or reference link in the table or list to display the individual record.

3. Choose **Integrity Reports** from the Options menu.

The Reports export options display in a pop-up window.

4. Choose a Report Type (options vary according to Knowledge Area):
    *   **Drugs & Biologics** – Product Report, Sales and Intellectual Property, Chemistry Report
    *   **Targets & Pathways** – Pipeline Report
    *   **Biomarkers** – Biomarker Full Record, Biomarker References, Biomarker Genomics, Biomarker Companies
    *   **Organic Synthesis** – Organic Synthesis Report
    *   **Experimental Pharmacology** – Experimental Pharmacology Report
    *   **Pharmacokinetics/Metabolism** – Pharmacokinetics Report
    *   **Clinical Studies** – Clinical Studies Report
    *   **Companies & Research Institutions** – Companies Report
    *   **Literature** – Literature Report
    *   **Patents Report** – Patents Report with Related Information

    The report export will be created in Microsoft® Word format. Reports are not available for content from the Genomics or Disease Briefings Knowledge Areas.

5. Enter a **Name** for the report to be saved as.

6. Click **Generate** to initiate the process (generates a report from the selected content).

    Reports are generated 'off line', and this may take some time, depending on the number of records selected.

7. Optional. Any reports you create appear listed and can be accessed via

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Reports (on the Integrity toolbar), where you can view the progress of a report as it is generated, download the report when it is available (opens in MS Word) and delete any reports that are no longer required.

ACCESSING SAVED REPORTS

Report Status

Status and details of recently generated reports. To generate a new report, obtain search results in the Knowledge Area of interest and then use the Options pull-down menu to select Integrity Reports.

Knowledge Area	Report Type	Report Name	Date	Download
Drugs & Biologics	Product Report	Celecoxib	31 Aug, 2010	Word

Any reports you create appear listed and can be accessed via the Reports screen, where you can view the progress of a report as it is generated, download the report when it is available (opens in MS Word) and delete any reports that are no longer required.

1. On the **Integrity toolbar**, click **Reports**.

   The Reports pop up shows the status and details of recently generated reports. For each entry the Knowledge Area, Report Type, Report Name, Date (the report was requested) and Download and Delete options are included.

   • Saved Reports is limited to showing 10 queries per page. If there are more than 10 then the queries list is separated into multiple pages that you can navigate between using the paging number links at the top right of the display.

2. Optional. Select **Download** (click the Word hyperlink), or **Delete** 🗑 for the desired report.
   • **Download** – when a report is available, opens the report in MS Word.
   • **Delete** – removes the report from your user account. If the report generation is still in progress, then the process is cancelled and any information processed is discarded.

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