

Global Substance Registration System (GSRS)

User Guide

GSRS User Guide (v3.x)

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Introduction

This is a guide explaining how to browse, search, and register a new substance (Chemical, Protein, Nucleic Acid, Polymer, Structurally diverse, mixture and concept) in GSRS. This document contains screen shots from GSRS version 3.x. The chemical and protein registration processes are given in detail and some parts of other substance types refer to these details.

The substance type should be identified, and the correct registration form should be used.

GSRS system has registration forms for:

1. Chemical
2. Protein
3. Nucleic Acid
4. Polymer
5. Structurally Diverse
6. Mixture
7. Concept
8. Group 1 Specified Substance – will be covered in a future version

Homepage

General Homepage Navigation

1. The blue menu bar also known as the Navigation Pane is accessible from all pages of GSRS, it includes the following:
 - a. Menu “hamburger” expands the menu in order to access the features that are also listed in the Quick Links panel on the left

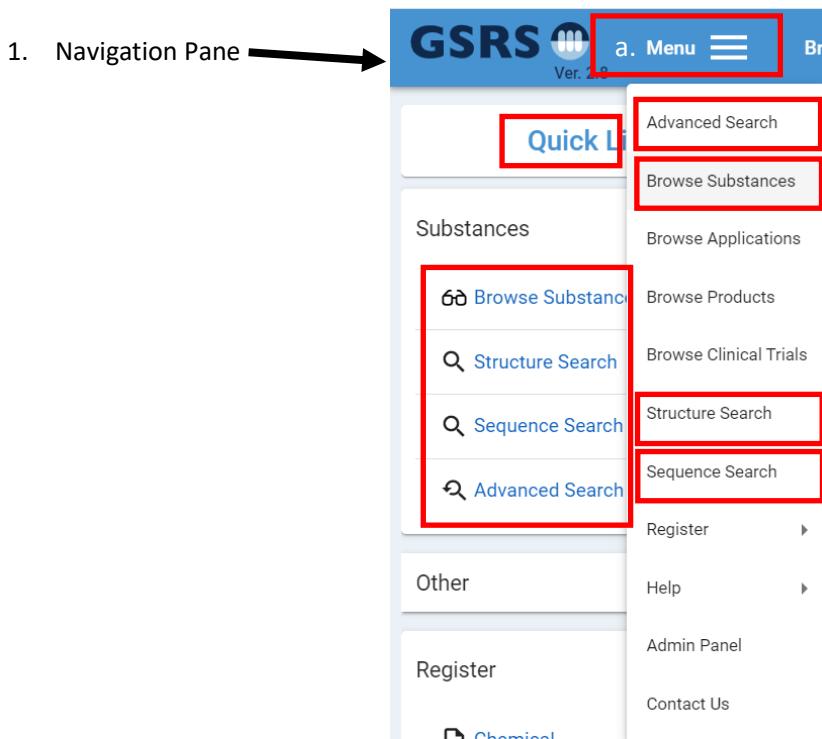


Figure 1: Navigation Pane, Quick Links, and Hamburger Menu

- b. Browse Substances (discussed in detail below)

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- c. Browse Other which is based on your GSRS instance implementation of additional non-substance modules
- d. Register (discussed in detail below)
- e. Advanced Search (discussed in detail below)
- f. Search Substances, often referred to as global search, which allows you to enter free-text and search across all substance types at once
- g. Login which is based on your GSRS instance and may be hidden if your agency is using single sign-on



Figure 2: Navigation Pane

2. The announcement may be displayed or hidden based on the GSRS instance's configuration
3. In the center pane are options for features which are also accessible from the menu
 - a. Under the Total Substances is a break-down with quick link to the browse page, for total substances for each substance type
 - b. Below the total substances quick links, are Helpful Resources which are publicly available to support users of GSRS

2. Announcement (Insert Text Here)

Global Substance Registration System - GSRS

The main goal of the GSRS software is to assist agencies in registering and documenting information about substances found in medicines. The Global Ingredient Archival System provides a common identifier for all of the substances used in medicinal products, utilizing a consistent definition of substances globally, including active substances under clinical investigation, consistent with the ISO 11238 standard.

Search Substances

3. [Browse Substances](#) [Browse Applications](#) [Structure Search](#) [Sequence Search](#)

a. All substances: 126,046

Chemicals	82,352	Polymer	2,252	Structurally Diverse Concepts	26,254
Proteins	5,321	Nucleic Acids	329	Concepts	6,666

b. Helpful Resources

[GSRSFind Excel tools](#)

GSRSFind is an add-in for Microsoft Excel that gives a user access to data in GSRS for both search/browse and creation/modification purposes. (Note: write access requires valid credentials!) GSRSFind can augment an existing spreadsheet with data from GSRS. For example, you can add chemical structures to a column of names or identifiers.

[User Registration Guide](#)

Introduction

This is a guide explaining how to register a new substance (Chemical, Protein, Nucleic Acid, Polymer, Structurally diverse, mixture and concept) in GSRS. This document contains screen shots from GSRS version 2.3.7. The chemical and protein registration processes are given in detail and some parts of other substance types refer to these details.

The substance type should be identified, and the correct registration form should be used. GSRS system has registration forms for:

1. Chemical
2. Protein
3. Nucleic Acid
4. Polymer
5. Structurally Diverse
6. Mixture
7. Concept
8. Group 1 Specified Substance - will be covered in a future version

Chemicals

Chemical is a small molecule and single entity. The first step of any registration should be duplicate check. Each substance is unique in GSRS.

Check for Duplicates

There are several options to check for duplicates (using all will ensure an exhaustive search):

- Search by name/code (CAS RN or another identifiers) using:
 - Advanced Search (FDA Only)
 - Query Builder
- Structure search:
 - Flex search - insensitive to stereo, salt and isotope
 - Similarity Search - If nothing comes up, do 90-95% similarity search

The GSRS user registration guide is comprehensive set of instructions for registering new substances of all types in GSRS.

Figure 3-Homepage Center Pane

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Registration Page Access Navigation Options

1. There are several options for selecting the substance registration page.
 - a. Select a substance type under Register in the Quick Links section of the Left Nav
 - b. Select the Menu hamburger and scroll down to Register and select the type of substance you want to register

The screenshot shows the Global Substance Registration System (GSRS) homepage. On the left, there is a vertical navigation pane with a 'Quick Links' section containing 'Substances' and 'Other' categories. Under 'Other', item 'a. Register' is highlighted with a red box. At the top right, there is a 'Menu' button with a red box around it, which opens a dropdown menu. In the dropdown menu, the 'Register' option is also highlighted with a red box. The main content area displays a banner message 'announcement test' and a search bar. Below the search bar are four buttons: 'Browse Substances', 'Browse Applications', 'Structure Search', and 'Sequence Search'. A table shows the total number of substances: 114,538, broken down by category: Chemicals (75,078), Proteins (3,619), Polymers (2,096), Nucleic Acids (176), Structurally Diverse (25,059), Concepts (6,005). At the bottom, there is a 'Help' and 'Contact Us' link.

Figure 4-Registration Page Access Navigation Options

- c. After login the Register menu appears in the center of the navigation pane if you have the right user access.
Scroll down to select the type of substance you want to register
- d. After login the Registrars Link appears on the far right and takes you to the Registrars homepage (this may be hidden based on your user type).

The screenshot shows the same GSRS homepage as Figure 4, but after logging in. The 'Register' menu item is now located in the center of the top navigation bar, highlighted with a red box. On the far right of the top navigation bar, the 'Registrars' link is also highlighted with a red box. The rest of the interface remains the same, including the announcement banner, search bar, and substance statistics table.

Figure 5-Registration Type Access and Registrar's Page

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Registrars Page

In addition to the general homepage, users with elevated permissions will have access to the Registrars homepage and can add this to their browser bookmarks. Below is the view of the Registrars page

1. Left Search column gives option to browse or search data
2. Middle Register column allows you to select the type of substance you want to register
3. Far right column is the Registrar's Quick Links-Statistics/Quick Search pane that includes links to browse results for substances. This particular feature allows registrars to go directly into substances with a UNII in the first column or pending substances in the second column

The screenshot shows the GSRS Registrars Page with three main sections highlighted by red boxes:

- 1. Search:** Contains links for various search functions: Search GSRS, Browse Substances, Browse Applications, Browse Clinical Trials, Structure Search, Sequence Search, Advanced Search, Application, and Clinical Trial.
- 2. Register:** Contains links for registering different types of substances: Register a Substance, Chemical, Protein, Polymer, Nucleic Acid, Structurally Diverse, Concept, Mixture, Specified Substance Group 1, and Application.
- 3. Registrar's Quick Links:** Contains links for Statistics/ Quick Search, Chemicals (9), Polymers (1), Structurally Diverse (1), Proteins (2), Nucleic Acids (1), Concepts (4), SSG1 (1), Pending Chemicals (1), Pending Polymers (0), Pending Structurally Diverse (0), Pending Proteins (0), Pending Nucleic Acids (0), Pending Concepts (0), and Pending SSG1 (0).

Figure 6-Registrars Page

Browse

Browse Substance Page Components

The Browse Substances page displays a summary view of substances and is divided into three major components, as noted in red in the screenshot below:

1. Filter/Facets Pane
2. Header Section
3. Substance Results pane

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The screenshot shows the GSRS user interface. On the left is the 'Filter/Facets' pane, which includes a dropdown menu for 'Facet View' set to 'Default'. Below it are various filter categories like Record Status, Substance Type, Source Tag, etc., each with a dropdown arrow. To the right of the facets is the 'Browse Substances' area, featuring a 'Substance Results' pane containing a single record for 'test protein name 1' (PROTEIN). The header section at the top right displays sorting information ('Sort By Newest Change'), export options, and pagination ('Items per page: 10 | 1 - 10 of 114553'). A vertical sidebar on the far right lists facet categories: Record Data, User Data, CMC Data, and Medical Data.

Figure 7-Filter/Facets and Substance Home Page Labeling

Filter/Facets (Filters) Pane

The filter view pane is located on the far left of the dashboard. The filter will show “default” until you select the down arrow to view the options by data type. Once the filter view is selected, the items on the facet will dynamically be available for selection for the data type criteria. Expand using the down arrow/caret highlighted above. The user can see the number of substance records stored in the GSRS database that match the filter criteria to the right.

This screenshot shows the 'Search Code System' facet expanded. It lists various code systems with checkboxes: RNCAS2 (unchecked), PUBCHEM (checked), EPA CompTox (unchecked), ECHA (EC/EINECS) (unchecked), WIKIPEDIA (checked), MERCK INDEX (unchecked), EVMPD (unchecked), NCI THESAURUS (unchecked), ChEMBL (unchecked), and NCBI TAXONOMY (unchecked). A red box highlights the 'More...' link and the 'advanced options' link below it. At the bottom are 'All Match' and 'Clear' buttons, with 'Apply' highlighted in a red box. To the right of the list, detailed descriptions for each facet are provided:

- Record Status: Under each filter title is a “Search [Facet name]...” box to search filter options that are not explicitly displayed. Enter text (full or partial) and search for the filter category within the filter.
- Substance Type: To the left of each filter category name is a checkbox.
- Source Tag: At the bottom of the displayed list is a link to “More...”. This will expand the filter list to display the next 20 options.
- Relationships: After making your filter selections the “All Match” option is displayed. By default, the filters are applied as “Any Match” and will return all records that match any one of the selected options. Select “All Match” to return records that match all of the selected options.
- Code System: Select “Apply” to filter substances based on the selected filters (for one or more filters at once). In this example we selected the Target->inhibitor Relationships and the PUBCHEM and WIKIPEDIA Code System facets. The applied facets are at the top of the display pane in the headers section boxed in red below and can be removed which will update the substance record results. The filtered substances are displayed in the Substance Results pane to the right in the large red box.

Filter Example:
Relationships = Target -> Inhibitor
Code System = PUBCHEM AND WIKIPEDIA

Figure 8-Filter Categories

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The screenshot shows the GSRS interface with the following components:

- Left Sidebar:** A tree view of search relationships under "Search Relationships".
 - ACTIVE MOIETY: 5023
 - BINDER->LIGAND: 483
 - TARGET->INHIBITOR:** 417 (This item is selected, indicated by a checked checkbox).
 - PARENT->CONSTITUENT ALWAYS PRESENT: 382
 - METABOLITE->PARENT: 346
 - PARENT->IMPURITY: 292
 - IMPURITY->PARENT: 247
 - TRANSPORTER->INHIBITOR: 243
 - TARGET->AGONIST: 224
 - METABOLIC ENZYME->SUBSTRATE: 181
- Header:** Three dropdown menus: "Code System: PUBCHEM", "Code System: WIKIPEDIA", and "Relationships: TARGET->INHIBITOR". A "RESET" button is also present.
- Browse Substances:** A main panel titled "Browse Substances" with a red border around it. It displays the following information for ZIDOVUDINE:
 - Names:** ZIDOVUDINE ✓, LAMIVUDINE/ZIDOVUDINE TEVA COMPONENT ZIDOVUDINE, ZIDOVUDINUM [WHO-IP LATIN], NSC-602670.
 - Codes:** RNCAS2: [30516-87-1](#), WHO-ATC: [J05AR05, J05AF01, J05AR04, J05AR01](#), EVMPD: SUB00153MIG.
 - EMA ASSESSMENT REPORTS:** [COMBIVIR \(AUTHORIZED: HIV INFECTIONS\)](#), [LAMIVUDINE/ZIDOVUDINE TEVA \(AUTHORIZED: HIV INFECTIONS\)](#).
 - FDA ORPHAN DRUG:** [8185](#).
 - Relationships:** 31.
 - Mol. Weight:** 267.2413.
 - Formula:** C₁₀H₁₃N₅O₄.
- Chemical Structure:** A small image of the Zidovudine chemical structure.
- Buttons:** Download (blue arrow), Search (magnifying glass), and Substance Hierarchy (dropdown menu).
- Page Navigation:** Items per page: 10, 1 - 10 of 417, Page: 1 of 42.
- Right Sidebar:** A red-bordered box containing the identifier 4B9XT59T7S and a link to "Insight Drugs".

Figure 9-Browse Substance Views and Results Pane

Header Features

The header for the results or browse screen displays the total number of records returned by GSRS that match the filter criteria. It also includes pagination in order to navigate to a specific page of results. The Items per page can be edited as well as the Sort By using the arrow to see the options.

The screenshot shows the GSRS interface with the following components:

- Header:** Three dropdown menus: "Code System: PUBCHEM", "Code System: WIKIPEDIA", and "Relationships: TARGET->INHIBITOR". A "RESET" button is also present.
- Browse Substances:** A main panel titled "Browse Substances" with a red border around the "Sort By" dropdown.
- Sort By:** A dropdown menu set to "Newest Change".
- Items per page:** A dropdown menu set to 10.
- Page Navigation:** 1 - 10 of 1027, Page: 1 of 103.
- Buttons:** Export (blue arrow).

Figure 10-Sort by and Browse Substance Results Quantity

Export Results

If you have logged into your user account, an Export button appears on the right. The Export button allows the user to export the substance records to one of the following formats in the red box below. If you want private records be sure to select the "Include Private Data" box.

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The screenshot shows the GSRS interface for browsing substances. At the top, there are three code system dropdowns: PUBCHEM, WIKIPEDIA, and TARGET->INHIBITOR, followed by a RESET button. Below these are sorting options: Sort By (Newest Change) and an Export button (highlighted with a red box). A dropdown menu is open next to the Export button, listing various file formats: CSV (csv) File, Codes File, Excel (xlsx) File, Json Export (gsrs) File, Legacy SRS Dictionary File, Names File, SD (sdf) File, SPL term validation (xml) File, and TSV (tab) File. A checkbox for 'Include Private Data' is also present. On the left, the substance 'ONDANSETRON' is shown with its names (ONDANSETRON, ONDANSETRON [USP-RS], ONDANSETRON [JAN], ONDANSETRON [ORANGE BOOK]), codes (BDNUMBER: 0126082AB, RNCAS2: 99614-02-5, WHO-ATC: A04AA01, EVMPD: SUB09445MIG, MESH: D017294), and relationships (13). A chemical structure of ONDANSETRON is displayed.

Figure 11-Export Options

After initiating an export, enter a filename (or accept the default date/time) and select Save.

A modal dialog titled 'Enter a Filename' appears. It contains a text input field labeled 'Filename' with the value 'export-03-05-2021_10-25-59' (highlighted with a red box) and a file extension '.xlsx'. Below the input fields are 'Cancel' and 'Save' buttons (the 'Save' button is highlighted with a red box).

Figure 12-Confirm File Name

While the download is generating, you can continue using GSRS.

A dialog box displays the status of a download named 'export-05-05-2021_14-53-49.xlsx'. The status is 'RUNNING'. It shows 'Records Processed So Far: 483' and the 'Original Query' details: Relationships: TARGET->INHIBITOR, Code System: PUBCHEM, Code System: WIKIPEDIA, Deprecated: Not Deprecated, Sort By: lastEdited - descending. A 'Running task ...' message with a '(click to cancel)' link is shown. A 'Delete' button is at the bottom right. A note at the bottom states: 'The download is preparing on the server. This dialog can be closed and the file downloaded by clicking on 'user downloads' in the user icon menu'. At the very bottom is a 'Show All Downloads' link.

Figure 13-Sample of Download generation in process

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When you are ready to access your export, select the down arrow next to your profile from the Navigation pane, and select User Downloads.

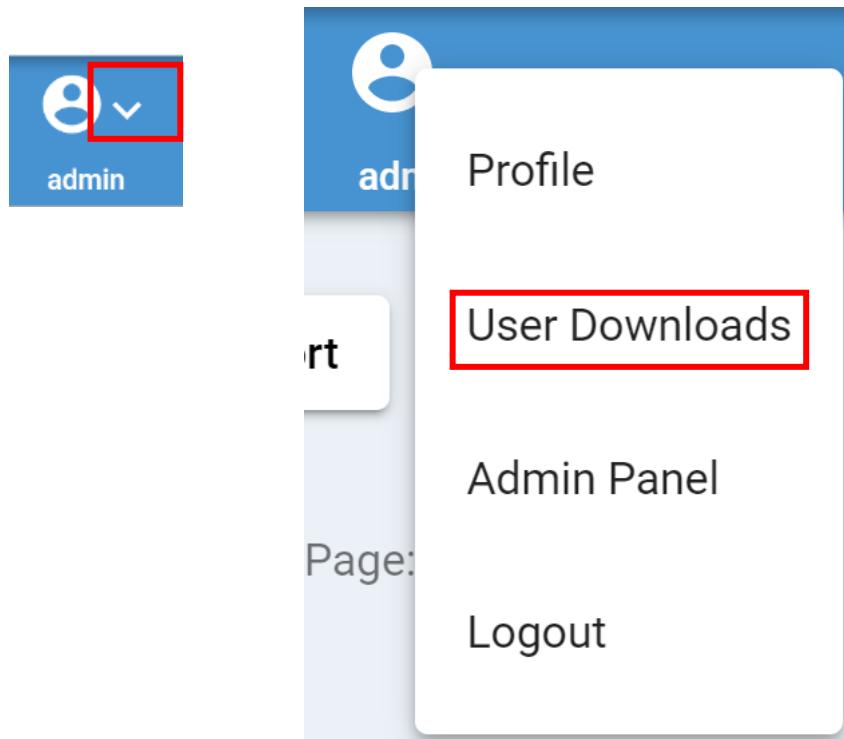


Figure 14-User Download in pulldown menu

The User Downloads page displays all downloads that your account has exported from GSRS. Select the Download button to view the results in the selected format. Select Original Query to re-open the substance records results.

A screenshot of the "User Downloads" page. It shows a single download entry for "export-05-05-2021_14-53-49.xlsx". The entry includes the following details:

- Status:** COMPLETE
- Records Processed:** 1025
- Relationships:** TARGET->INHIBITOR
- Code System:** PUBCHEM
- Code System:** WIKIPEDIA
- Deprecated:** Not Deprecated
- Sort By:** lastEdited - descending

There are three buttons at the bottom of the entry:

- A red box highlights the "Original Query" link.
- A red box highlights the "Download" button.
- A red box highlights the "Delete" button.

Figure 15-User Download Page

Browse Substance Results Pane View Options

In the header section, the user can select one of three icons to display the results pane in different views formats.



Figure 16-Browse Substance Results Pane View Options

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The middle icon is the default format for the “full view”. The left icon is the “table view” and the right icon is the “tile view”.

Results Pane Full View Default Option

The results pane is shown in the screenshot below, outlined in the red box. Here, the substance answers are displayed in the format selected. By default, the full view provides a summary for each record returned by the GSRS database, (this view will contain a high-level preview of Names, Codes, Relationships).

The screenshot shows the GSRS Results Pane Full View for Crotonic Acid. The top section displays the substance name "CROTONIC ACID" in a red-bordered box, its stereochemistry as "ACHIRAL", and its chemical structure. Below this, sections for "Names", "Codes", "Mol. Weight", and "Formula" provide detailed information. A "Substance Hierarchy" section is also present. The bottom navigation bar includes "CROTONIC ACID" and "YW5WZZ405Q". On the right side, there are links to "Inxight Drugs" and a unique identifier "YW5WZZ405Q".

Figure 17-Results Pane Full View

Additional information depending on substance type is presented in the detailed view of each substance if you select the underlined substance name. This is the display name also known as the preferred term. An example of the default full view for a chemical substance record is shown below.

The screenshot shows the GSRS Detailed View for Dalfampridine. The left sidebar lists various tabs: Overview, Products, Applications, Clinical Trials, Adverse Events, Structure, Names (23), Classification (10), Identifiers (25), Metabolites (1), Active Moiety (1), Relationships Visualization, Notes (1), Audit Info, References (46), Moieties (1), and Characteristic Attributes (2). The main content area for "DALFAMPRIDINE" (Record UNII: BH3B640KL9) includes sections for Overview (Substance Class: Chemical, Record Protection Status: Public record), Products, Applications, Clinical Trials, Adverse Events, and Structure. The Structure section shows the chemical formula CsHsNz, Molecular Weight (94.1145), Optical Activity (UNSPECIFIED), and Stereochemistry (ACHIRAL). A chemical structure diagram is shown with a central nitrogen atom bonded to two methyl groups and an amino group (NH₂). Tags for various databases like USAN, INN, ORANGE BOOK, MART, EMA EPAR, HSDB, USP-RS, WHO-DD, VANDF, MI, and VANDF are listed.

Figure 18-Detailed View of Substance

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The additional information incorporated into the detailed view of each substance type is included below:

- Chemical
 - Formula
 - Number of moieties
 - Stereochemistry
 - 2D structure
- Structurally diverse
 - Whole/Part/Full fields
- Mixture
 - Number of components
- Polymer
- Protein
 - Display structure
 - SRUs generation
- Nucleic Acid
 - Number of subunits
 - Disulfide Links
 - Glycosylation
- Sugars
- Linkages

Results Pane Table View Option

The table view of Browse Substances provides basic information which includes the substance approval ID (UNII code, if any), names, codes (e.g., CAS, WHO-ATC, EVMPD, MESH, Drug Bank.) An example of the Table View is shown below:

Name	Approval ID	Names	Codes	Actions
ONDANSETRON	4AF302ESOS	ONDANSETRON [MI]; (+/-)-2,3-DIHYDRO-9-METHYL-3-((2-METHYLLIMIDAZOL-1-YL)METHYL)CARBAZOL-4(1H)-ONE; A04AA01; ONDANSETRON [MART.]	BNUM: 0126082AB CAS: 99614-02-5 WHO-ATC: A04AA01 EVMPD: SUB09445MIG MESH: D017294	
TRIPROLIDINE	2L8T9S52QM	TRIPROLIDINE [WHO-DD]; TRIPROLIDINE; TRIPROLIDINE [MI]; TRIPROLIDINE [VANDF]	BNUM: 0126073AB CAS: 486-12-4 WHO-ATC: R06AX07 EVMPD: SUB11323MIG DRUG BANK: DB00427	
		IMMUNOGLOBULIN G2, ANTI-(HUMAN NERVE GROWTH FACTOR) (HUMAN MONOCLONAL 4D4	BNUM: 0125948AB	

Figure 19-Table View of Substances

Results Pane Tile View Option

The tile view of Browse Substances solely presents the approval ID (if any), the preferred name of the substance, and the structure (if the substance is either a chemical or a polymer). It also gives information about the substance record access. An example of the Tile View displaying several chemical substance records is shown below:

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Substance Class: chemical Substance Class: protein RESET

Browse Substances Sort By Newest Change Export

Items per page: 10 1 – 10 of 87673 | < < > > | Page: 1 of 8768

Display Match Application Names Applications ?

5743F6U086 ACHIRAL CINOQUIDOX	S1SDI2FJIY ABSOLUTE CEFPROZIL ANHYDROUS, (E):	N2161X1050 PROTEIN DEXTRANASE PENICILLIUM	MH07KB041M PROTEIN THAUMATIN II
XL8ALU0JFD PROTEIN TIAHUMATIN	5Z6C6451WY PROTEIN DADOTATIN	763UCG980J PROTEIN O 04	NI016E55WW PROTEIN COMTOPROUKINTFLUOROC

Figure 20-Tile View of Substances

Substance Actions

From the Browse results pane, frequently used substance actions are available from the icons below the structure/substance icon.

DALFAMPRIDINE BH3B640KL9

ACHIRAL Names: DALFAMPRIDINE ✓ Inxight Drugs

Codes: RNCAS2: 504-24-5 Created: 4/3/19

WHO-ATC: N07XX07 Created By: admin

EVMPD: SUB07505MIG Status: Validated (UNII)

INN: 7283 Validated By: FDA_SRS

PUBCHEM: 1727 Last Modified: 4/3/19

Relationships: 2 Last Modified By: admin

Mol. Weight: 94.1145 Version: 11

Formula: C₅H₆N₂

Substance Hierarchy DALFAMPRIDINE BH3B640KL9 (ACTIVE MOIETY)

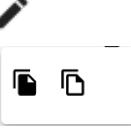
Figure 21-Browse Substances Pane Action Icons

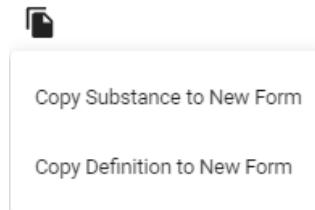
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All users are able to:

- Download 
 - Chemicals – Molfile, JSON
 - Protein – Fasta, JSON
 - Polymer – Molfile, JSON
 - Nucleic Acid – Fasta, JSON
 - Download not applicable for Structurally Diverse, Concept, Mixture, Group 1 and Group 3 Specified Substance
- Search 
 - Chemicals – transfer the structure to the Structure Search interface; there is right click option to open in new tab/window.
 - Protein – Sequence Search; select subunit Similarity Search
 - Polymer - transfer the structure to the Structure Search interface
 - Nucleic Acid - Sequence Search; select subunit Similarity Search
 - Search not applicable for Structurally Diverse, Concept, Mixture, Group 1 and Group 3 Specified Substance

For all substance types users with elevated privileges are also able to:

- Edit 
- Copy 
 - You can select Copy Substance to New Form for the whole substance record or select Copy Definition to New Form to get the definition to register a new substance



Search

GSRS supports several means for searching substances based on user-specified criteria. These are Global Search, Advanced Search, Structure Search, and Sequence Search.

1. Global Search
 - a. Name – enter name of the substance
 - b. Code (CAS RN or another identifiers): enter the numeric and/or alphabetic (numbers/letters) code
 - c. Sequence Search – copy and paste a sequence
2. Advanced Search
3. Structure Search
 - a. Reference Export Structure from Structure Search once you have confirmed your substance is new and unique
4. Sequence Search

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Global Search

Global search is a free-text search box in the top center of every page as shown in the screen shot below.

1. Type the text you are looking for. Some searches may require your text to be in quotes. You can also try adding an asterisk at the end to make it a begins with search.
2. The type-ahead feature will display the top matches for approval ID and names separated by preferred names and all other name types.
3. You can select from one of the matches from the list or use the magnifying glass for a wider search.
4. Results are presented in the display pane.
5. This search also allows for fielded, wildcard, fuzzy, group, and Boolean searches using word based [Lucene query syntax](#) (It will look for a dash or a space in the search string when doing the search.) You can also use an Inchi key as well.

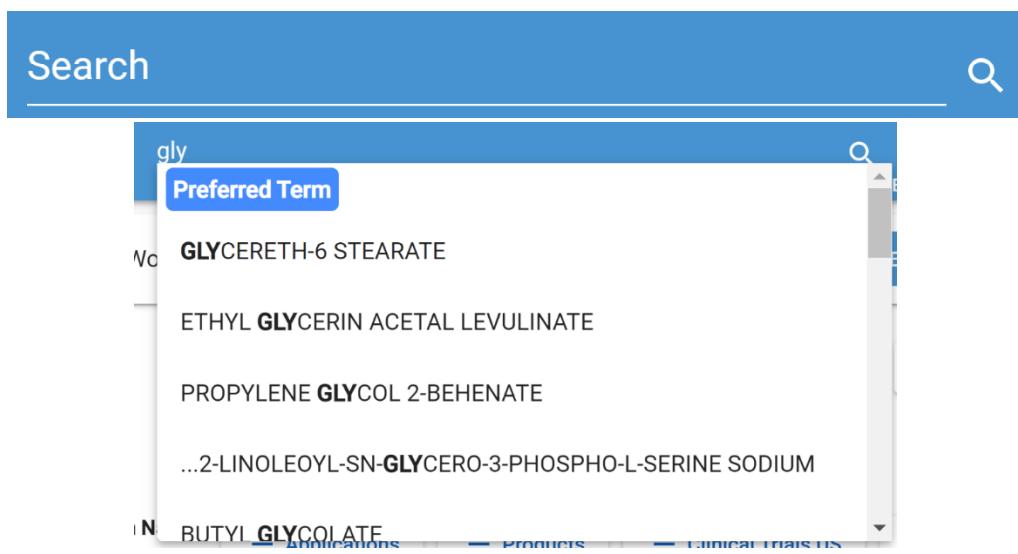


Figure 22-Global Search on Navigation Bar

Advanced Search

There are few ways to access Advanced Search:

- Next to the Global Search bar, select Advanced Search
- From the hamburger icon on the navigation pane, select Advanced Search
- From the home page Quick Links select Advanced Search

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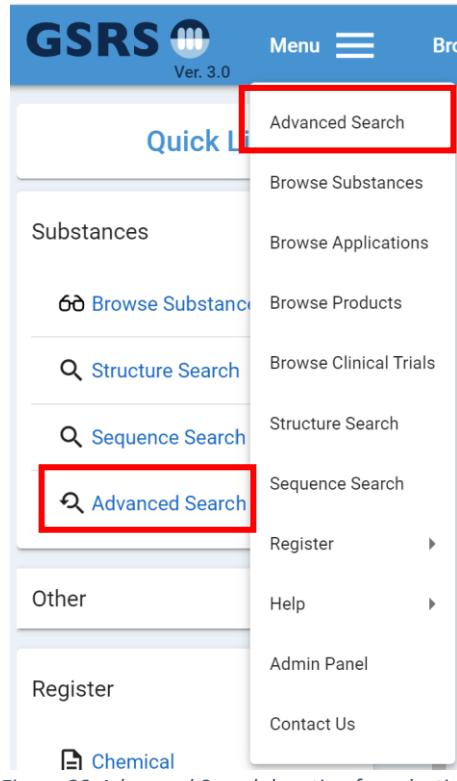


Figure 23-Advanced Search location for selection

Check for Duplicate Substances

1. To check for duplicate substances using Advanced Search make the following selections:
 - a. **Substance tab**
 - b. **Search in Fields:** Using the pulldown menu
 - c. **For:** Select Contains, Exact Match, Starts with, or Show More Options
 - d. **Enter search value**
2. Click the Search button
3. Review the results to ensure the new entry is not already represented by another

A screenshot of the 'Advanced Search' interface. At the top, tabs for 'Substance' (204,482), 'Application' (243,666), 'Product' (44,024), 'Clinical Trial' (0), and 'Adverse Event' (PT (5,470,148) DME (49,014) CVM (211,948)) are shown. Below is a search bar with 'Search in Fields' dropdown set to 'All', 'Or' dropdown, 'Contains' dropdown, and an 'Enter search value *' input field. Buttons for 'Show all fields', 'Show More Options', and 'Example: sodium' are present. A '+' button is also visible. Below the search bar is a 'Query' section with a large text input field and a 'Search' button at the bottom right. A 'Filter by Substance Facets(19)' dropdown is located below the query section.

Figure 24-Advanced Search Options

User also has the option to add additional searches to do conditional searching using AND, OR, or NOT. You can delete multiple search criteria by selecting the minus sign.

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The screenshot shows the 'Advanced Search' page. At the top, there are tabs for Substance (126,046), Application (0), Product (0), Clinical Trial (0), Adverse Event, Structure Search, and Sequence Search. A 'Search' button is located in the top right corner. Below the tabs, there are three sections for search conditions: AND, OR, and NOT. Each section has a dropdown menu for 'Condition' (AND, OR, NOT) and a dropdown menu for 'Search in Fields' (All). To the right of each section are search fields for 'Contains' with an 'Enter search value *' input field and an 'Example: sodium' placeholder. There are also 'Show More Options' and '⊖' buttons. A red box highlights the AND condition section. In the bottom right corner of the search area, there is a red-bordered '+' button.

Figure 25-Advanced Search Conditions

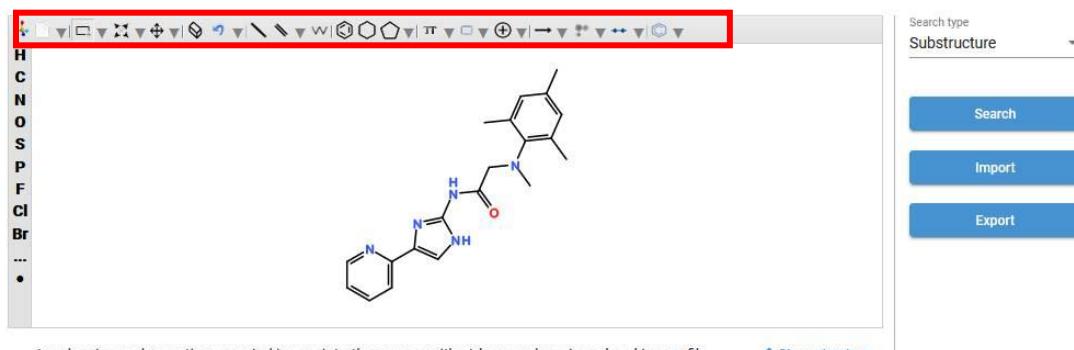
Obtaining Chemical Structures for GSRS

GSRS is a chemically aware system and can make use of chemical structure formats for searching and registration. There are many ways to import, draw or obtain a machine-readable chemical structure. The four main ways that we import structures are:

1. Draw Structure
2. Get Structure from Name
3. Load Image
4. Import Structure from Molfile or SMILES

Draw Structure

1. Use either the default web editor directly or you can import molfiles or SMILES strings from standalone chemical editors using one of the methods below.
 - a. Symyx Draw is the preferred standalone because the molfile is its native format.
 - b. Scifinder provides an option to export molfiles
 - c. Chemdraw generate structures from systematic names



Get Structure From Name

Search

Figure 26-Draw Structure

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Get Structure from Name

1. Below the canvas, enter the substance name in the search field
2. Select magnify glass

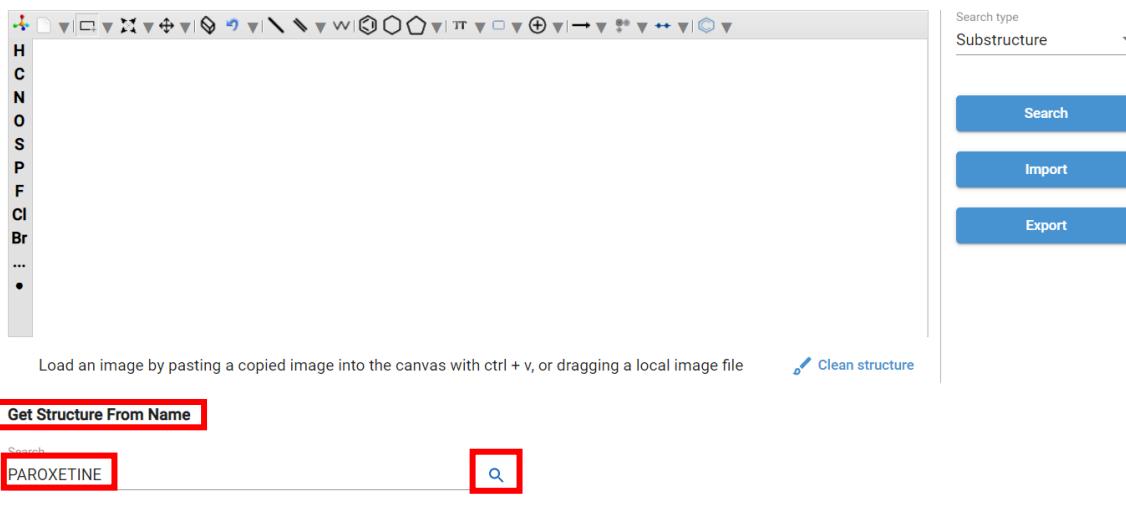


Figure 27-Get Structure from Name

3. Select one of the matching substances (this example selects the one in the red box below).
4. Select Apply Structure to populate the canvas
5. Verify the imported structure, minor adjustments may be required, use the chemical web editor toolbar to make your edits before selecting Search

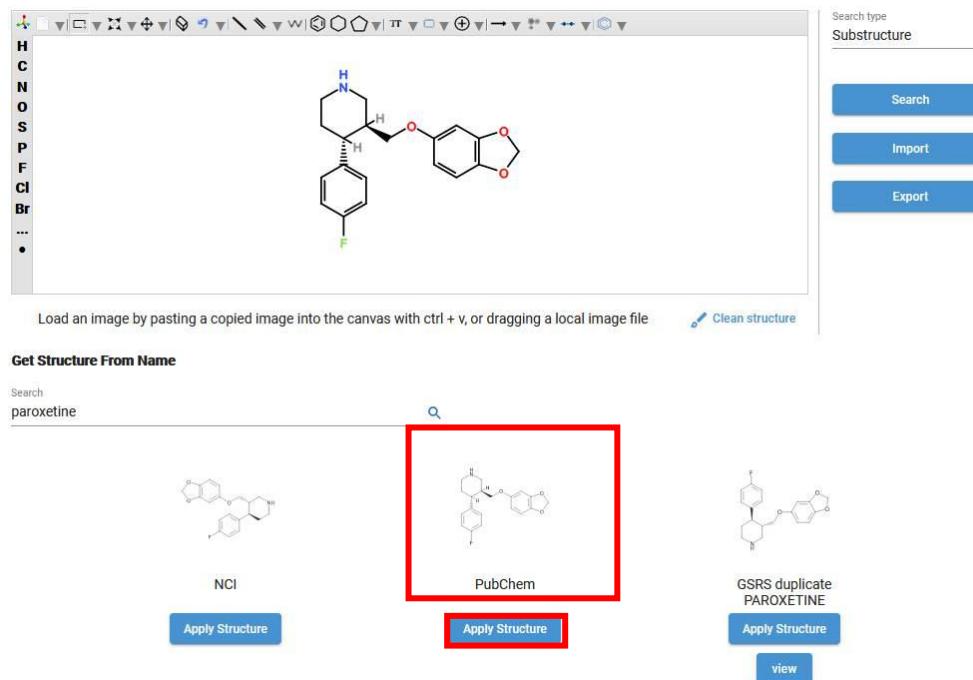


Figure 28-Apply Structure

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Load Image (via copy/paste or drag local file)

GSRS can convert images to structures when it is pasted onto the canvas

1. Copy a source image (ctrl+c) or use a snipping/screenshot tool to load the structure image into your clipboard
2. Click on canvas (canvas border will turn blue),
3. Press ctrl+v or drag a local image file
4. Verify the imported structure, minor adjustments may be required, for example in the structure shown below was not converted correctly, use the toolbar to make your edits before selecting Search

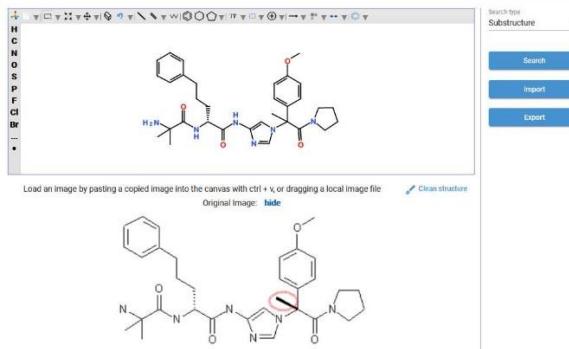


Figure 29-Load Image

Import Structure from Molfile or SMILES

1. Select Import
2. Select Browse
3. Navigate to structure location (where it's saved on your computer) and select the image name (e.g., molefile or SMILES string)

Molfile

1. Select Open and the Molfile appears
2. Select Import to display the structure on the canvas.

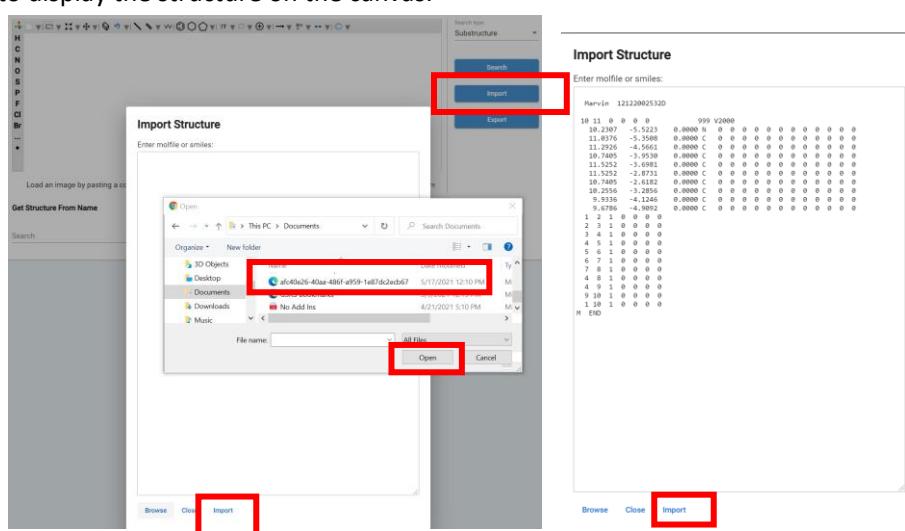


Figure 30-Enter Molfile

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- Verify the imported structure, minor adjustments may be required. Use the chemical web editor toolbar to make your edits before you use the structure.

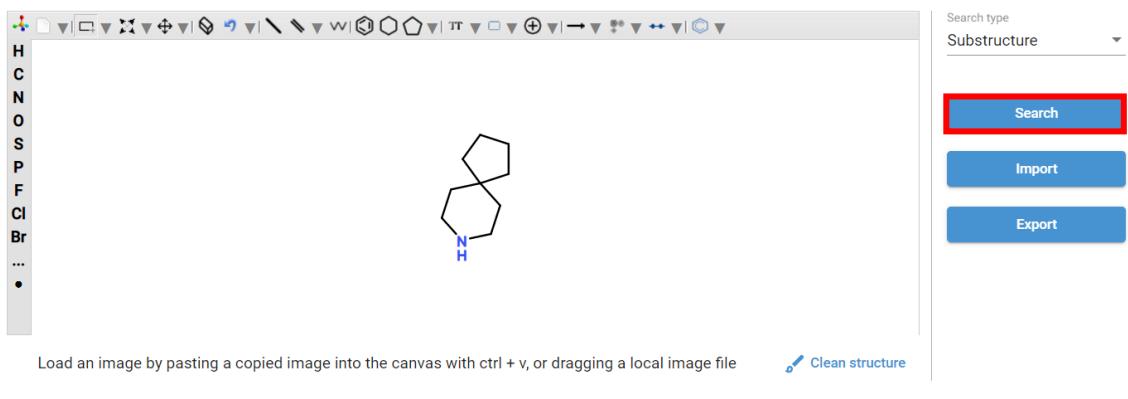


Figure 31-Search for Structure

SMILES String

- Paste the SMILES string directly into the text box and select Import

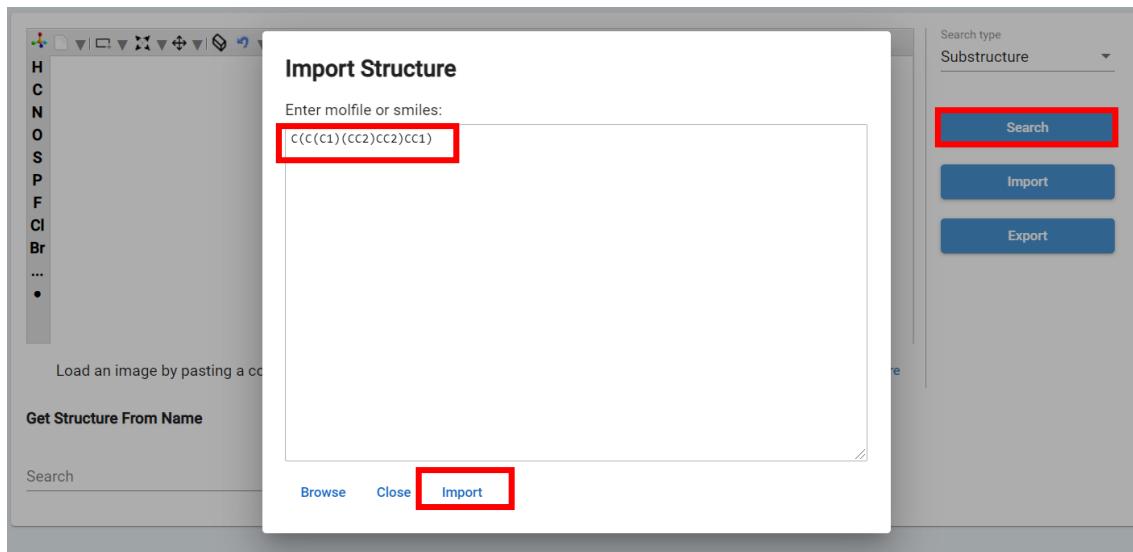


Figure 32-Enter SMILES

- Verify the imported structure, minor adjustments may be required. Use the chemical web editor toolbar to make your edits before selecting Search

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Structure Search

GSRS Structure Search is a means for searching for specific chemical and polymer records based on their two-dimensional chemical structure. The structure search is available from the home page, Quick Links or at any time from the Menu hamburger. The canvas displays the structure editor pane shown below. The canvas must have a structure in order to perform a meaningful search. You can populate the structure search canvas by obtaining a chemical structure as shown in section above.

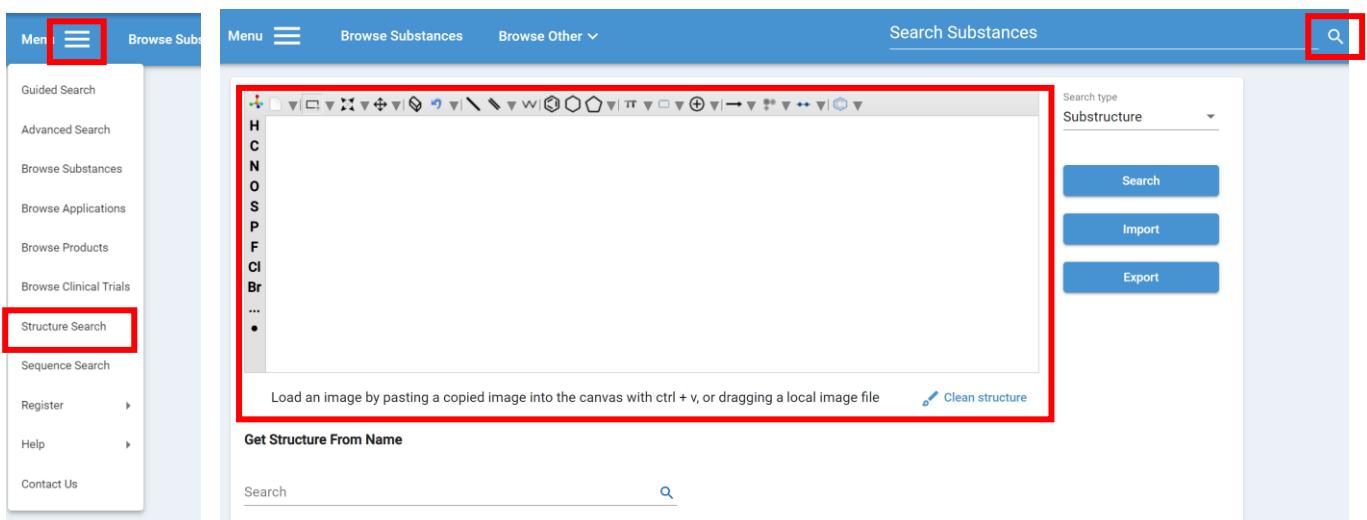


Figure 33-Structure Search

Structure Search Type Options

Note, there are four Search Type options in the upper right corner displayed to the right of the Chemical web editor plug canvas; they are:

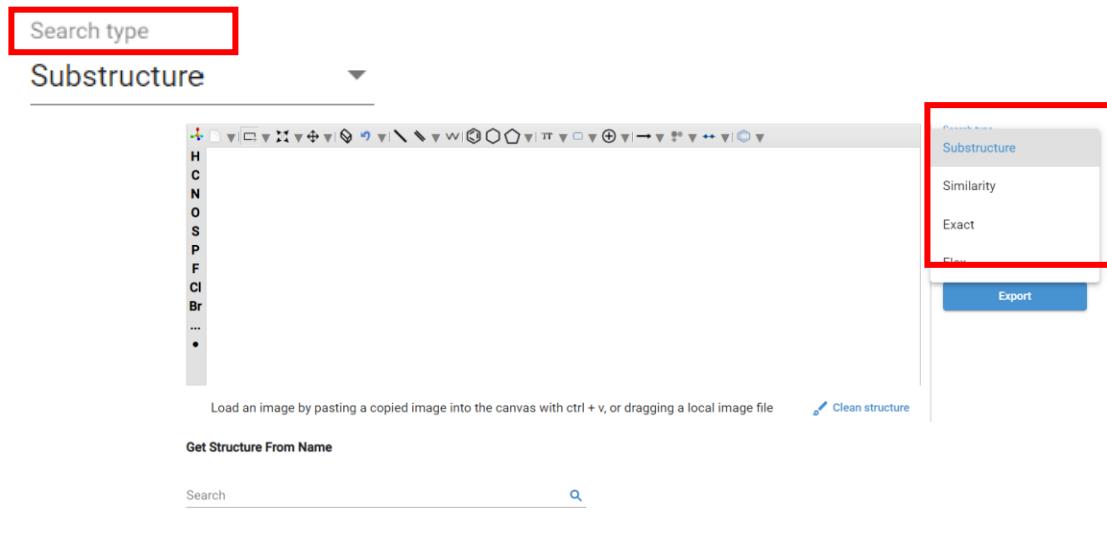


Figure 34-Search Substructure

1. **Substructure:** Find chemical structures that have an embedded query "substructure". This is like a chemical structure "contains" search. This kind of search supports query bonds and query atoms for complex structure searches. This search type is useful for finding a set of compounds that share a common "substructure" or "motif". After populating the Structure, select "Substructure" criteria and select Search as shown on the left, the search results are on the right.

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The screenshot shows the GSRS interface for a substructure search. On the left, the 'Structure Search' panel has a dropdown menu set to 'Substructure' with a red box around it. Below it are buttons for 'Add Explicit Hydrogens', 'Remove Stereochemistry Bonds', 'Search' (which is highlighted with a red box), 'Import', and 'Export'. A chemical structure of 2-hydroxyacetophenone is displayed on the canvas. On the right, the 'Browse Substances' panel shows a list of results for the substructure query Oc(=O)c1cc(O)cc(C)c1. The results include: AMV9L2WTBK (ACHIRAL), 0798E1C152 (ACHIRAL), 29JTXN99TW (ACHIRAL), 433PEB167C (ACHIRAL), and 66R5KVZ43T (ACHIRAL). Each result shows a small chemical structure thumbnail and its name.

Figure 35-Substructure Search and Tile View

2. **Similarity:** Find chemical structures that have structural features that are similar to those of the query structure. This similarity search is based on a chemical feature fingerprint and the "tanimoto" similarity metric. This kind of search also requires a numeric similarity cutoff; a left to right scroll appears below. A common similarity cutoff to use is 80% (aka 0.80), which suggests that 80% of the shared chemical features between the query and target are found in both the query and target. This search type is useful for finding chemical structures that have similar functional groups and similar overall structure. After populating the Structure, select "Similarity" and "Similarity cutoff" criteria and select Search as shown on the left, the search results are on the right.

The screenshot shows the GSRS interface for a similarity search. The 'Structure Search' panel on the left has a dropdown menu set to 'Similarity' with a red box around it. Below it are buttons for 'Similarity cutoff (tanimoto)' (with a slider set to 0.8), 'Search' (highlighted with a red box), 'Import', and 'Export'. A chemical structure of 2-hydroxyacetophenone is displayed on the canvas. On the right, the 'Browse Substances' panel shows results for a similarity query of 0.8. The results include: SALICYLIC ACID (ACHIRAL) with a similarity of 1.000, and CEROUS SALICYLATE (ACHIRAL) with a similarity of 0.922. Each result shows a small chemical structure thumbnail and its name.

Figure 36-Similarity Search and Cutoff

The screenshot shows detailed substance information for SALICYLIC ACID and CEROUS SALICYLATE. SALICYLIC ACID has a similarity of 1.000 to the query. CEROUS SALICYLATE has a similarity of 0.922 to the query. Both entries show their chemical structures, names, codes, and various identifiers like CAS numbers and regulatory status. The right side of the screen shows administrative details for each substance.

Substance	Similarity to Query
SALICYLIC ACID	1.000
CEROUS SALICYLATE	0.922

Figure 37-Similarity Value

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3. **Exact:** Find chemical structures that match the query structure definition exactly. This search type does allow for returned chemical structures to be of a different tautomeric form or resonance structure, but requires that the returned results are functionally equivalent to the query structure, including stereochemical bonds. This kind of search is useful in finding chemical structures that are essentially identical to the provided structure. Note that an exact match on structure doesn't necessarily mean that the full definitions are equivalent, as there are other defining attributes of substances outside of the chemical structure.
4. **Flex:** Find chemical structures that have isolated connected covalent structures which match the query structure definition, allowing for differences in stereochemistry. This search type does allow for returned chemical structures to be of a different tautomeric form or resonance structure, but requires that the returned results contain a fully isolatable structure that, when charge normalized, is functionally equivalent to the query structure, ignoring stereochemical bonds. This kind of search is useful for finding all salts, solvates, hydrates and stereoisomers of a given covalent structure.

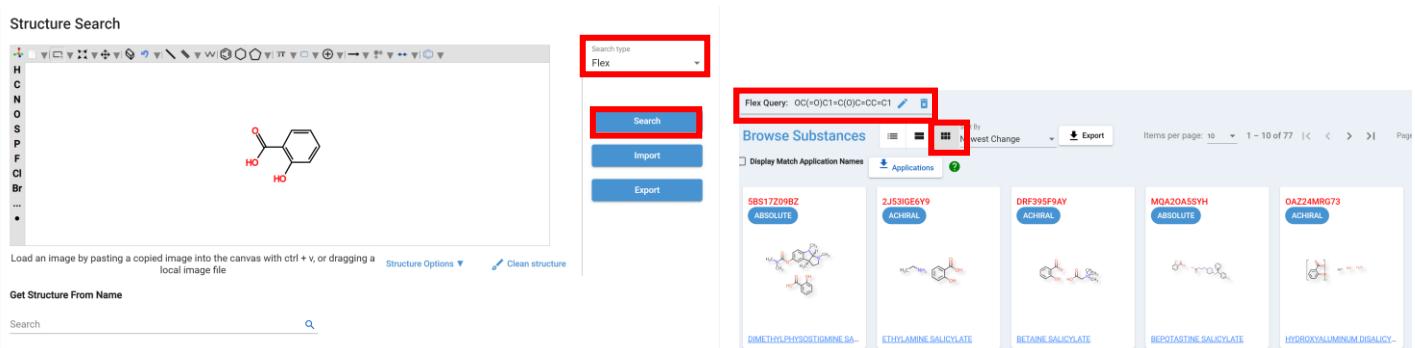


Figure 38-Flex Search and Results in Tile View

Export Structure from the web drawing tool

After drawing or obtaining a chemical structure into the Chemical web editor you can export into a molfile or SMILES string using the export feature. The Molfile by default is going to use Mol 2000.

1. Select Export

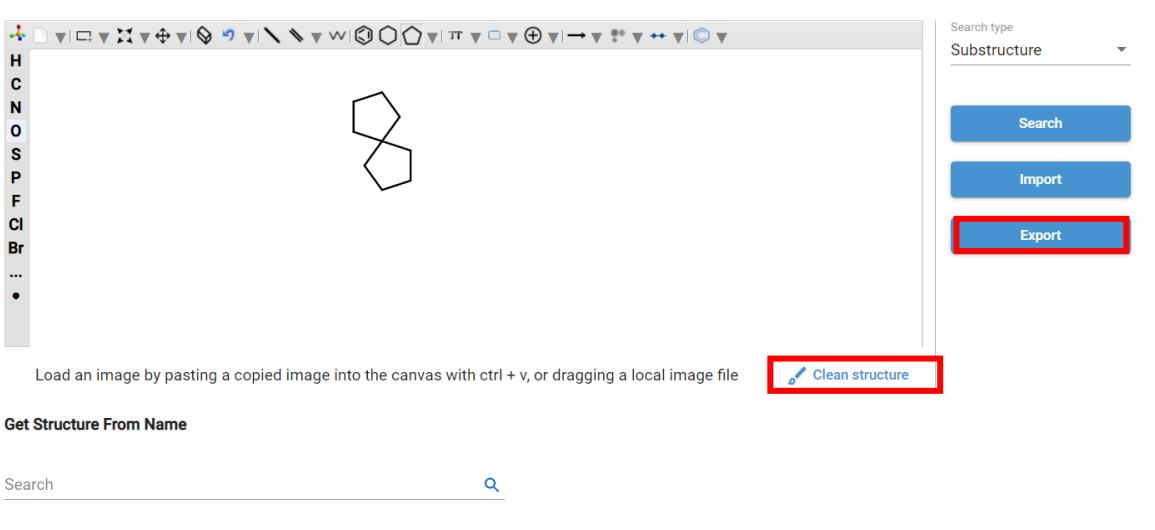


Figure 39-Export Structure

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2. The Export Screen appear with two tabs, Molfile and SMILES

Export

The screenshot shows the 'Export' interface. At the top, there are two tabs: 'Molfile' (highlighted with a red box) and 'Smiles'. Below the tabs, the 'Molfile' tab displays a large block of numerical data representing a molecule's structure. The 'Smiles' tab displays the chemical structure in SMILES format: c(c(c1)cc2)cc2)cc1. At the bottom of each section are 'Close' and 'Download' buttons.

Figure 40-Export Results=Molfile and Smiles

3. Select Download, the file will be saved locally when you are ready to re-use. Clean the structure using Accelrys draw or Chemdraw for cyclic structures. Both Chemical web editor and Accelrys are not for cyclic structures.

Structure Search from an existing GSRS Substance

From an existing GSRS substance record, you can transfer a structure found during a search or browse session from the browse results pane to the Structure Search screen.

1. From your substance, select the magnify glass
2. Select the words "Search Structure"
3. The structure populates on the canvas
4. Select Search.

The screenshot shows the 'Structure Search' interface. On the left, a substance record for 'PAROXETINE HYDROCHLORIDE HEMIHYDRATE' is displayed. It includes fields for 'Names', 'Codes', and various identifiers like BDNUMBER, RNCAS2, EVMPD, PUBCHEM, and MERCK INDEX. A 'Search Structure' button is highlighted with a red box. On the right, the 'Structure Search' interface shows the molecule's structure in a canvas. The 'Search type' dropdown is set to 'Substructure'. Below the canvas are buttons for 'Search' (highlighted with a red box), 'Import', and 'Export'. A note at the bottom says 'Load an image by pasting a copied image into the canvas with ctrl + v, or dragging a local image file'.

Figure 41-Select Magnify Glass to Search Stucture

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Sequence Search

GSRS also supports searching on sequences to locate protein and nucleic acid substance records via sequence alignment search for DNA, RNA and amino acid sequences using a BLAST-like alignment search.

- From any page in GSRS select the Menu hamburger icon and scroll to Sequence search. The Sequence Search box displays as shown to the right of the pulldown menu below.

Sequence Search

Search Identity
0.9

Cutoff Type
Global Alignment Match

Sequence Type
Protein

Search

A clean sequence

Figure 42-Sequence Search

- The default search is Search Identity = 0.9, Cutoff Type = Global Alignment Match.

Sequence Search

Search Identity
0.9

Contains Alignment Match

Global Alignment Match

Local Alignment Match

Sequence Type
Protein

Search

A clean sequence

Figure 43-Sequence Search Defaults

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3. Cutoff Type provides options for:

- Contains Alignment Match. This sequence alignment search type searches for substance sequences (proteins, RNA, DNA) which contain a subsequence similar to the query. This kind of search is useful when searching for a relatively short sequence motif which may be found in a much larger sequence with a few small edits. The score for this alignment is based on how closely the full query aligns with a portion of the target sequence. Searching for a small sequence may return much larger sequences. Searching for a large sequence will not return much smaller sequences. The actual alignment score is based on the global alignment score for the isolated section of the target which is aligned with the query.
- Global Alignment Match. This sequence alignment search type searches for substance sequences (proteins, RNA, DNA) which are similar to the complete query. This kind of search is useful when searching for a complete sequence (e.g. a protein subunit, peptide, oligonucleotide, etc) where the goal is to find a substance with a nearly exact complete sequence match. This can be useful in finding potential transcribing errors and typos on existing protein and nucleic acid substances as well as helping to find analogs to a given substance. As with all sequence search types, the search is done across all subunits within a given sequence-containing substance (proteins and nucleic acids). Alignment scores are based on the Levenshtein edit distance between the query and target, divided by the length of the larger sequence.
- Local Alignment Match. This sequence alignment search type searches for substance sequences (proteins, RNA, DNA) which share sufficient overlapping sequence portions. This kind of search is useful when searching for either a larger or smaller sequence which share some motifs. This search type is also currently the fastest returning sequence search type. However, the results from these searches may contain some sequences which simply happen to share a few very small regions of sequence overlap. The score for this alignment is based on the global alignment score for the isolated section of the target which is aligned with the isolated section of the query. Some short sequence matches without gaps may rank higher than longer sequence matches with gaps. Care must be taken when using this type.

4. Paste the subunit into the text box.

5. Select Search.

Sequence Search

Search Identity 0.9	Cutoff Type Global Alignment Match	Sequence Type Protein
EVQLVESGGGLVQPGRSLRLSCAASGFTFDDYAMHNVRQAPGKLEWVAITWNSGHIDYADSVEGRFTISRDNAKNSLYLQMSLRAEDTAVY YCAKVSYLSTASSLDYNGQQLTVSSASTKGPSVFLAPSSKSTSGGTAALGCLVKDYFPEPVTVWSNSGALTSGVHTFPALVLQSGLYSLSS VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEELLGGPSVFLFPPPKDTLMSRTPEVTCVVVDVSHDPEVKFNWY VDGVEVHNAKTPREEQYNSTYRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIASKAKGQPREPQVYTLPPSRDELTKNQVSLCLVKGF YPSDIAWESENQGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSVMEALHNHYTQKSLSLSPKG		
<input type="button" value="Search"/>	<input type="button" value="Clear"/>	<input type="button" value="clean sequence"/>

Figure 44-Sequence Search Subunit

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6. Matching records are displayed in the Results Pane with additional details about how the records matched the sequence search criteria.

Figure 45-Sequence Search Results

Sequence Search from Existing Substance Record: Transfer a structure found during a search or browse session using the results pane search icon.

From an existing GSRS substance record, you can transfer a sequence found during a search or browse session from the browse results pane to the Sequence Search screen.

1. From your substance, select the magnify glass 
 2. Select the subunit (if more than one)
 3. The sequence search screen will be displayed and populated with the selected subunit and default matching criteria.

ADALIMUMAB		FYS6T7F842
PROTEIN		Inxight Drugs
 Download Edit File Search	Names: ADALIMUMAB ✓ ADALIMUMAB, LICENSE HOLDER UNSPECIFIED ADALIMUMAB [INN] ADALIMUMAB [MART.]	Created: 4/3/19 Created By: admin Status: Validated (UNII) Validated By: FDA_SRS Last Modified: 4/3/19 Last Modified By: admin Version: 43
	Codes: BDNUMBER: 0126172AB RNCAS2: 331731-18-1 WHO-ATC: L04AB04 EVMPD: SUB20016 LIVERTOX: 15	
Substance Hierarchy	subunit 1 (451) similarity search	
> ADALIMUMAB	subunit 2 (451) similarity search	
	subunit 3 (214) similarity search	
	subunit 4 (214) similarity search	
	FYS6T7F842 (ACTIVE MOIETY)	

Figure 46-Sequence Search Magnified Glass Subunit Options

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Register Chemicals

A chemical is a small molecule and single entity. The first step of any registration should be to -. If no duplicates are found, proceed by selecting Register Chemical. If duplicates are found you will need to investigate further to determine if it's a true duplicate. Each substance is unique in GSRS. Select Register then Chemical from one of the various options explained in the Registration Page Navigation Options section of this document.

The chemical registration form will be displayed. Section cards are collapsible to ease navigation, however the elements in this form are:

1. Overview
2. Names
3. Structure
4. Codes
5. Relationships
6. Notes
7. Properties
8. References

Below is the Registering New Chemical entry form

The screenshot shows the 'Registering New Chemical' entry form. At the top, there are fields for 'Definition Type' (Primary) and 'Definition Level' (Complete), both with dropdown menus. There is also a checkbox for 'Deprecated' and a 'Record Level Access' button. Below these are 'Substance tags' input fields and a 'Definitional References' section with a 'Create new' button and a 'Definition Access' link. The main area contains several collapsible section cards: 'Names' (with 'Add Names' button), 'Structure' (collapsible), 'Codes' (with 'Add Codes' button), 'Relationships' (with 'Add Relationships' button), 'Notes' (with 'Add Notes' button), 'Properties' (with 'Add Properties' button), and 'References' (with 'Add References' button). Each card has a collapse/expand arrow icon to its right.

Figure 47-Register Chemical Entry Form with Card Options

Overview – Registering New Chemical

In order to register a chemical structure (which is the substance identity), and in general for any substance, you need

- a substance identity
- at least one name and
- at least one definitional reference

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1. Definition Type - hover over and select the down arrow to activate the Edit drop-down.

The screenshot shows two side-by-side sections of a web form. The left section is titled 'Overview' and 'Registering New Chemical'. It has a 'Definition Type' dropdown menu where 'Primary' is selected. A red box highlights the dropdown arrow. Below it is a 'Substance tags' input field with placeholder text 'Enter new tags (and press Enter after each entry) or select...' and a 'Definitional References' link. The right section is also titled 'Overview' and 'Registering New Chemical'. It has a similar 'Definition Type' dropdown menu, which is currently set to 'Alternative'. A red box highlights the dropdown arrow. Below it is a 'Primary Substance' input field with a placeholder 'Search (entry) or select from suggested terms...' and a 'Definitional References' link.

Figure 48-Definition Type Field Options

There are two options:

- a. Primary
- b. Alternative - Chemical alternative definition of a protein, nucleic acid, polymer, ring/open sugar etc. Once Alternative is selected a Primary Substance Search field appears

This screenshot shows the same 'Registering New Chemical' form as Figure 48, but with a different selection in the 'Definition Type' dropdown. The dropdown is now set to 'Alternative', and a red box highlights this selection. To the right of the dropdown is a 'Primary Substance' input field with a magnifying glass icon and a placeholder 'Search (entry) or select from suggested terms...'. Below these fields is a 'Substance tags' input field.

Figure 49-Definition Type-Alternative reveals a Primary Substance Search Option

- i. Type the Primary Substance name in search box and select. As you begin, typing a list containing those letters will appear. Make a selection and then select search and the Primary Substance will populate

This screenshot shows a search interface for 'Preferred Term'. At the top, there is a search bar with 'Sodium' typed in, a magnifying glass icon, and a 'Definition Level' dropdown set to 'Complete'. Below the search bar is a list of terms under the heading 'Preferred Term'. The term 'TRABEDERSEN SODIUM' is highlighted with a red box. Other terms listed include 'SODIUM', 'SODIUM CHLORIDE', 'PHENYTOIN SODIUM', and 'SODIUM CITRATE, UNSPECIFIED FORM'. To the right of the search results is a detailed view of 'TRABEDERSEN SODIUM' enclosed in a red box. This view includes a blue circular icon with a DNA double helix, a pencil icon, and a delete icon. The text 'Primary Substance' is visible above the icon, and 'TRABEDERSEN SODIUM' is repeated below it.

Figure 50-Primary Substance Search, Selection and Result

- ii. After submission, the system generates a relationship connecting both definitions
- iii. Alternative definition registration is similar to Primary definitions, but Names and Codes are not included

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2. Definition Level – select the down arrow to activate the Edit drop-down.

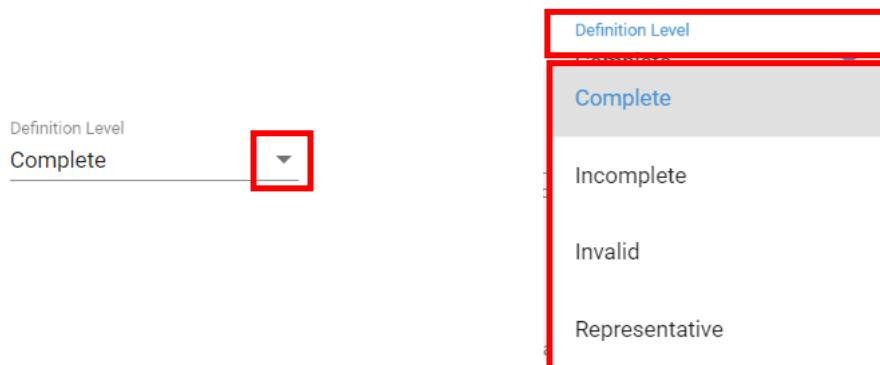


Figure 51-Definition Level Options

- a. Always try to enter a Complete definition
 - b. Incomplete are allowed for incompletely defined substances.
 - c. Representatives are too complex to define completely
3. Deprecated box. Selecting this box means it is semi-deleted, or a candidate for deletion". There are other flags for deprecation elsewhere in GSRS, but that one also tells the browse/search functions not to show this record Unless you specifically click the box allowing it to show

Registering New Chemical

A screenshot of the "Registering New Chemical" form. It shows fields for "Definition Type" (Primary), "Definition Level" (Complete), and a "Deprecated" checkbox. The "Deprecated" checkbox is highlighted with a red box. To the right are buttons for "Record Level Access" and "Definition Access". Below the form is a section for "Substance tags" with a text input field and a "Create new" button.

Figure 52-Registering a Chemical - Deprecated Box

4. Record Level Access. Some substances are public in which case set the Record Level Access to Public by deselecting Protected under Record Level Access. Some substance are private in which case we select Protected. Private means not readily available in public sources, domains, website, etc. (e.g., Scifinder, pubchem)

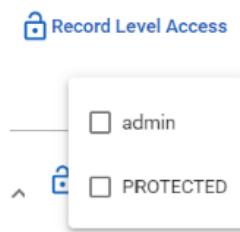


Figure 53-Record Level Access Types

5. Definitional Reference(s)
a. Select the Create new + button

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Definitional References ⁰

Create new

Definition Access

Type Citation Public Domain Access Open Remove Delete

Figure 55-Adding a new Definitional Reference

- b. The Add Reference screen appears and additional fields will be displayed
 - i. Select the down arrow next to Source Type

Add Reference

Source Type * Source Text/Citation * Public Domain

URL Source Id Tags

[Upload Document](#) [Use Previous Substance Reference](#)

Figure 52-Add Reference Source Type Down Arrow

- ii. Use the scroll on the right to navigate and select a Source Type

Source Type *

- ACD
- ALANWOOD
- ALGAEBASE
- AMERICAN BOTANICAL COUNCIL
- ANDA

Source Text/Citation * Public Domain

Source Id Tags

[Cancel](#) [Save](#)

Figure 53-Add Reference Source Type Options

- iii. Source Text/Citation – identifies where the information comes from
- iv. Based on the release sensitivity,
 - a. Check Public Domain if public
 - I. If public, add Tags for Public-Domain-Release
 - b. Update the Access by deselecting PROTECTED, if applicable
 - c. Select Save

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Add Reference

The screenshot shows the 'Add Reference' form. It includes fields for 'Source Type *' (dropdown), 'Source Text/Citation *' (text input with a red box around it), 'Public Domain' (checkbox with a red box around it), 'Access' (button with a lock icon), 'URL' (text input), 'Source Id' (text input), 'Tags' (text input), 'Upload Document' (button), 'Use Previous Substance Reference' (link), and 'Cancel/Save' buttons. A modal window titled 'Access' is open, showing 'admin' and 'PROTECTED' checkboxes, with 'PROTECTED' checked.

Figure 54-Add Reference Source Text/Citation, Public Domain and Access Options

- v. In order to make something Public it has to be made public three times.
 - a. Undo the lock
 - b. Select the Public Domain checkbox
 - c. Enter the Tag as Public Domain Release
- c. Verify the Reference is attached to the Definitional References section located in the upper left hand corner of the record
 - i. The 0 is replaced with 1; the number will correspond to the number of references added
 - ii. "Apply to" hamburger pull down menu has the options of All, All without references, chemical, or relationships.
 - a. Relationships has a right arrow with the options
 - i. All relationships
 - ii. All Relationships without references

The screenshot shows the 'Definitional References' section. It includes a header with 'Definitional References' (0) and a button to 'Create new'. Below is a table with columns: Type, Citation, Public Domain, Access, Open, Remove, and Delete. A row shows CAS, Cass, Yes, Public, and buttons for Open, Remove, and Apply to (with a red box around it). A dropdown menu titled 'Apply to' is open, showing options: All, All without references, chemical (checked), relationships (with a red box around it), All relationships, and All relationships without references.

Figure 55-Definitional References Quantity Notation and Apply to Options

2. Click on Create new + to add more references. Or select a previously used ref by clicking on reuse to select a previous substance reference

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Names

The Names card accommodates multiple names. By default, the section is collapsed but can be expanded to view more names.

1. Select the Add names + button or the down arrow next to Add Names

Names



- a. The Names screen appears and additional fields will be displayed
- b. Names
 - i. All CAPS – select the Standardize Names button prior to leaving the Names card
 - ii. No Brackets – use parenthesis for brackets. Exception to the bracket is when referencing substance tags (e.g., [USP], [EP])
- c. Type – select using the down arrow to the right

Names



Standardize Names Collapse All More ▾

A screenshot of the "Names" card interface. It includes fields for "Name *", "Type * (Common Name)", and "Language" (English). A dropdown menu for "Type" is open, showing options like "Code", "Common Name", "Official Name", etc. Other sections visible include "Domains" and "Jurisdiction". Buttons for "Create new" and "Reuse" are at the bottom.

Figure 56-Names Card and Field Options

- i. Scroll, on the right, to view all name types and navigate and select a Type (Codes are usually seen as letters dash numbers (e.g., ABC-123); Systematic Name for a Chemical is a name you can derive a structure from directly). Common name is the default for any new name being entered and must be changed if the name being entered into GSRS is a code, systematic name, etc; an official name is a name from an official body such as INN, USAN, JP, etc

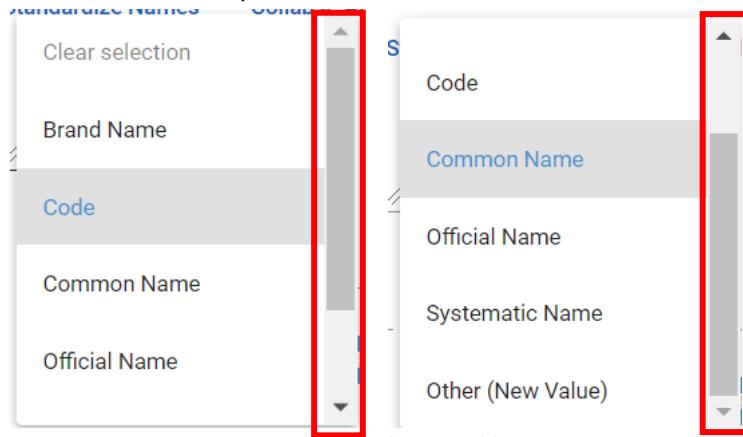


Figure 57-Names Card Type Field Options

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- a. Access - Update the Access by deselecting PROTECTED, if applicable

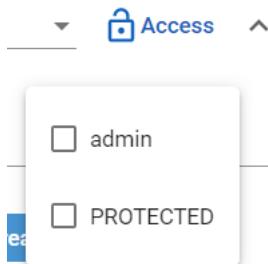


Figure 58-Names Card Access Options

- b. Languages – Select inside the Language field to pull up the Language menu; scroll on the right to view all Languages and select a Language
- c. Domains – Select inside the Domains field to pull up the Domains menu; scroll on the right to view all Domains and select a Domain; this is typically done when adding an official name to the document. Any other type of name (e.g., code, systematic name) you do not need to select a Domain.
- d. Jurisdiction – Select the Jurisdiction field to pull up the Jurisdiction menu; scroll on the right to view all Jurisdictions and select a Jurisdiction

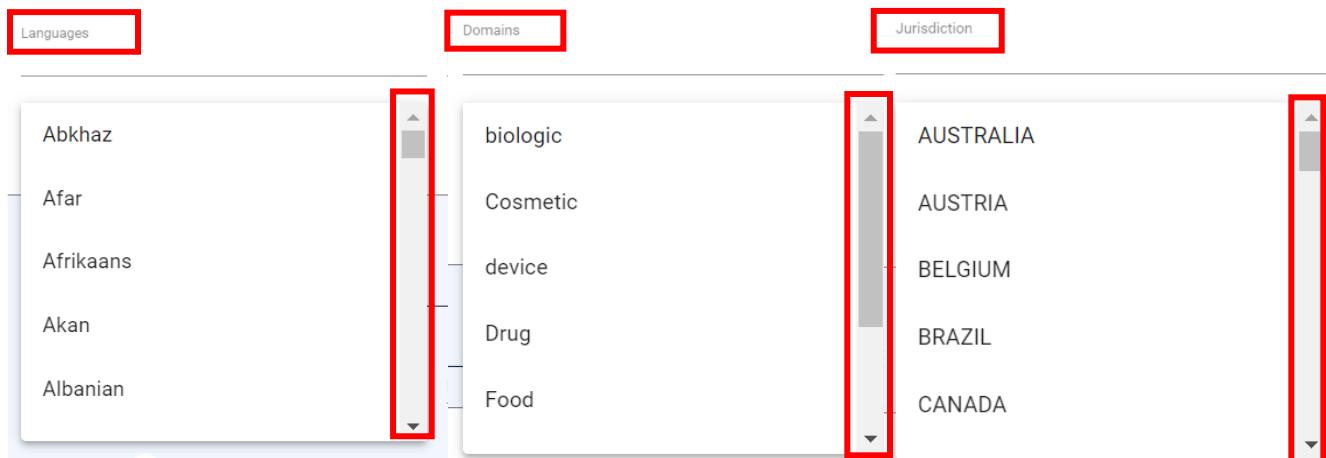


Figure 59-Names Card Language, Domains, and Jurisdiction Field Options with Scroll bars

- e. References – a reference is required for each name that is added. Add a Reference as explained in Overview section above or if references already exist, you can select an existing reference.
 - i. To Reuse an existing Reference select the down arrow next to Reuse button



- ii. Reuse Substance References window appears with a list of previously used references. Select using the Apply box(es) on the left

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iii. Select Save

The screenshot shows the 'Reuse Substance References' window. At the top left is a checked checkbox labeled 'Filter Out System / Validation references'. Below it is a table with two rows. The first row has columns: 'Type' (WEB PAGE), 'Citation' (testing test), 'Public Domain' (No), and 'Access' (Public). The second row has columns: 'Type' (WEBSITE), 'Citation' (Web), 'Public Domain' (No), and 'Access' (Public). To the left of the table is a red box around the 'Apply' button. To the right are 'Cancel' and 'Save' buttons, with 'Save' also enclosed in a red box.

Figure 60-Reuse Substance References window, Select and Save

- f. Access – if you are adding a Reference instead of reusing one, update the Access by deselecting PROTECTED, if applicable

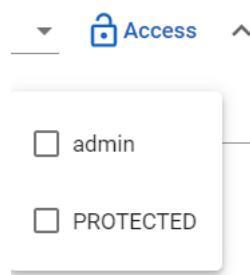


Figure 61-Access Options

3. Select Add Names + to add additional Names.

4. Apply reference to all Names at one time

The screenshot shows the 'References' section. On the left, under 'Languages', 'English' is selected. In the center, there's a table with one row: Type (ALANWOOD), Citation (testing test), Public Domain (Yes), Access (Public), Open (checkbox checked), Remove (X), Delete (checkbox), and 'names' (dropdown menu). To the right is a 'Jurisdiction' section with a dropdown menu showing 'All', 'All without references', and 'chemical' (checkbox unchecked). A blue 'Reuse' button is next to the dropdown. At the bottom right is a red box around the 'Apply to' button with three horizontal lines.

Figure 62- References Apply to Options

Structure

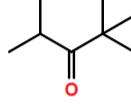
The Structure card canvas is populated using any method described in the **Structure Search** to upload a structure.

1. After entering the structure in the Chemical web editor canvas, click Check for Duplicates button
2. Verify the system correctly auto populated the remaining fields:

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- a. Molecular Formula
- b. Stereochemistry – calculated based on stereo bond, update as needed
 - i. Ex: Asenapine is racemic, however GSRS would recognize the structure as “absolute, chiral” because it has stereo bonds and user would have to change the identify to racemic
- c. Optical Activity
- d. Additional Stereochemistry (e.g., axial stereochemistry)
- e. Molecular Weight
- f. Defined Stereocenters
- g. EZ Centers
- h. Structure Charge
- i. Access – update to Protected for nonpublic substances
- j. Stereo Comments - Add if applicable, e.g. meso, Assumed racemic (if one stereo center and we can safely assume racemic), AXIAL, S; AXIAL, R; AXIAL, RACEMIC for additional stereochemistry

Structure



Load an image by pasting a copied image into the canvas with **ctrl + v**, or dragging a local image file Clean structure

Check for duplicates Import... Export View stereochemistry

SUCCESS Structure is valid and unique X

Molecular Formula *	Stereochemistry	Optical Activity	Additional Stereochemistry
C8H16O	Achiral	None	NO

Molecular Weight	Defined Stereocenters	EZ Centers	Structure Charge	Access
128.212	0 / 0	0	0	

Stereo Comments
Enter text here

Figure 63- Structure card canvas, Check for Duplicates, Success renders completed fields

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Codes

The Codes card accommodates multiple codes. By default, the section is collapsed but can be expanded to view more codes.

1. Select the Add Codes + button or the down arrow next to Add Codes



2. The Codes screen appears and additional fields will be displayed

A screenshot of the GSRS interface showing the 'Codes' screen expanded. The expanded section includes several input fields and dropdown menus:

- 'Code System *' dropdown menu with a red border around its selection area.
- 'Type' dropdown menu with a red border around its selection area.
- 'Code *' dropdown menu with a red border around its selection area.
- 'Access' button with a lock icon.
- 'Url' input field.
- 'Code text' input field containing placeholder text 'Enter text here'.
- 'Comments' input field containing placeholder text 'Enter text here'.
- 'References' button with a red border around its selection area.
- 'Create new +' button.
- 'Reuse' button with a red border around its selection area.

Figure 64- Codes Card

- a. Code System - Select the Code System field to pull up the Codes menu; scroll on the right to view all Codes and select a Code
- b. Type - Select the Type field to pull up the Type menu, scroll on the right to view all Types and select a Type

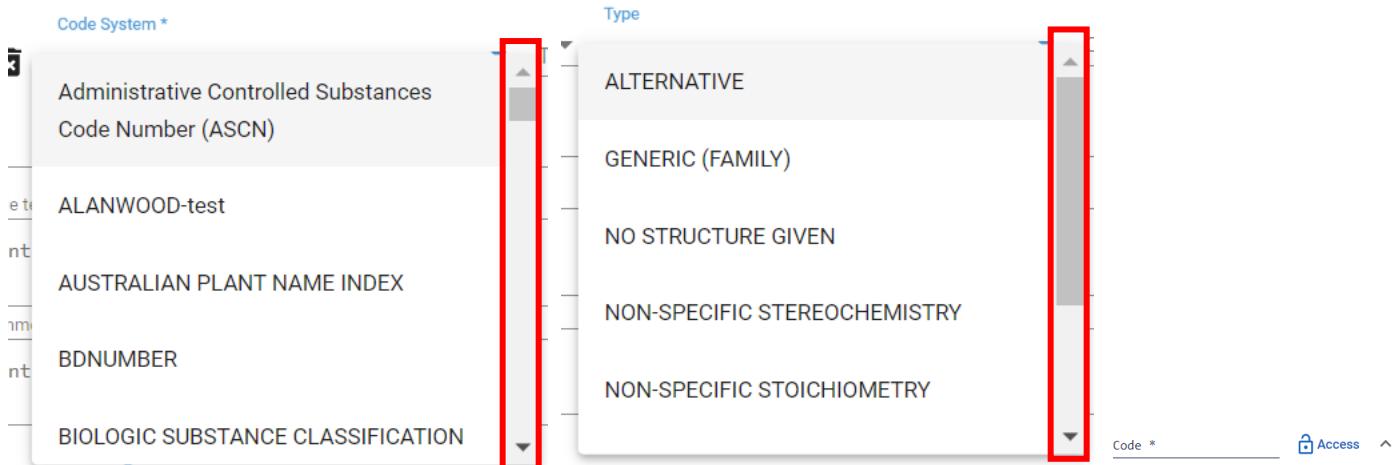


Figure 64- Codes Card – Code System and Type

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- c. Code - Enter a Code in the Code field
- d. Access - update the Access by deselecting PROTECTED, if applicable
- e. GSRS will automatically construct URLs for the following Code Systems which can be accessed in the hyperlink on the view page

ALANWOOD	GRIN	NCI THESAURUS
CAS	INN	NDF-RT
CFR	ITIS	PHAROS
CHEMBL	IUPHAR	PUBCHEM
CLINICAL_TRIALS.GOV	JECFA EVALUATION	RXCUI
CODEX ALIMENTARIUS (GSFA)	JMPR-PESTICIDE RESIDUE	UNIPROT
DEA NO.	MERCK INDEX	USDA PLANTS
DRUG BANK	MEX	WHO-ATC
FOOD CONTANT SUBSTANCE NOTIF, (FCN NO.)	NCBI TAXONOMY	

Figure 65 - Register Chemicals - URL Construction for Code Systems

3. References - If references already exist, you can select Reuse to Add a [References](#)

Once cards have been completed for Overview, Names, Structure and Codes, user can select Validate and Submit to enter a Chemical.

The screenshot shows the 'Register Chemicals' interface with a blue header bar containing 'Menu', 'Browse Substances', 'Browse Other', 'Register', and 'Search Substances'. Below the header are buttons for 'Show JSON', 'Import JSON', 'Advanced Features', 'Validate and Submit' (which is highlighted with a red box), and 'Approve'. The main area contains several cards: 'Overview' (highlighted with a red box), 'Names' (with 'Add Names' button), 'Structure', 'Codes' (with 'Add Codes' button), 'Relationships' (with 'Add Relationships' button), 'Notes' (with 'Add Notes' button), and 'Properties' (with 'Add Properties' button). Each card has a small dropdown arrow icon at the top right.

Figure 66- Minimum Cards Needing Completion in order to Validate and Submit

Once the Substance is Valid message appears, select Submit

The screenshot shows the 'Register Chemicals' interface with a blue header bar containing 'Show JSON', 'Import JSON', 'Advanced Features', 'Validate and Submit' (highlighted with a red box), and 'Approve'. A message box in the center asks 'Substance is Valid. Would you like to submit?'. Below the message is a large blue 'Submit' button with a red box around it.

Figure 67- Valid Substance Message

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Success screen appears with the message Update was performed. Select View Substance.

Success

Update was performed.

[Continue Editing](#)

[Go to Browse](#)

[View Substance](#)

Figure 68- Success Screen

PENTAMETHYLACETONE
4BGD3V6DXM

Overview

Substance Class: Chemical

Record UNII: 4BGD3V6DXM

Record Protection Status: Public record 

Record Status: Validated (UNII)

Record Version: 5

Tags

Show Definitional References 

Definitional Access: Public definition 

Figure 69- Substance View

Names

Search

Filter Name Type  [Reset](#)

Name	Type	Language	Details	References
PENTAMETHYLACETONE 	Common Name	English	View	View
NSC-892	Code	English	View	View
NSC-139131	Code	English	View	View
ISOPROPYL TERT-BUTYL KETONE	Common Name	English	View	View
3-PENTANONE, 2,2,4-TRIMETHYL-	Systematic Name	English	View	View
2,2,4-TRIMETHYL-3-PENTANONE	Systematic Name	English	View	View

Items per page: 10  1 – 6 of 6 |< < > >|

Figure 70- Substance Names

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Overview >

Products, Applications, Clinical Trials, Adverse Events >

Structure >

Names 1 >

Identifiers 2 >

Audit Info >

References 2 >

Moieties 1 >

History >

Structure

Stereochemistry **ACHIRAL**

Molecular Formula C₈H₁₆O

Molecular Weight 128.212

Optical Activity **NONE**

Defined Stereocenters 0 / 0

E/Z Centers 0

Charge 0

Additional stereochemistry **No**

Show References ▾

Show SMILES / InChi ▾

No Systematic Names

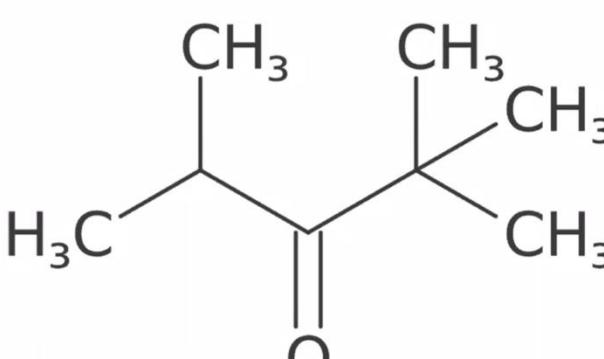


Figure 71- Substance Structure

Identifiers				
Code System	Code	Type	Comments	References
PUBCHEM	138611	PRIMARY	<button>View</button>	<button>View</button>
CAS	5857-36-3	PRIMARY	<button>View</button>	<button>View</button>
FDA UNII	4BGD3V6DXM	PRIMARY	<button>View</button>	<button>View</button>

Items per page: 5 ▾ 1 – 3 of 3 |< < > >|

Figure 72- Substance Identifiers

Relationships

The relationships card accommodates multiple relationships. By default, the section is collapsed but can be expanded to view more relationships. When relationships are added, the inverse relationship is added to the related substance.

1. Expand the Relationships card

Relationships

Add Relationships + ▾

2. Select the Add Relationships + button

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Relationships

Add Relationships

Collapse All



Related Substance



Type *



Access

Mediator Substance



Qualification

Interaction Type

Comments

Enter text here

Amount

Type *



Average

Low

High

Low Limit

High Limit

Units

Non-numeric Value

References

Create new

Reuse



Figure 73- Relationships Card

3. Both the Related Substance and Mediator Substance are search fields. Type ahead is also available for these fields.
 - a. Begin entering the name
 - b. Select the correct substance if more than one option is available
 - c. If no matching substances are returned, you cannot create a relationship to an unregistered substance
4. Select Relationship Type and if applicable, using the down arrow select Qualification, Interaction Type, and Amount.

Relationships

Add Relationships

Collapse All

Related Substance

Type * METABOLITE ACTIVE -> PARENT

Access Cyto

Qualification USP

Interaction Type CHROMATOGRAPHIC PURI...

Comments
Enter text here

Amount

Type * Average Low High Low Limit High Limit Units Non-numeric Value

References

Create new

Desloratadine

Chemical Structure

Preferred Term

CYTOCHROME P450 11B1, MITOCHONDRIAL

CYTOSINE DEAMINASE

CYCLOPENTENYL CYTOSINE

CYTOSOLIC PHOSPHOLIPASE A2

CYTOCHROME P450 3A4

Figure 74- Relationships Card Sample Completed

Impurity Relationships should be added to the active ingredient - to the salt record, if the substance is a salt

1. The relationship Type should be IMPURITY → PARENT
 - a. The related substance is always on left side of the arrow and main substance is on right side of the arrow

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e.g.: PRASUGREL HYDROCHLORIDE is in USAN (https://online.uspnf.com/uspnf/document/GUID-6F4D7843-1F3E-43B5-949B-F88DBD6DFA74_5_en-US?highlight=Prasugrel%20Hydrochloride)

Table 3			
Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Desacetyl hydroxy-prasugrel	0.74	1.0	0.15

Figure 75 - Relationships - IMPURITIES USP/NF monograph; Mode LC

2. Based on this information, the additional details are:
 - a. Qualification = USP
 - b. Interaction Type = ASSAY (HPLC)
3. To add the USAN specification of this impurity is “NOT MORE THAN” 0.15 %, go to the High Limit field under Amount to add amount.
 - a. Select the amount Type: Percent Peak Area
 - b. Enter “0.15” as the High Limit
 - c. Enter Units

Related Substance

Type *
IMPURITY -> PARENT

Qualification
USP

Interaction Type
CHROMATOGRAPHIC PURI...

Comments
Enter text here

DESACETYL HYDROXYPRASUGREL

Amount

Type * Average Low High Low Limit High Limit Units PERCENT PE... Non-numeric

References ¹

Create new + Reuse

Figure 76 - Relationships - Impurity Details

Metabolite relationships always link to active moiety/prodrug. The relationship options between metabolites and the active moiety/prodrug are:

- Metabolite Active
- Metabolite Active → (as) Parent
- Metabolite Active → Prodrug
- Metabolite Inactive → Parent
- Metabolite Less Active → Parent
- Metabolite → Parent (unknown)
- Metabolite Toxic → Parent (without any activation)
- Metabolite Reactive Type → Parent

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- Those should be covalently bind to proteins and nucleic acids for the toxicity
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2952084/>

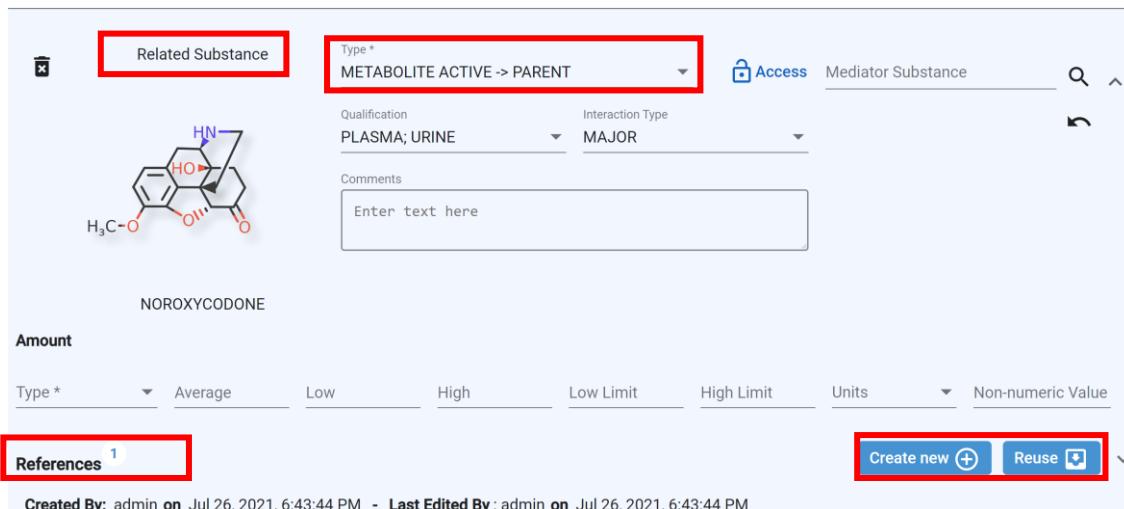


The screenshot shows the 'Relationships' card for Noroxycodone. The card includes fields for 'Related Substance' (set to 'NOROXCODONE'), 'Type' (set to 'METABOLITE ACTIVE -> PARENT'), 'Qualification' (set to 'PLASMA; URINE'), 'Interaction Type' (set to 'MAJOR'), and a 'Comments' field ('Enter text here'). Below the card is an 'Amount' section with various input fields. A dropdown menu is open, listing five relationship types: METABOLITE ACTIVE -> PARENT, METABOLITE ACTIVE -> PRODRUG, METABOLITE INACTIVE -> PARENT, METABOLITE LESS ACTIVE -> PARENT, and METABOLITE TOXIC -> PARENT.

Figure 77 - Relationships - Metabolite Types

Metabolite relationships Example below: Noroxycodone is an active metabolite of oxycodone.

- Edit Oxycodone
- In the Relationships card, click Add another relationship
- In Related Substance, search and select "Noroxycodone"
- For Type, select "METABOLITE ACTIVE -> PARENT"
- Add a Reference – a reference is required. If references already exist, you can select an existing reference or Add a Reference



The screenshot shows the 'Relationships' card for Noroxymorphone. The card includes fields for 'Related Substance' (set to 'NOROXCODONE'), 'Type' (set to 'METABOLITE ACTIVE -> PARENT'), 'Qualification' (set to 'PLASMA; URINE'), 'Interaction Type' (set to 'MAJOR'), and a 'Comments' field ('Enter text here'). Below the card is an 'Amount' section with various input fields. At the bottom right, there are 'Create new' and 'Reuse' buttons. A red box highlights the 'References' button, which has a value of '1'. Another red box highlights the 'Create new' and 'Reuse' buttons.

Figure 78 - Relationships - Noroxymorphone Metabolite

- Mediator Substance - Finding information to register the mediator substance relationship. Example: R-138727 is an active metabolite of Prasugrel, which is a prodrug. R-138727 is a mixture of four isomers. It is a major metabolite in plasma and involves a two step conversion.
 - First conversion step in the article below is mediated by esterase (not specified and therefore cannot be captured)
 - Second step is specific and is mediated by four CYP enzymes. So, one relationship should be added for each CYP enzyme.

<https://accpjournals.onlinelibrary.wiley.com/doi/pdf/10.1592/phco.29.9.1089>

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extensively metabolized to one active metabolite (Figure 1) and to several inactive metabolites.²³ However, there are some differences in the metabolism of prasugrel and clopidogrel. Although both are metabolized by carboxylesterases, the metabolism of clopidogrel involves two CYP-dependent steps, whereas the metabolism of prasugrel involves only one CYP-dependent step.²⁴⁻³⁰ The conversion of the clopidogrel prodrug to the intermediate compound

involves liver CYP1A2, CYP2C19, and CYP2B6, whereas liver CYP3A, CYP2C19, CYP2C9, and CYP2B6 are involved in the conversion of the intermediate to the active metabolite. The conversion of the prodrug of prasugrel to the intermediate form is accomplished primarily by intestinal esterases; both the intestines (CYP3A, CYP2C9, CYP2C19) and liver (CYP3A, CYP2B6, CYP2C9, CYP2C19) are involved in the conversion of prasugrel from the intermediate to the active form.

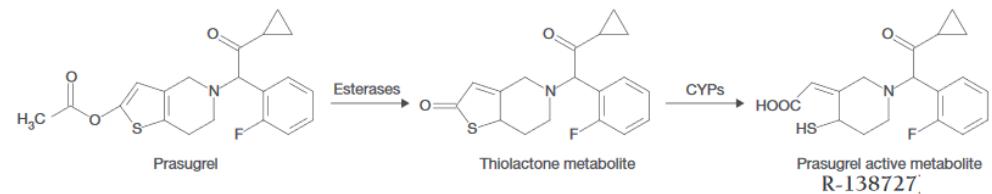


Table 1. Pharmacokinetic Parameters of Prasugrel's Major Metabolites After a 15-mg Radiolabeled Dose in Healthy Volunteers

Parameter	R-95913	R-138727 ^a	R-106583	R-119251
AUC ₀₋₁₂ (ng•hr/ml)	117	122	604	103
AUC _{0-last} (ng•hr/ml)	118	122	827	104
C _{max} (ng/ml)	67	80	120	58
T _{max} (hr)	0.5	0.5	1.0	0.5
Half-life, median (hrs)	3.9	3.7	8.7	2.9

Data are mean except for half-life.

AUC₀₋₁₂ = area under the plasma concentration-time curve from 0–12 hrs; AUC_{0-last} = AUC from time zero to time of last quantifiable concentration; C_{max} = peak plasma concentration; T_{max} = time to C_{max}.

^aActive metabolite.

Adapted from reference 28.

Figure 79 - Extracts of Pharmacokinetics and Pharmacodynamics of Prasugrel, a Thienopyridine P2Y12 Inhibitor

The screenshot shows the GSRS software interface for managing substance relationships. On the left, there is a 'Delete' button and a 'Related Substance' section with a blue gear icon. Below it is a link to 'R-138727' and a 'View in new tab' button. In the center, there is a 'Type' field set to 'METABOLITE ACTIVE -> PRODRUG'. To the right, there are sections for 'Qualification' (set to 'PLASMA Mediator Substance') and 'Interaction Type' (set to 'MAJOR'). Further right are 'Comments' and 'Amount' fields, both set to '122 ng-hour/ml (average)'. At the bottom, there are 'References', 'Access', 'Hide Details', and 'Options' buttons.

Figure 80 - Relationships – Metabolite for Prasugrel

Ionic moiety is a reflexive substance attribute. It is indicated when the chemical structure is not charge-balanced. Active moiety may be a reflexive substance attribute but may also reference another substance

Notes

While you can add a note, you will notice that notes will also be automatically added to track Warning messages and other information related to substance validation.

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Notes

Add Notes

^

Search

Items per page: 5 1 – 5 of 8 | < < > > |

Note

[Validation]WARNING:Code 'N0000175684'[NDF-RT] collides (possible duplicate) with existing code & codeSystem for substance:
[UIE599785171FENTANVI]

Access

References

Create new

Reuse

▼

Created By: admin on Jul 26, 2021, 6:43:44 PM - Last Edited By: admin on Jul 26, 2021, 6:43:44 PM

Figure 81 – Notes Sample

Property

Additional substance details can be added to the Properties card. Properties are not significant for a chemical though.

Properties

Add Properties

^

Name * Volume of Distribution (not in C... add) Property Type * PHARMACOKINETIC (not in CV) add Defining Referenced Substance Access

Parameters

Amount

Type * 2.6 Average Low High Low Limit High Limit Units Liters/Kilogr... Non-numeric Value

References

Create new

Reuse

▼

Figure 6 - Register Chemical – Properties (Prasugrel)

References

The References card automatically accumulate the references added during registration in one section. References can be added, updated, or removed from this card.

Submit

1. Submit the substance by clicking Submit button on top right-hand corner
2. GSRS will validate the submission, you may receive prompts for
 - a. Errors (red) – substances with errors cannot be submitted, click Go Back to return to the substance form, make corrections and resubmit
 - b. Warnings (yellow) – warnings should be reviewed
 - i. If warnings are accepted, click Dismiss and continue
 - ii. If warnings should be address, click Go Back to return to the substance form, make corrections and resubmit
3. The Success window will provide three options:
 - a. Continue Editing –return to the registration edit form
 - b. Go to Browse – close this substance registration form and return to the substance browser of all substances

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- c. View Substance – close this substance registration form and display the view version of the substance

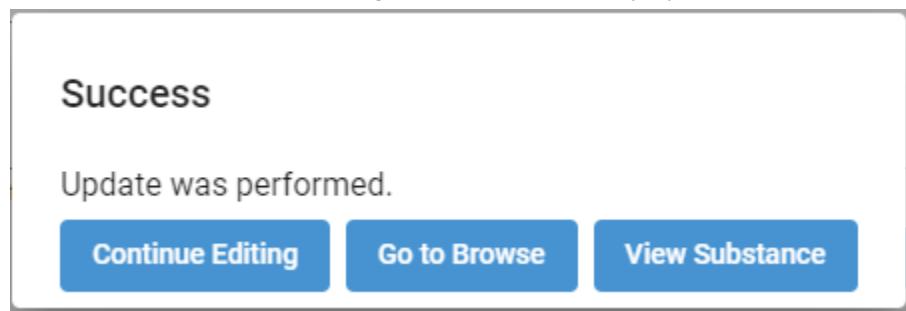


Figure 83 - Chemical Submission Success

4. If you select View Substance, you can confirm your registration. The submitted substance will be assigned the status of Pending and will not have an approval ID. Continue to [Approve Substances](#) to review the next phase of substance registration.

The top part shows the "DYNORPHINS" chemical registration page with various metadata fields like Substance Class, Record UNII, Record Protection Status, Record Status, Record Version, Tags, and Definitional Access. The bottom part shows a "Submit Substance" dialog with error messages about missing references and possible duplicates, followed by a confirmation dialog asking if the user is sure they want to submit.

Figure 84 - Register Chemical - Submission Validation

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5. After successfully submitted you will have the following options:
 - a. Continue Editing – the registration form remains, and changes can be made
 - b. Return to Browse – loads the Browse Substances screen
 - c. View Substance – displays the current substance in view-only mode



Figure 85 - Register Chemical – Submission

Register Chemical Stereoisomers

Now that you have registered a Chemical substance, the user should identify any relevant stereoisomers that should also be registered. SciFinder can be quite useful in identifying isomers referenced in chemical literature and those that are available from commercial sources. Since many GSRS users also have access to SciFinder, we will show some of the most commonly used features. The following example illustrates the 7 stereoisomeric GSRS records typically required when a chemical possesses 2 stereocenters and has no plane of symmetry.

The SciFinder homepage is shown below. Select Draw to import chemical information. In the drawing tool, you can draw a query structure, import a molfile, or use the text box to import a structure using a CAS registry number, SMILES, or InChI.

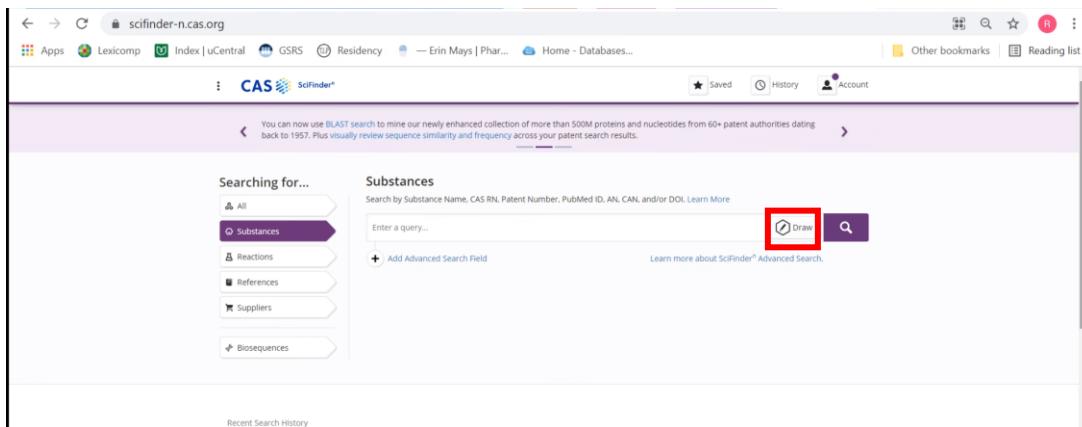


Figure 86 – CAS SciFinder– Draw

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1. Copy and paste CAS number in the search field into CAS Draw and select enter, a molecule drawing will appear. Select Ok on the bottom right to exit the drawing tool

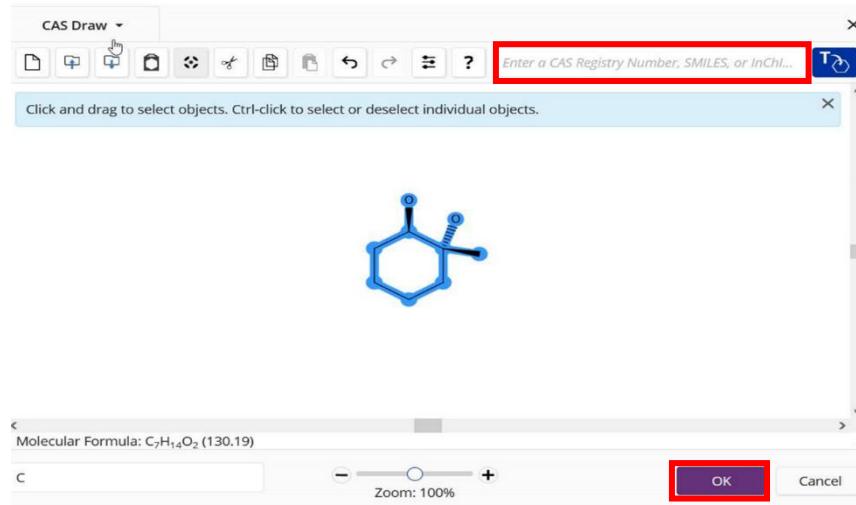


Figure 87 – CAS SciFinder– Enter CAS Number

2. Select Search

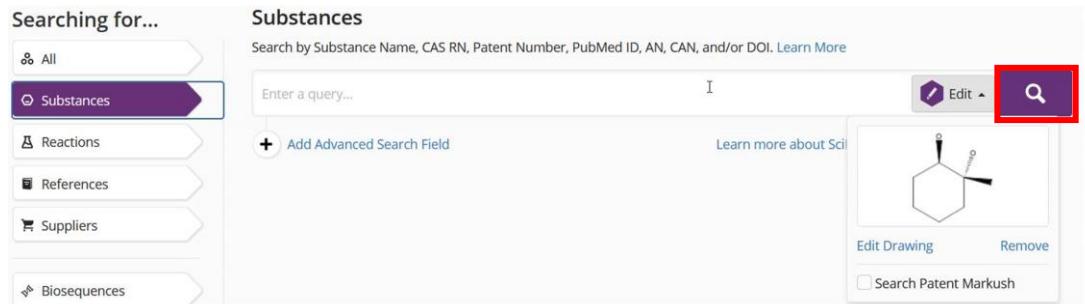


Figure 88 – CAS SciFinder– Search

Some stereoisomers may not appear in the Scifinder search results due to filters which the user can clear. The initial search results show absolute and relative stereochemistry in SciFinder. After all filters are cleared, the 7 relevant chemical structures are shown.

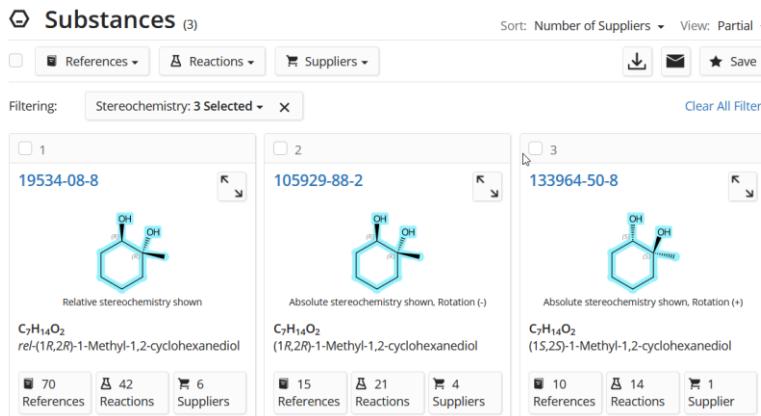


Figure 88 – CAS SciFinder– absolute and relative stereochemistry

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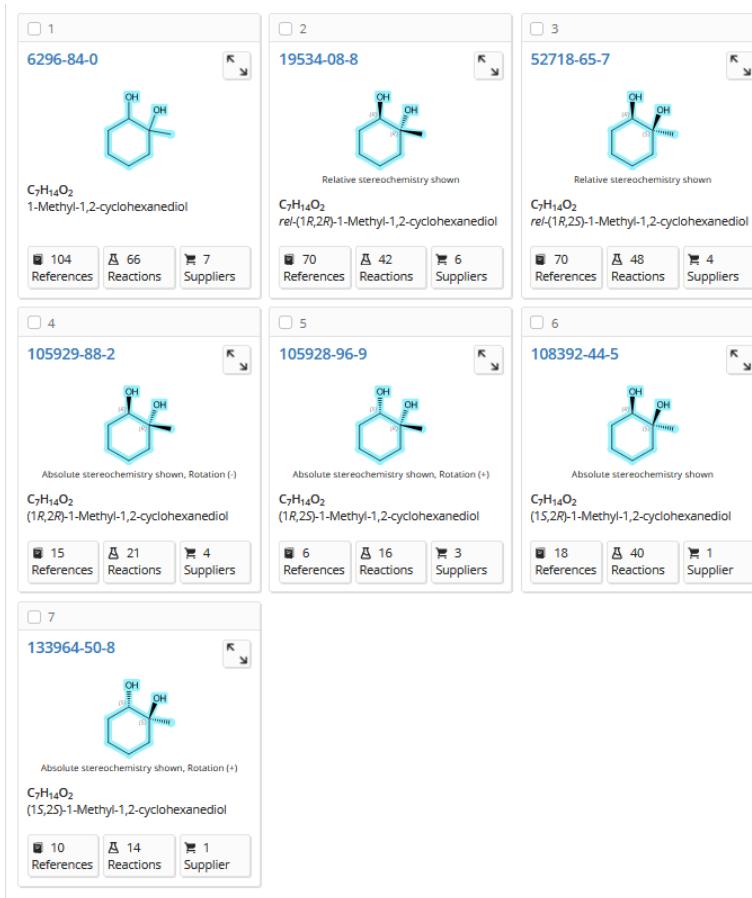


Figure 89 – CAS SciFinder – relevant chemical structures

The following chemical on the left hand side is the +/- trans isomer. The GSRS drawing tool assumes that structures drawn with dashes and wedges infer absolute stereochemistry. The initial structure input is shown in the screen shot on the right. This molecule on the other hand is racemic.

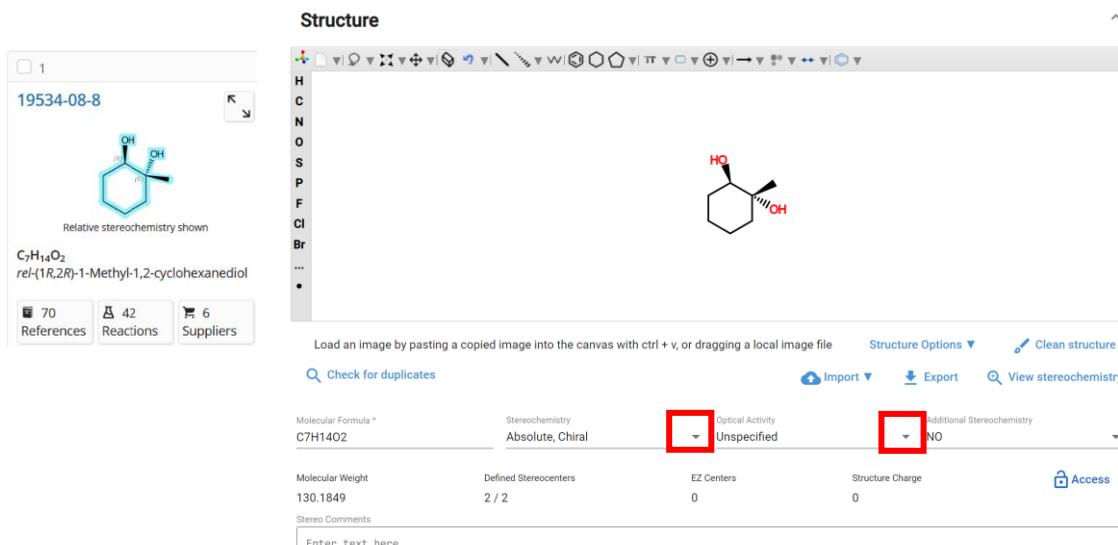


Figure 90 – +/- Trans isomer and initial structure input

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We must therefore explicitly select racemic from the Stereochemistry drop down menu. We also must explicitly select the +/- Optical Activity from that drop down menu. These additional steps result in an accurate description of the molecule. Several of the structures above are absolute. Their Optical Activity defaults to unspecified, but can be selected using the information from SciFinder.

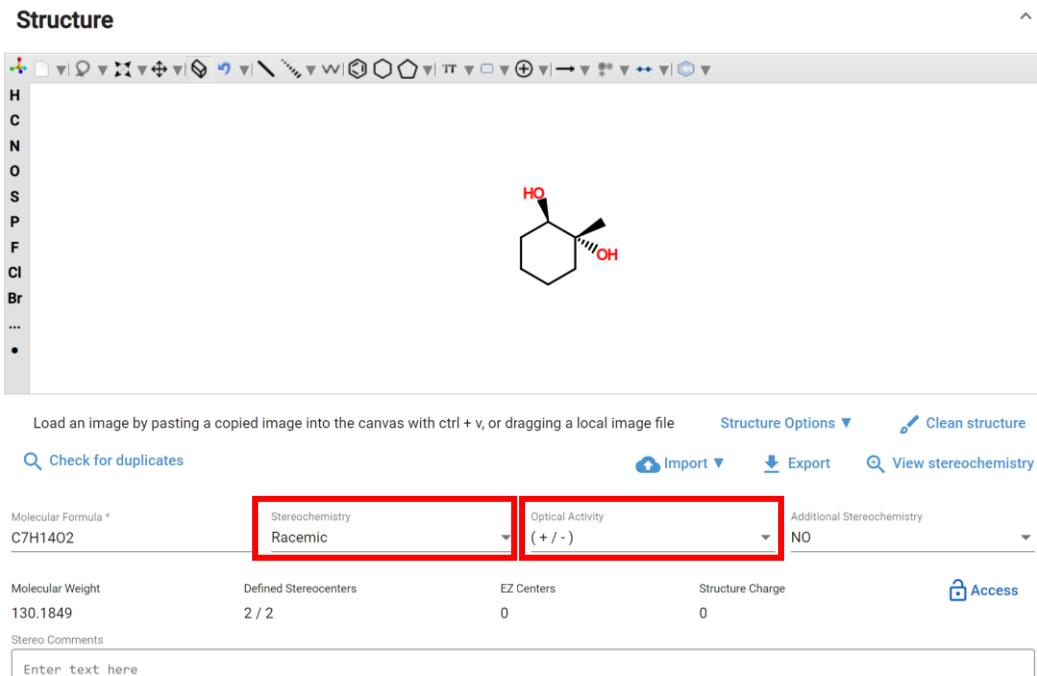


Figure 91 – Stereochemistry-Racemic and Optical Activity (+/-)

Molecule 6296-84-0 is the compound with no stereochemistry. In this case GSRS describes the molecule as a mixture of the +/- trans isomer 19534-08-0 and the +/- cis isomer 52718-65-7 as shown below. The latter structure must be registered first in GSRS. The mixture substance is then registered with the other two compounds as components.

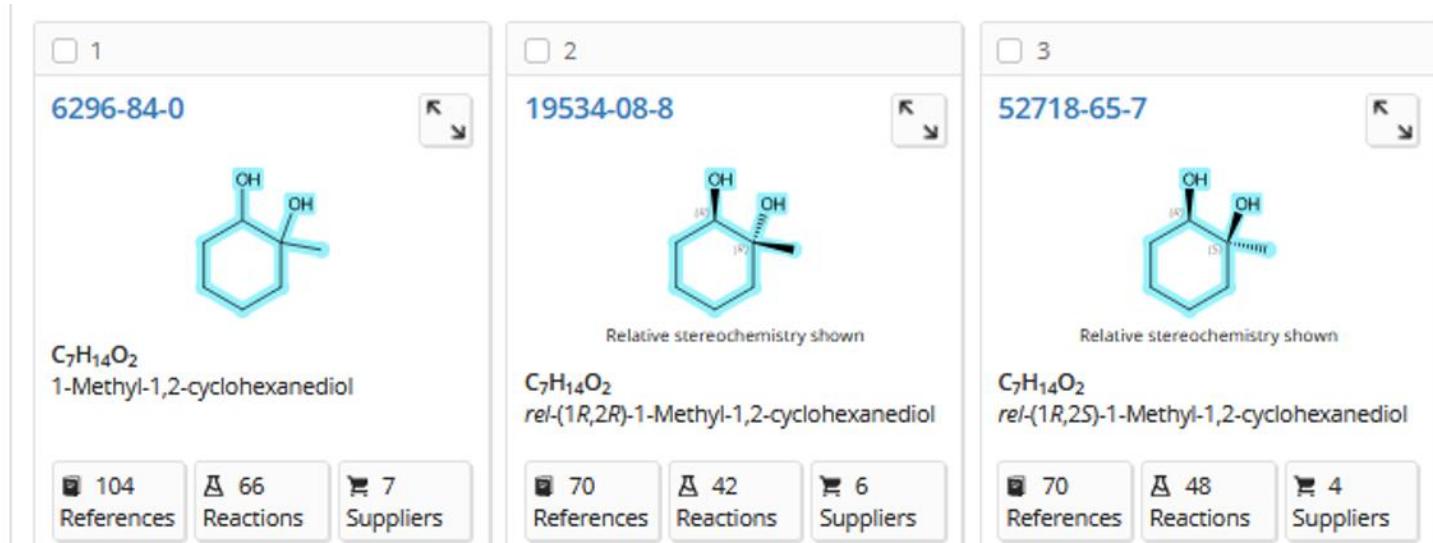


Figure 92 – Molecule 6296-84-0 is compound with no stereochemistry; mixture of +/- trans isomer 19534-08-0 and +/- cis isomer 52718-65-7

Complete registering a chemical Stereoisomers as previously described in [Register Chemicals](#).

GSRS User Guide (v3.x)

Register Proteins

Check for Duplicates

Global Search

Utilize the [Global Search options](#)

Sequence Search

Same as in [Sequence Search](#)

Protein Registration

1. After verifying the substance is not registered in GSRS via your Check for Duplicates, use the [Protein Registration form](#) to register the new substance.
 - a. User accounts with registration permissions will have access to the registration menus. If you believe your account is not properly configured, contact your site admin.
2. The protein registration form will be displayed. Section cards are collapsible to ease navigation, however the elements in this form are:
 - a. Overview - Definitional Information
 - b. Names
 - c. Protein Details
 - d. Subunits
 - e. Other links
 - f. Disulfide links
 - g. Glycosylation
 - h. Agent modification
 - i. Structural modification
 - j. Physical modification
 - k. Code
 - l. Relationships
 - m. Notes
 - n. Properties
 - o. References

Definitional Information

Same as in [Chemical registration - Overview Definitional Information](#)

Names

Same as in [Chemical registration - Names](#)

Protein Details

1. Add Protein Details for: Protein Type, Protein SubType, Sequence Origin, Sequence Type and Access level, all of which are driven by the controlled vocabulary of your instance
 - a. Access level should be set to protected if the sequence information is not public, even if name and target information is public

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Protein Details

protein subType
CYTOCHROME P450

Protein Type: ENZYME Sequence Origin: HUMAN Sequence Type: COMPLETE

Access

Created By: admin on Jun 25, 2021, 10:17:57 PM - Last Edited By: admin on Jun 25, 2021, 10:17:57 PM

Figure 93 - Protein Details Card

Subunits

Add subunits one at a time.

1. Press Add subunits button, the card will expand and have the following options:
 - a. Add Feature
 - b. Add Any Site Type
 - c. Subunit 1
 - i. Clean
 - ii. Save
 - iii. Convert
 - iv. Sequence Search
 - v. Copy Disulfide links
2. Paste the sequence into the canvas
3. Press the clean button, this tool removes numbers, spaces if any
4. Press the save button

Subunits

Add Subunits +

Add Feature + Add Any Site Type +

Subunit 1	save	clean	convert	sequence search	copy disulfide links
GRMKQIEDKI PNSKNEKALG NTKNDKOMVO	EEILSKIYHV RKINSWESSR VTVKVTSVPRD	ENEIARIKEL SGHSFLSNLH DTIIMKSARM	IGEDGVRERG LRNGELVIHE SCWSKDAEVG	PQRVAAHITG KGFYIYSQT IVSTYOGGTE	TRGRSNTLSS YFRFQEEIKE EIKENDRTEV

Figure 94 - Subunits

5. For some subunits, you may want to highlight specific regions of a protein that are of interest
 - a. Other registrars will easily identify these regions through the display highlights
 - b. Browse or Query users will have access to this information in the substance property of the Characteristic Attributes card
6. If you need to highlight a specific region, the subunit will need to be saved first (steps 1-4 of this section). Next, press the Add Feature button
7. In the Add/Modify Feature pop-up:
 - a. Add a Name for display

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- b. Select the range
- c. Press the Save button

Add / Modify Feature

Name: ISOLEUCINE "ZIPPER" (ILZ)

Site Range: 1_2 - 1_33 X

Click a new site to add an additional range

Key:

- C-Glycosylation
- O-Glycosylation
- N-Glycosylation
- Modification
- Disulfide Link
- Feature
- currently selected

Subunit 1

10	GRMKQI E DKI	EEILSKIYHV	ENEIARIKEL	IGEDGVRERG	PQRVAAHITG	50
60	TRGRSNTLSS	PNSKNEKALG	RKINSWESSR	SGHSFLSNLH	LRNGELVIE	100
110	KGFYYIYSQT	YFRFQEEIKE	NTKNDKQMVK	YIYKYTSYPD	PILLMKSARN	150
160	SCWSKDAEYGG	LYSIYQGGIF	ELKENDRIFV	SVTNEHLIDM	DHEASFFGAF	200
203	LVG					

Cancel
Save

Figure 95 - Subunits "Feature"

8. Your browser will display a message that reads Feature added under "Properties". Press OK to the browser notification.
9. The display is updated to highlight the region

Subunits

Add Feature +
Add Any Site Type +
Add Subunits +

	Subunit 1	edit	clean	convert	sequence search	copy disulfide links
10	GRMKQI E DKI	EEILSKIYHV	ENEIARIKEL	IGEDGVRERG	PQRVAAHITG	50
60	TRGRSNTLSS	PNSKNEKALG	RKINSWESSR	SGHSFLSNLH	LRNGELVIE	100
110	KGFYYIYSQT	YFRFQEEIKE	NTKNDKQMVK	YIYKYTSYPD	PILLMKSARN	150
160	SCWSKDAEYGG	LYSIYQGGIF	ELKENDRIFV	SVTNEHLIDM	DHEASFFGAF	200
203	LVG					

Add Subunit +

Figure 96 - Subunits Feature Highlight

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10. For some subunits, you will need to add Glycosylation, Disulfide, Modification, and Other link types from the subunit card.
11. Press the Add any site type button
12. In the Select Sites pop-up:
 - a. Select the link type from the drop-down (first)
 - b. Then, select the range
 - c. Press the Save button
 - d. Repeat for as many links as you would like to add
 - e. These can also be added in the [link type] card

Select Sites

Sites:

Select link type to add

Key:

C-Glycosylation	Other Link
O-Glycosylation	Modification
N-Glycosylation	Disulfide Link
Feature	currently selected

Subunit 1

G R M K Q I E D K I	E E I L S K I Y H V	E N E I A R I K E L	I G E D G V R E R G	P Q R V A A H I T G
60 T R G R S N T L S S	70 P N S T N E K A L G	80 R K I N S W E S S R	90 S G H S F L S N L H	100 L R N G E L V I H E
110 K G F Y Y I Y S Q T	120 Y F R F Q E E I K E	130 N T K N D K Q M V Q	140 Y I Y K Y T S Y P D	150 P I L L M K S A R N
160 S T W S K D A E Y G G	170 L Y S I Y Q G G I F	180 E L K E N D R I F V	190 S V T N E H L I D M	200 D H E A S F F G A F
203 L V G				

Figure 97 - Subunits Select Sites pop-up

13. To verify, scroll to the Glycosylation card.
14. Press the Add subunits button to add more subunits, or continue to another card.

Other Links

Add other links one at time.

1. Press the Add Other Links button
2. Select the Sequence Type drop-down to identify the linkage type
3. Press the  pencil button to select sites to display

GSRS User Guide (v3.x)

Other Links

Add Other Links

Sequence Type

Sequence Type Coordination Compound

link

link

1_424; 1_426; 1_428; 1_430; 1_432

Created By: admin on Jun 27, 2021, 12:29:19 AM - Last Edited By: admin on Jun 27, 2021, 12:29:19 AM

Figure 98 - Other Links - Linkage Type

4. A new pop-up will be displayed with the populated subunits.
 - a. Select the subunits and the site box will populate.
 - b. You can continue for each pair, press Save

Select Sites

Sites:

1_424; 1_426; 1_428; 1_430

Key:

C-Glycosylation	Other Link
O-Glycosylation	Modification
N-Glycosylation	Disulfide Link
Feature	currently selected

Subunit 1

F N L D A E A P A V	L S G P P G S F F G	F S V E F Y R P G T	D G V S V L V G A P	K A N T S Q P G V L
Q G G A V Y L C P W	G A S P T Q C T P I	E F D S K G S R L L	E S S L S S E G E	E P V E Y K S L Q W
F G A T V R A H G S	S I L A C A P L Y S	W R T E K E P L S D	P V G T C Y L S T D	N F T R I L E Y A P
C R S D F S W A A G	Q G Y C Q G G F S A	E F T K T G R V V L	G G P G S Y F W Q G	Q I L S A T Q E Q I
A E S Y Y P E Y L I	N L V Q G Q L Q T R	Q A S S I Y D D S Y	L G Y S V A V G E	S G D D T E D F V A
G V P K G N L T Y G	Y V T I L N G S D I	R S L Y N F S G E Q	M A S Y F G Y A V A	A T D V N G D G L D
D L L V G A P L L M	D R T P D G R P Q E	V G R V Y V Y L Q H	P A G I E P T P T L	T L T G H D E F G R
F G S S L T P L G	L D Q D G Y N D V A	I G A P F G G E T Q	Q G V V F V F P G G	P G G L G S K P S Q
V L Q P L W A A S H	T P D F F G S A L R	G G R D L D G N G Y	P D L I V G S F G V	D K A V V Y R G R P
I V S A S A S L T I	F P A M F N P E E R	S C S L E G N P V A	C I N L S F C L	S G K H V A D S I G

Cancel

Save

Figure 99 - Other Links - Site Selector

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Disulfide Links

Add disulfide links one at a time with the pre-populated sites for pairing

1. Press the Add Disulfide Links button

The screenshot shows the 'Disulfide Links' page. At the top right is a blue button labeled 'Add Disulfide Links' with a plus sign. Below it, a red box highlights the 'Add Multiple Links' button. To its right, the text 'Number of unspecified Cysteine residues: 7' is displayed. In the center, there are two dropdown menus labeled 'To' and 'From' with a red box around them, and a pencil icon. At the bottom left is a 'Delete All Links' button.

Figure 100 –Add Disulfide Links

2. There are several options to add disulfide links:

- a. Use the To and From drop-downs to select sites, one pair at a time



- b. Use the pencil icon to select sites which will populate in the drop-down menu, one pair at a time
- c. Press the Add Multiple Links button
 - i. The Select Sites window will pop-up
 - ii. Select pairs of sites which will be updated in the Links section
 - iii. Press Save and return to the registration form

The screenshot shows the 'Select Sites' window. It includes a legend for link types: C-Glycosylation (grey), O-Glycosylation (red), N-Glycosylation (blue), Feature (magenta), Other Link (purple), Modification (green), Disulfide Link (yellow), and currently selected (cyan). The main area displays a sequence alignment for 'Subunit 1' with residue numbers 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290, 300, 310, 320, 330, 340, 350, 360, 370, 380, 390, 400, 410, 420, 430, 440, 450, 460, 470, 480, 490, 500. A red box highlights the 'Save' button at the bottom left.

Figure 101 –Add Multiple Disulfide Links

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3. Repeat for each pair
4. At any time, if you need to start over, press the Delete all links button

Glycosylation

1. Press Glycosylation to expand the card
2. Select the Glycosylation Type – optional, based on the controlled vocabulary of your instance

3. For C, N and O Glycosylation Sites, press  and the current sequence selector will be displayed

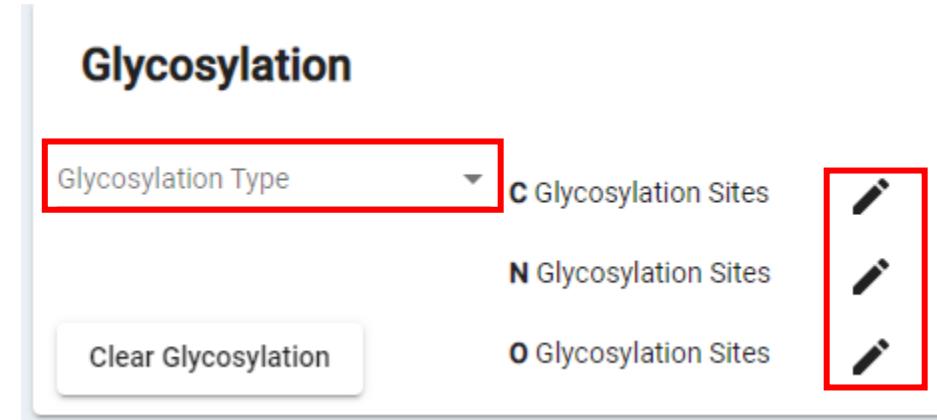


Figure 102 - Glycosylation

4. Sites should be in the form of subunit_residue, use hyphen “-” to indicate a range, this will be automatically applied if you select the sites within the pop-up window.
5. Press the Save button

Select Sites

Sites:

Key:

C-Glycosylation	Other Link
O-Glycosylation	Modification
N-Glycosylation	Disulfide Link
Feature	Currently Selected

Subunit 1

10	20	30	40	50
M D I L C E E N T S	L S S T T N S L M Q	L N D D T R L Y S N	D F N S G E A N T S	D A F N W T V D S E
60 N R T N L S C E G C	60 L S P S C L S L L H	70 L Q E K N W S A L L	80 T A V V I I L T I A	90 G N I L V I M A V S
110 L E K K L Q N A T N	110 Y F L M S L A I A D	120 M L L G F L V M P V	130 S M L T I L Y G Y R	140 W P L P S K L C A V
160 W I Y L D V L F S T	160 A S I M H L C A I S	170 L D R Y V V A I Q N P	180 I H H S R F N S R T	190 K A F L K I I A V W
210 T I S V G I S M P I	210 P V F G L Q D D S K	220 V F K E G S C L L A	230 D D N F V L I G S F	240 V S F F I P L T I M
260 V I T Y F L T I K S	260 L Q K E A T L C V S	270 D L G T R A K L A S	280 F S F L P Q S S L S	290 S E K L F Q R S I H
310 R E P G S Y T G R R	310 T M Q S I S N E Q K	320 A C K V L G I V F F	330 L F V V M W C P F F	340 I T N I M A V I C K
360 E S C N E D V I G A	360 L L N V F V W I G Y	370 L S S A V N P L V Y	380 T L F N K T Y R S A	390 F S R Y I Q C Q Y K
410 E N K K P L Q L I L	410 V N T I P A L A Y K	420 S S Q L Q M G Q K K	430 N S K Q D A K T T D	440 N D C S M V A L G K
460 Q H S E E A S K D N	460 S D G V N E K V S C	470 V		450

[Cancel](#) [Save](#)

Figure 103 - Glycosylation Site Selector

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Agent Modifications

The modifications without sufficient information to capture as structural modifications should be added as agent modifications.

1. Press Add Agent Modifications button to expand the card, the following fields can be populated:
 - a. Agent Substance – substance selector, search for other substance records in your instance
 - b. Modification Process – drop-down values from the controlled vocabulary of your instance
 - c. Modification Type – drop-down values from the controlled vocabulary of your instance
 - d. Modification Role – drop-down values from the controlled vocabulary of your instance
 - e. Amount – pop-up window to enter amount parameters, press Save after adding values
 - f. Group – text box
2. Repeat for additional agent modifications

Agent Modifications

[Add Agent Modifications](#)

	Agent Substance	Modification Process	Modification Type	Modification Role
	P-ISOTHIOCYANATOBENZYL- DESFERROXAMINE	RADIOLABELLING	RADIOLABEL	CHELATING AGENT
	Amount			Group *
	<input type="text" value="1"/>			

P-ISOTHIOCYANATOBENZYL-
DESFERROXAMINE

Created By: admin on Jun 26, 2021, 4:54:03 PM - Last Edited By: admin on Jun 26, 2021, 4:54:03 PM

Figure 7 - Agent Modifications

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Structural Modifications

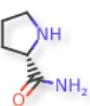
The common modifications are Amino Acid Removal, Amino acid replacement, Ligand Binding, Metal Binding and moiety.

1. To add a structural modification, press the Add Structural Modification button to expand the card, the following fields should be populated:
 - a. Molecular Fragment – substance selector, search for other substance records in your instance
 - b. Modification Type – drop-down values from the controlled vocabulary of your instance
 - i. Moiety: Use moiety modification for salts or solvates
 - ii. Ligand Binding or Metal Binding: Use to describe chelates, metal binding sites
 - c. Sites – from the site selector pop-up, select the site and press Save to return to the registration form
 - d. Extent – select partial or complete
 - i. If Partial press the pencil button and enter the amount details in the Edit Parameter pop-up, press Save to apply the amounts and return to the registration form
 - e. Location – drop-down values from the controlled vocabulary of your instance; If modification is residue specific, sites will disappear and list of amino acids will appear. Selected the correct amino acid
 - f. Amount – pop-up window to enter amount parameters, press Save after adding values
 - g. Group – text box

Structural Modifications

[Add Structural Modifications](#)

Molecular Fragment



PROLINAMIDE

Modification Type

Amino Acid Replacement

Sites

1_32

Extent

Complete

Location

C-TERMINUS

Group *

1

Amount

Created By: admin on Jun 25, 2021, 8:52:34 PM - Last Edited By: admin on Jun 25, 2021, 8:52:34 PM

Figure 105 - Structural Modifications

2. Select the Fragment via substance search

- a. In some instances, the fragment substance may not be included in GSRS. Below is an example to register a fragment for Amino Acid Replacement
 - i. Identify the substance type and register it using appropriate registration form
 - ii. Draw the structure to show clearly how the modifying group would connect to the amino acid
 - iii. If the modifying group has multiple connecting points consider it as multiple modifications and register all the possible isomers.
1. Ex: Two lysine modifications and two leucine modifications for this example

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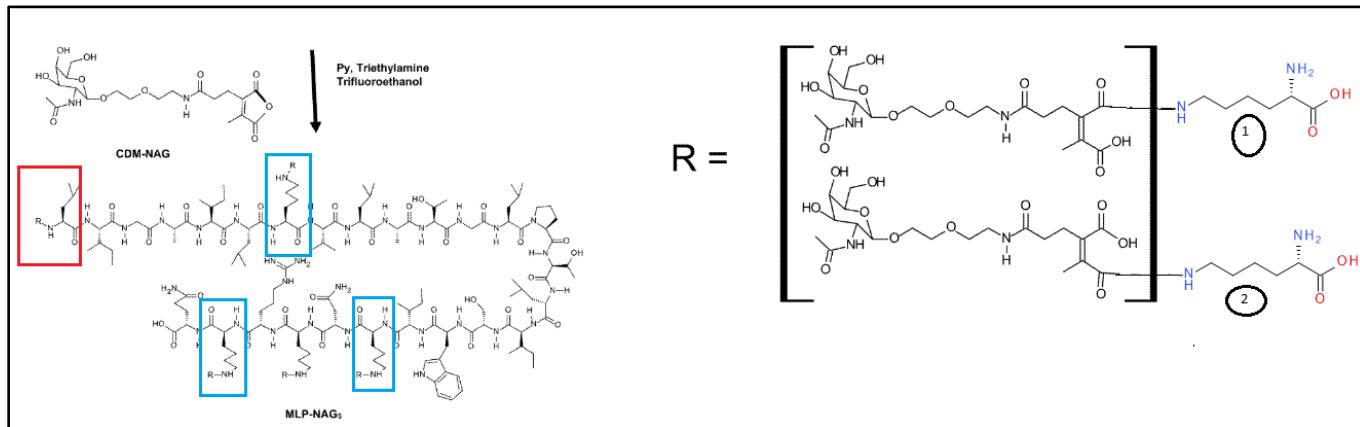


Figure 8 - Structural Modifications – Amino Acid Replacement Fragment

3. Select the location type:

- If the Location Type is Residue-Specific, the Residue Modified field will be displayed. Select an option from the controlled vocabulary of your instance

Structural Modifications

Add Structural Modifications +

<input checked="" type="checkbox"/> Molecular Fragment	Modification Type: Amino Acid Replacement	Residue Modified: Lysine ×
	Extent	Location: RESIDUE-SPECIFIC
	Amount	Group *: 1 Access
LYSINE, THIOUREA-BENZYL-DEFEROXAMINE-(89)ZR	Created By: admin on Jun 27, 2021, 1:13:43 AM	- Last Edited By: admin on Jun 27, 2021, 1:13:43 AM

Figure 107 - Structural Modifications - RESIDUE-SPECIFIC Location Type

- If the Location Type is N-terminus, C-terminus or Site Specific, the Site field will be displayed. Press the pencil button which will display the site selector pop-up, select the sites and press Save to return to the registration form

Structural Modifications

Add Structural Modifications +

<input checked="" type="checkbox"/> Molecular Fragment	Modification Type: Amino Acid Replacement	Sites: 1_1 -pencil
N-(MPEG-20000-PROPYL)-METHIONINE	Extent: Partial	Location: N-TERMINUS
	Amount	Group: 1 Access
MOLE PERCENT 100 % (average)		
Created By: admin on Jun 26, 2021, 4:42:17 PM - Last Edited By: admin on Jun 26, 2021, 4:42:17 PM		

Figure 108- Structural Modification – N-TERMINUS Location Type

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4. Repeat for additional structural modifications

Physical Modifications

1. To add a Physical Modification, press Add Physical Modifications button to expand the card, the following fields should be populated:
 - a. Modification Role – drop-down values from the controlled vocabulary of your instance
 - a. Parameters – in the pop-up window, name the parameter, ex: Temperature and complete the amount fields
 - i. Press save to apply the parameters and return to the registration form
 - b. Group – text box
2. Repeat for additional physical modifications

Physical Modifications		
Modification Role <input type="button" value="x"/> Sterilization	Parameters <input type="button" value="+"/> <input type="button" value="x"/> TEMPERATURE - 121 °C (average) <input type="button" value="edit"/>	Group * 1

Created By: admin on Jun 25, 2021, 9:20:26 PM - Last Edited By: admin on Jun 25, 2021, 9:20:26 PM

Figure 109 - Physical Modifications

Codes

Same as in [Chemical registration - Codes](#)

Relationships

Same as in [Chemical registration - Relationships](#)

Notes

Same as in [Chemical registration - Notes](#)

Properties

Same as in [Chemical registration - Properties](#)

References

Same as in [Chemical registration - References](#)

Submit

Same as in [Chemical registration - Submit](#)

Register Nucleic Acids

Check for Duplicates

There are several options to check for duplicates (using all will ensure an exhaustive search).

1. Search by name/code (CAS RN or another identifiers) using:
 - a. Global Search
 - b. Advanced Search
2. Sequence search

Global Search

Same as in [Global Search](#)

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Sequence Search

Same as in [Sequence Search](#)

Nucleic Acid Registration

1. After verifying the substance is not registered in GSRS via your Check for Duplicates, use the [Nucleic Acid Registration form](#) to register the new substance.
 - a. User accounts with registration permissions will have access to the registration menus. If you believe your account is not properly configured, contact your site admin.
2. The nucleic acid registration form will be displayed. Section cards are collapsible to ease navigation, however the elements in this form are:
 - a. Overview - Definitional Information
 - b. Names
 - c. Nucleic Acid Classification
 - d. Subunits
 - e. Links
 - f. Sugars
 - g. Physical modifications
 - h. Agent modifications
 - i. Structural modifications
 - j. Codes
 - k. Relationships
 - l. Properties
 - m. Notes
 - n. References

Overview - Definitional Information

Same as in [Chemical registration - Overview Definitional Information](#)

Names

Same as in [Chemical registration - Names](#)

Nucleic Acid Classification

1. Select Nucleic Acid Classification to expand the card
2. Select Nucleic Acid Type, Nucleic Acid Subtype, Sequence Origin, Sequence Type, which are all drop-down options driven by the GSRS Controlled Vocabulary
3. Access level should be protected if the sequence information is not public, even if name and target information is public

Nucleic Acid Classification

Nucleic Acid Type OLIGONUCLEOTIDE	Nucleic Acid SubType ANTI-SENSE	Sequence Origin HUMAN	Sequence Type COMPLETE	Access
--------------------------------------	------------------------------------	--------------------------	---------------------------	--------

Created By: admin on Jun 26, 2021, 6:10:40 PM - Last Edited By: admin on Jun 26, 2021, 6:10:40 PM

Figure 110 - Register Nucleic Acid - Classification

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Subunits

Same as in [Protein registration - Subunits](#)

Links

1. Select the Add Links button
2. The Links card will expand and display the number of remaining links, Sequence Type drop-down, add remaining [#] sites button, pencil edit button for link

Links

Add Links

Remaining Links: 19

Sequence Type add remaining 19 sites

Figure 111 - Register Nucleic Acid – Add Links

3. Select a Sequence Type from the controlled vocabulary
4. Select the add remaining [#] sites button
5. If more than one link, press the for the site selector pop-up.
 - a. Either select or type in the text box in the format subunit_residue; use “-” for a range
 - b. Press the Save button to update the link’s site list and be returned to the registration page

Select Sites

Sites:
1_20-1_21; 2_20-2_21

Subunit 1

AUG GAA AUACU CU UGG GUUA C T

Subunit 2

GU ACC CAAG A GU AUU CC CAU T

Cancel Sequence Type

1 2 1 5 1 6 1 12 1 14 1 17 1 19 2 7 2 17

Figure 112 - Register Nucleic Acid – Links Select Sites

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6. Repeat for additional links

Sugars

1. Press the Add Sugars button
2. If the nucleic acid has one sugar, press Add remaining [#] sites button and it will auto populate all the sugars

Sugars

Add Sugars

Remaining Sugars: 42

Sequence Type sugar

Figure 113 - Register Nucleic Acid - Sugars

3. If more than one sugar, Click on for the site selector pop-up.
 - a. Either select or type in the text box in the format subunit_residue; use “-” for a range
 - b. Press the Save button to update the sugars and be returned to the registration form.

Select Sites

Sites:

Subunit 1

A **U** G G **A** A U A C U 10 C **U** U **G** G **U** U A **C** T 20 T 21

Subunit 2

G U A A C C **A** A G A 10 G U A U U C **C** A U T 20 T 21

[Cancel](#) [Save](#)

Figure 114 - Register Nucleic Acid - Sugars - Site Selector

4. Repeat for additional sugars

Agent Modifications

Same as in [Protein registration - Agent Modifications](#)

GSRS User Guide (v3.x)

Structural Modifications

Follow the steps in the [Protein registration – Structural Modifications](#).

The common structural modifications for nucleic acids are:

- Nucleoside substitution - 5'-terminus location type
- Nucleotide substitution - invert sugars with 3'-3' linkages
- Nucleobase substitution - for inner base modifications

Note: Nucleoside substitution has been using for both 5' and inner base modifications to remove the ambiguity of the connectivity between base and sugar. This practice may have to continue with unusual bases

Molecular Fragment
Modification Type: NUCLEOSIDE SUBSTITUTION
Extent: Location: 5'-TERMINUS
Amount:
2'-O-(2-METHOXYETHYL)-5-METHYLURIDINE
Created By: admin on Jun 26, 2021, 11:05:11 PM - Last Edited By: admin on Jun 26, 2021, 11:05:11 PM
Group *: 1
Access

Figure 115 - Register Nucleic Acid - Structural Modifications

Fragment registration for Nucleoside/nucleotide substitution:

Follow the steps in the [Protein Registration – Fragment](#) section to identify the substance type and register it using appropriate registration form. Draw the structure to show clearly how modifying group would connect to the nucleoside/nucleotide.

Physical Modifications

Same as in [Protein registration - Physical Modifications](#)

Codes

Same as in [Chemical registration - Codes](#)

Relationships

Same as in [Chemical registration - Relationships](#)

Notes

Same as in [Chemical registration - Notes](#)

Properties

Same as in [Chemical registration - Properties](#)

References

Same as in [Chemical registration - References](#)

Submit

Same as in [Chemical registration - Submit](#)

Register Polymers

Check for Duplicates

There is only one systematic way to search for polymer duplicates, using the Global Search feature.

Global Search

Same as in [Global Search](#)

GSRS User Guide (v3.x)

Polymer Registration

1. After verifying the substance is not registered in GSRS via your Check for Duplicates, use the [Polymer Registration form](#) to register the new substance.
 - a. User accounts with registration permissions will have access to the registration menus. If you believe your account is not properly configured, contact your site admin.
2. The polymer registration form will be displayed. Section cards are collapsible to ease navigation, however the elements in this form are:
 - a. Overview - Definitional Information
 - b. Names
 - c. Polymer Classification
 - d. Monomers
 - e. Idealized Structure
 - f. Structural Units
 - g. Agent Modifications
 - h. Structural Modifications
 - i. Physical Modifications
 - j. Codes
 - k. Relationships
 - l. Notes
 - m. Properties
 - n. References

Definitional Information

Same as in [Chemical registration - Overview Definitional Information](#)

Names

Same as in [Chemical registration - Names](#)

Polymer Classification

1. Select Polymer Classification to expand the card
2. Select:
 - a. Polymer Class - drop-down driven by the CV
 - b. Source Type - drop-down driven by the CV
 - c. Parent Substance – substance search/selector
 - i. Use the substance search box to search and select the record of the Parent Substance which should be pre-registered
 - ii. If the Parent Substance is not in GSRS, determine the substance type and register the new record
 - d. polymer subclass – multi-select drop-down driven by the CV
 - e. Polymer Geometry - drop-down driven by the CV
3. Access level should be protected if the defining information is not public, even if the name is public.

GSRS User Guide (v3.x)

Polymer Classification

Polymer Class: Copolymer Source Type: Biosynthetic Parent Substance: 
polymer subclass: Random Polymer Geometry: Linear

Access:  Access

Created By: admin on Apr 3, 2019, 8:25:32 PM - Last Edited By: admin on Apr 3, 2019, 8:25:32 PM

Figure 116 - Polymer Registration - Polymer Classification

Monomers

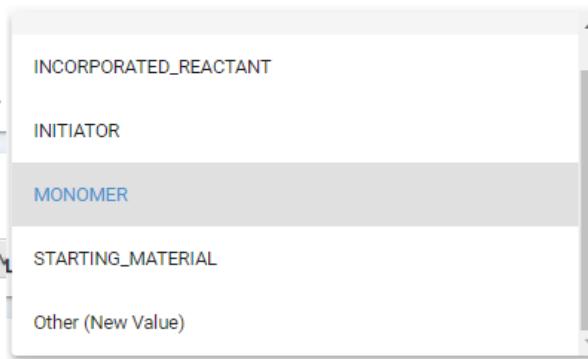
The monomers should be preregistered.

1. Select Monomers to expand the card.
2. Select
 - a. Monomer Substance - substance search/selector
 - b. Monomer Type - drop-down driven by the CV

Monomers

Monomer Substance: 
ETHYLENE OXIDE
Created By: admin on Apr 4, 2019, 6:00:38 AM

Idealized Structure

Monomer Type: 
INCORPORATED_REACTANT
INITIATOR
MONOMER
STARTING_MATERIAL
Other (New Value)

Amount:  MOL RATIO 15 (average)
Defining:

Figure 117 - Polymer Registration – Monomers

3. To add the pop-up window will be displayed to Edit Parameter
4. The amount type should be Mol Ratio or Weight ratio.
 - a. The amount could be a range, average or limits.
 - b. The units should be per polymer for homopolymers and no units for copolymers.
5. Select Save and you are returned to the Polymer registration form and the amount details are displayed on the Monomers card.

amount, select on  . A

GSRS User Guide (v3.x)

Edit Parameter

Type *	Average
MOL RATIO	15
Low	High
Low Limit	High Limit
Units	Non-numeric V...

Cancel **Save**

Figure 118 - Polymer Registration - Monomers - Amount

Idealized Structure

Follow the steps to import the structure similar to the [chemical registration structure](#).

- The bracket types [] can be found in the JS Draw Canvas tool bar
 - o SRUs can be labelled as you draw them
- Free sites can be used to show the possible sites of substitution. To create free sites:
 - o Bring the cursor to the site
 - o Do not select the site, but on hover the site should high in green
 - o Use the keyboard to hold Shift and * together

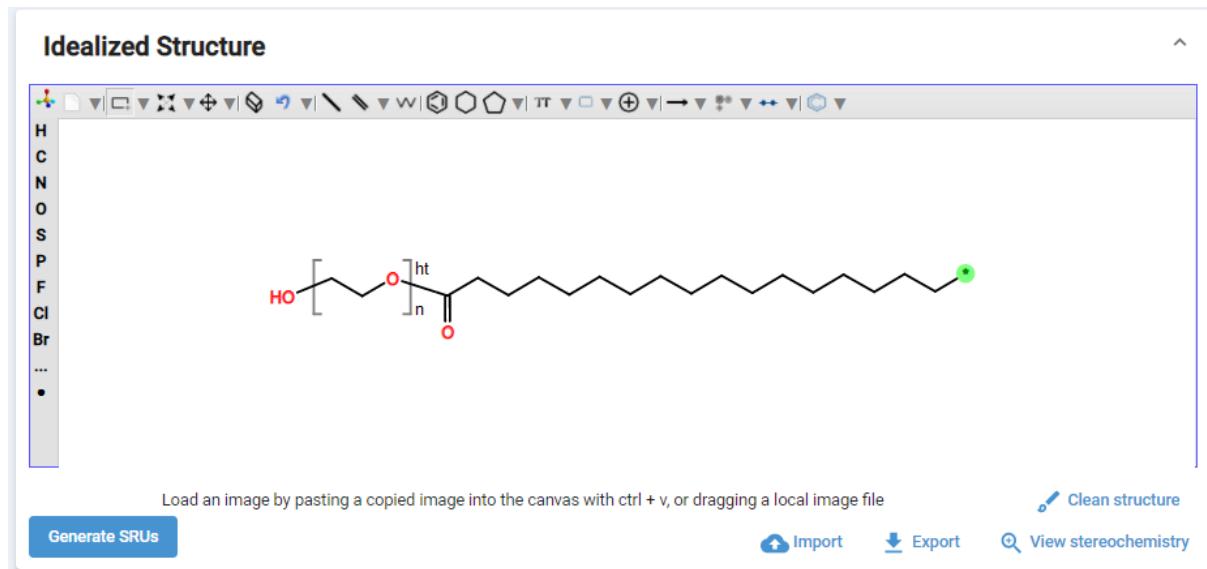


Figure 119 - Polymer Registration - Brackets and Free Site

Structural Units

1. From the Idealized Structure canvas, select the Generate SRUs button
 - a. The values can be manually updated

GSRS User Guide (v3.x)

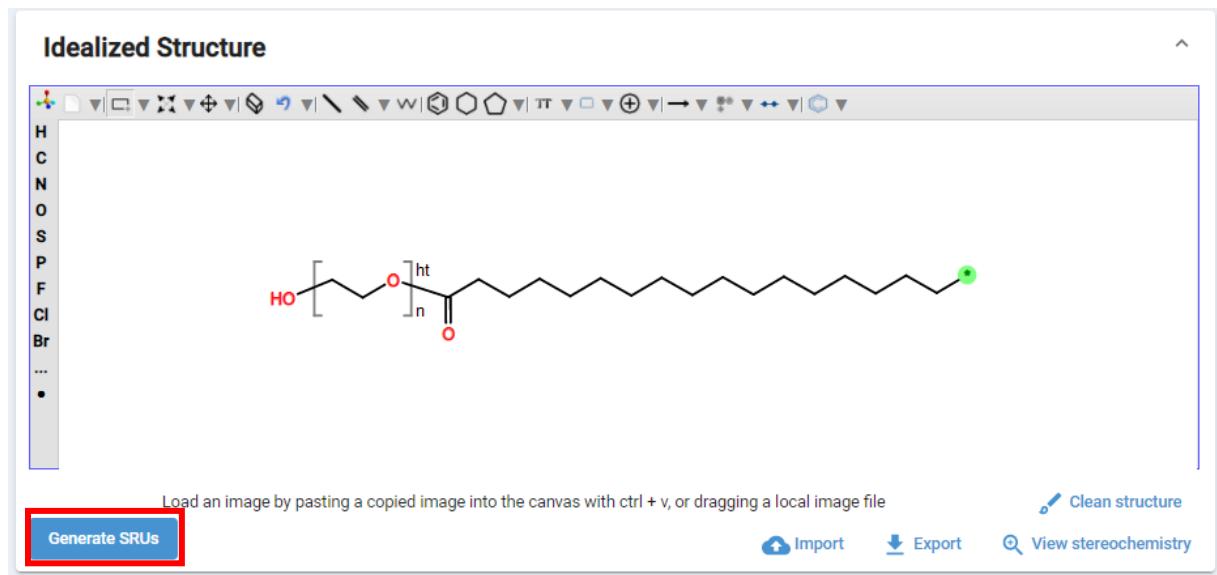


Figure 120 - Polymer Registration – Generate SRUs

2. Select Structural Units to expand the card

Structural Units

SRU Type: SRU:HEAD-TO-TAIL Label: n attachment count: 5
Amount: + Connectivity: n_R3-n_R4; n_R4-n_R3;

SRU Type: SRU:HEAD-TO-TAIL Label: A attachment count: 1
Connectivity:

SRU Type: SRU:HEAD-TO-TAIL Label: B attachment count: 1
Connectivity:

Figure 121 - Polymer Registration - Structural Units

3. Each Structural Unit has fields for:
 - a. SRU Type – drop-down driven by the CV
 - b. Label
 - c. Attachment Count – computed, cannot change
 - d. Amount - to add the amount, select on . A pop-up window will be displayed to Edit Parameter
 - i. Type – set to:
 1. Degree of polymerization for structural repeat units

GSRS User Guide (v3.x)

2. Degree of Substitution for substituents.
 - ii. The amount can be a range, average or low/high limits.
 - iii. Any additional information can be captured under Non numerical values
 - iv. Select Save to be returned to the Polymer Registration form
 - e. Connectivity

Edit Parameter

Type * Average
 DEGREE OF ... ▾ 10 Low High Low Limit High Limit Units per polymer ▾ Non-numeric V...

[Cancel](#) [Save](#)

 	SRU Type End Group	Label * B	attachment count 1
Amount 	Connectivity B_R4-A_R2; B_R4-A_R3;		

DEGREE OF SUBSTITUTION 4 per polymer (average)

Figure 122 - Polymer Registration - Structural Unit – Amounts

Agent Modifications

Same as in [Protein registration - Agent Modifications](#)

Physical Modifications

Same as in [Protein registration - Physical Modifications](#)

Codes

Same as in [Chemical registration - Codes](#)

Relationships

Same as in Chemical registration - Relationships

Notes

Same as in Chemical registration - Notes

Properties

Same as in Chemical registration - Properties

References

Same as in Chemical registration - References

[Submit](#)

Same as in Chemical registration - Submit

Same as in Rint

Register Structurally Divergent

Check for Duplicates

There is only one systematic

Global Search

Same as in [Search](#)

GSRS User Guide (v3.x)

Structurally Diverse Registration

1. After verifying the substance is not registered in GSRS via your Check for Duplicates, use the [Structurally Diverse Registration form](#) to register the new substance.
 - a. User accounts with registration permissions will have access to the registration menus. If you believe your account is not properly configured, contact your site admin.
2. The structurally diverse registration form will be displayed. Section cards are collapsible to ease navigation, however the elements in this form are:
 - a. Overview - Definitional Information
 - b. Names
 - c. Source Material
 - d. Parts and Fractions
 - e. Agent modification
 - f. Structural modification
 - g. Physical modification
 - h. Code
 - i. Relationships
 - j. Notes
 - k. Properties
 - l. References

Overview Definitional Information

Same as in [Chemical registration - Overview Definitional Information](#)

Names

Same as in [Chemical registration - Names](#)

Source Material

1. Select Source Material to expand the card
2. Select the Source Material Class and Source Material Type
 - a. If you select Source Material Class = Organism, you will also have the opportunity to add the Source Material State

The screenshot shows the 'Source Material' section of the registration form. The 'Source Material' card is expanded. On the left, the 'Source Material Class' dropdown shows 'ORGANISM' selected. In the center, the 'Source Material Type' dropdown shows 'BACTERIUM' selected. On the right, the 'Source Material State' dropdown shows 'LIVE' selected. There are three radio buttons at the top right labeled 'Whole', 'Part/Fraction', and 'Full Fields'. An 'Access' button is also present.

Figure 123 - Structurally Diverse Registration - Source Material

3. There are three radio buttons to indicate record type and drive the display of the Parts and Fractions card.

GSRS User Guide (v3.x)

- a. Whole - whole organisms are plants, animals, microorganism, virus, modified virus, cell lines, modified cell lines. The Organism Details card will now include options to capture Family, Genus, Species, Author, Infra Specific Type, Infra Specific Name, Developmental Stage, Hybrid Paternal Organism and Hybrid Maternal Organism are captured
- b. Part/Fraction - additional cards for Organism Details appear as part of the form to capture Source Material Parent, Part(s) Part Location, Fraction Name, and Fraction Material Type
- c. Full Fields – structurally diverse substances will not be saved with both sets of fields. This option is for display during edit ONLY in order to view all available fields. Once changes are submitted, the record type will be saved as the original record type – either Whole or Part/Fraction.

Parts and Fractions

1. Select Parts and Fractions to expand the card
2. Whole Fields include:
 - a. Family – free text
 - b. Genus – free text
 - c. Species – free text
 - d. Author – free text
 - e. Infraspecific Type – drop-down driven by the CV
 - f. Infraspecific Name – free text
 - g. Developmental Stage – drop-down driven by the CV
 - h. Hybrid Paternal/Maternal Organism – substance search
3. Part/Fraction fields include:
 - a. Source Material Parent – substance search
 - b. Part(s) – multi-select driven by the CV
 - c. Part Location – drop-down driven by the CV
 - d. Fraction Name – free text
 - e. Fraction Material Type – drop-down driven by the CV
 - f. Developmental Stage – drop-down driven by the CV
4. If the record was switched from one Whole to Part or vice versa and data persists, select Full Fields to view and edit all the fields at once and clean up the data. Note: The record type will be saved as the original, either Whole or Part/Fraction.

GSRS User Guide (v3.x)

Organism Details

Whole Fields

Family *	Genus *	Species *	Author *
RUTACEAE	CITRUS	AURANTIUM	L.

Infra Specific Type	▼	Infra Specific Name *	Developmental Stage	▼
---------------------	---	-----------------------	---------------------	---

Hybrid Paternal Organism



CITRUS RETICULATA WHOLE

Hybrid Maternal Organism



CITRUS MAXIMA WHOLE

Part/Fraction Fields

Source Material Parent	🔍	Part(s)	Part Location
		WHOLE X	▼
		Fraction Name	Fraction Material Type

Figure 124 - Structurally Diverse Registration - Organism Details

Agent Modifications

Same as in [Protein registration - Agent Modifications](#)

Structural Modifications

Follow the steps in the [Protein registration – Structural Modifications](#).

Physical Modifications

Same as in [Protein registration - Physical Modifications](#)

Modifications for Gene and Cell Therapies Example

Gene therapy and cell therapy are rapidly evolving fields for treatment. These are complex modified biological materials and captured structurally diverse substances. All the modifications should be captured under these modifications.

Example: Ad5 [E1-, E2b-]-HER2/Neu vaccine ETBX-021: A cancer vaccine composed of a genetically engineered, replication-defective oncolytic adenovirus serotype 5 (Ad5) vector, in which the E1, E2b and E3 genes are deleted, that encodes a modified version of the tumor-associated antigen (TAA) human epidermal growth factor receptor 2 (HER2/neu; ErbB-2; ERBB2), with potential antineoplastic activity.

<https://www.cancer.gov/publications/dictionaries/cancer-drug/def/793072>

This was registered as structurally diverse whole organism with structural modifications.

GSRS User Guide (v3.x)

Source Material

Source Material Class ORGANISM	Source Material Type VIRUS	Source Material State LIVE GENETICALLY MODIFI... add	<input checked="" type="radio"/> Whole	<input type="radio"/> Part/Fraction	<input type="radio"/> Full Fields	
-----------------------------------	-------------------------------	---	--	-------------------------------------	-----------------------------------	--

Created By: admin on Feb 7, 2021, 11:23:52 PM - **Last Edited By:** admin on Feb 7, 2021, 11:23:52 PM

Organism Details

Family * ADENOVIRIDAE	Genus * MASTADENOVIRUS	Species * Human mastadenovirus C	Author *
Infra Specific Type SEROTYPE	Infra Specific Name * TYPE 5	Developmental Stage	

Hybrid Paternal Organism Hybrid Maternal Organism

Created By: admin on Feb 7, 2021, 11:23:52 PM - **Last Edited By:** admin on Feb 7, 2021, 11:23:52 PM

Figure 125 - Structurally Diverse Registration - Cancer Vaccine ETBX-021 Example

Most of the time, the sequence of deleted gene is not available. The expressed protein from that gene could be available. The available information has been captured when registering ETBX-021.

GSRS User Guide (v3.x)

Structural Modifications

[Add Structural Modifications](#)

Molecular Fragment  **Modification Type** PROTEIN NOT EXPRESS... [add](#)

Extent: Complete Location: viral genes early 1 (not i... [add](#)

Amount: 

Sites  Group * 1  Access

Created By: admin on May 20, 2021, 9:25:40 AM - **Last Edited By:** admin on May 20, 2021, 9:25:40 AM

Molecular Fragment  **Modification Type** VECTOR EXPRESSED P... [add](#)

Extent: Location: UNKNOWN

Amount: 

Sites  Group * 1  Access

Created By: admin on May 20, 2021, 9:25:40 AM - **Last Edited By:** admin on May 20, 2021, 9:25:40 AM

Figure 126 - Structurally Diverse Registration – Structural Modifications for ETBX-021

Codes

Same as in [Chemical registration - Codes](#)

Relationships

Same as in [Chemical registration - Relationships](#)

Notes

Same as in [Chemical registration - Notes](#)

Properties

Same as in [Chemical registration - Properties](#), Note that, capturing a Property may be important for cell/gene therapy drugs.

GSRS User Guide (v3.x)

The screenshot shows the 'Properties' section of the GSRS interface. At the top, there is a search bar with 'Tmax (not in CV)' and a dropdown menu for 'Property Type' set to 'PHARMACOKINETIC (not in CV)'. Below this, there is a 'Parameters' section with a note 'TISSUE MEASURED - peripheral blood'. Under 'Amount', there are fields for 'Type' (set to 'Average'), 'Low' (9), 'High' (10), 'Units' (days), and 'Non-numeric Value' (maximal expansion). A 'References' section shows one entry, with buttons for 'Create new' and 'Reuse'. The top right corner has a 'Add Properties' button.

Figure 127 - Structurally Diverse Registration – Property for TISAGENLECLEUCEL

References

Same as in [Chemical registration - References](#)

Submit

Same as in [Chemical registration - Submit](#)

Register Mixture

Substances that are isolated or synthesized together are considered a mixture. Common examples include coconut acid (Fatty acid isolated from coconut oil) or a mixture of isomers (most commercial products with chiral centers are mixtures of isomers).

Check for Duplicates

There is only one systematic way to search for structurally diverse duplicates, using the Global Search feature.

Global Search

Same as in [Search](#). Note that, a search by a component name generates a short list of substances which may include all the mixtures with that component, this list should be reviewed for duplicates.

Mixture Registration

1. After verifying the substance is not registered in GSRS via your Check for Duplicates, use the [Mixture Registration form](#) to register the new substance.
 - a. User accounts with registration permissions will have access to the registration menus. If you believe your account is not properly configured, contact your site admin.
2. The mixture registration form will be displayed. Section cards are collapsible to ease navigation, however the elements in this form are:
 - a. Overview - Definitional Information
 - b. Names
 - c. Mixture Details
 - d. Components
 - e. Agent modifications
 - f. Structural modifications
 - g. Physical modifications

GSRS User Guide (v3.x)

- h. Codes
- i. Relationships
- j. Notes
- k. Properties
- l. References

Definitional Information

Same as in [Chemical registration - Overview Definitional Information](#)

Names

Same as in [Chemical registration - Names](#)

Mixture Details

If the mixture substance is a mixture of substances that are isolated together, the Source Material Parent should be captured.

1. Select Mixture Details to expand the card
2. Use the parent substance search box to search for the record for parent substance which should be pre-registered
 - a. If the substance is not in GSRS, determine the substance type and register the new record
3. Access level should be protected if the component information is not public, even if name is public.

Components

1. Select Components to expand the card.
2. Select Add Components button
3. Use the Component Substance field to search GSRS for substances
4. Select the type from drop down
 - a. Typically the type will be “must be present (all of)”
 - b. At least two components are required

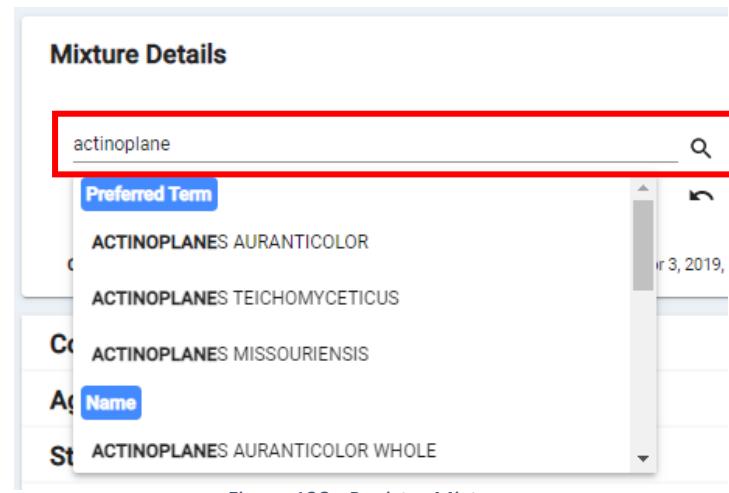


Figure 128 - Register Mixture - Mixture Details

The screenshot shows the 'Components' section of the 'Register Mixture' form. On the left, there is a list of mixture components:

- Mixture Component: MADUMYCIN I (with a chemical structure icon)

To the right, there is a dropdown menu for 'Mixture Component Type':

- May be present (any of)
- May be present (one of)
- Must be present (all of) (highlighted with a red box)
- Other (New Value)

Figure 129 - Register Mixture - Components

Agent Modifications

Same as in [Protein registration - Agent Modifications](#)

GSRS User Guide (v3.x)

Structural Modifications

Same as in [Protein registration – Structural Modifications.](#)

Physical Modifications

Same as in [Protein registration - Physical Modifications](#)

Names

Same as in [Chemical registration - Names](#)

Codes

Same as in [Chemical registration - Codes](#)

Relationships

Same as in [Chemical registration - Relationships](#)

Notes

Same as in [Chemical registration - Notes](#)

Properties

Same as in [Chemical registration - Properties](#)

References

Same as in [Chemical registration - References](#)

Submit

Same as in [Chemical registration - Submit](#)

The screenshot shows a detailed view of a chemical record in the GSRS system. At the top, the title "1-METHYL-1,2-CYCLOHEXANEDIOL" is displayed in bold blue text. To the left of the title is a blue circular icon containing the word "MIXTURE". Below the title, there are two sections: "Names:" and "Codes:". The "Names:" section contains "1-METHYL-1,2-CYCLOHEXANEDIOL ✓", "NSC-17487", and "1,2-CYCLOHEXANEDIOL, 1-METHYL-". The "Codes:" section contains "CAS: 6296-84-0". To the right of these sections is a large blue square icon featuring a stylized gear and hexagon pattern. At the bottom of the screen, there is a navigation bar with icons for edit, file, and search, followed by the text "Substance Hierarchy" and a blue button labeled "1-METHYL-1,2-CYCLOHEXANEDIOL". On the far right of the bar is a red button labeled "PENDING".

Figure 130 - Mixture

GSRS User Guide (v3.x)

Register Concept

Check for Duplicates

There is only one systematic way to search for concept duplicates, using the Global Search feature.

Global Search

Same as in [Search](#). Note that, a search by a concept name generates a short list of substances which may include all substance types, this list should be reviewed for duplicates.

Concept Registration

Concepts have no defining information but are collections of terms, codes and related information. They can be promoted to a defined substance later, when appropriate. Examples of concepts include herbal extract/tincture and biosimilars.

1. After verifying the substance is not registered in GSRS via your Check for Duplicates, use the [Concept Registration form](#) to register the new substance.
 - b. User accounts with registration permissions will have access to the registration menus. If you believe your account is not properly configured, contact your site admin.
2. The concept registration form will be displayed. Section cards are collapsible to ease navigation, however the elements in this form are:
 - a. Overview - Definitional Information
 - b. Names
 - c. Code
 - d. Relationships
 - e. Notes
 - f. Properties
 - g. References

Names

Same as in [Chemical registration - Names](#)

Codes

Same as in [Chemical registration - Codes](#).

Relationships

Same as in [Chemical registration - Relationships](#)

- Use the relationship type Substance -> Sub_concept for herbal extracts/tincture and biosimilars
- Use the Constituent Always Present -> Parent relationship types for components

GSRS User Guide (v3.x)

Relationships

Add Relationships + **Expand All**

Related Substance **VALERIAN**

Type * **SUBSTANCE -> SUB_CONCEPT**

Access **Mediator Substance** **Search**

Qualification **Interaction Type**

Comments **Enter text here**

Amount

Type * **Average** **Low** **High** **Low Limit** **High Limit** **Units** **Non-numeric Value**

References **1** **Create new +** **Reuse**

Related Substance **ACETOXYVALERENIC ACID** **Type *** **CONSTITUENT ALWAYS PRESENT -> PARENT** **Access** **Mediator Substance** **Search**

Related Substance **VALERENIC ACID** **Type *** **CONSTITUENT ALWAYS PRESENT -> PARENT** **Access** **Mediator Substance** **Search**

Figure 131 - Concept Registration – Relationships - New

Notes

Same as in [Chemical registration - Notes](#)

Properties

Same as in [Chemical registration - Properties](#)

References

Same as in [Chemical registration - References](#)

Submit

Same as in [Chemical registration - Submit](#)

Approve Substances

Substance registration require two subject matter experts to review, verify, and confirm that the registered definition is valid, unique, and descriptive of the substance. Once this has been determined, a second reviewer will approve/curate the substance.

1. There are several options to find recently registered substances:

- a. Share the link, ex: <https://gsrs.ncats.nih.gov/ginias/app/beta/substances/fa9f99b9-c77f-45c8-ab7f-a75b36ae65df>
- b. [Search](#)

GSRS User Guide (v3.x)

- c. Browse and filter on Record Created By and filter based on the registrar
- d. From the registrars landing page, under Quick Links, select Pending [by substance type]
2. After locating the pending substance, edit the substance
3. At the top of the registration form, the following buttons will be displayed:
 - a. Show JSON
 - b. Import JSON
 - c. Advanced Features
 - d. Validate and Submit
 - e. Approve – this button is activated if your user account did not register the subject substance and the substance is not already validated
4. If you have changes, request the originating registrar to make the required updates. If you make the updates, you will no longer be able to Approve the substance
5. If you have confirmed that the registration indicates that the substance is valid, unique, and descriptive, press the Approve button

The screenshot shows the GSRS software interface. At the top, there is a blue header bar with the GSRS logo, a 'Menu' button, a search bar labeled 'Search Substances', and a user profile icon labeled 'admin'. Below the header, there are several buttons: 'Show JSON', 'Import JSON', 'Advanced Features' (with a dropdown arrow), 'Validate and Submit', and 'Approve'. The 'Approve' button is highlighted with a red box. The main content area has a title 'Overview' and a section titled 'Editing Chemical'. Below this, it says 'Preferred Term: PSEUDOBUFARENOGIN'. There are two small links at the bottom left: 'Definition Term' and 'Definition Usage'. A caption 'Figure 132 – Substance - Approve' is located just above the screenshot.

6. GSRS may prompt with Warning messages that were previously dismissed. You may continue by pressing the Confirm Approval button

GSRS User Guide (v3.x)

Show JSON Import JSON Hide messages Advanced Features Validate and Submit Approve

Are you sure you'd like to approve this substance?

WARNING Substance BUFARENIGIN (ID: 9ca9e6aa-9f28-4851-8c90-747412c9ff51) is a possible duplicate [pending record]BUFARENIGIN

Confirm Approval

Preferred Term: PSEUDOBUFARENIGIN

Definition Type * Primary Definition Level Complete Deprecated Record Level Access Details page

Substance tags Enter new tags (and press Enter after each entry) or select from suggested tags below

Definitional References ¹ Create new + Reuse Definition Access

Created By: harmanpreet.kaur on Oct 30, 2020, 9:35:33 PM - Last Edited By: harmanpreet.kaur on Oct 30, 2020, 9:35:33 PM

Figure 133 – Substance – Confirm Approval

7. At the Success window, select View Substance, in order to can confirm your approval.
 - a. The approved substance record will be assigned the status of Validated
 - b. The approval ID will be displayed in red text next to the substance name. For US FDA, the approval ID is the Unique Ingredient Identifier (UNII).

PSEUDOBUFARENIGIN S3FD7P4VN5

Overview

Substance Class Chemical

Record UNII S3FD7P4VN5

BDNUM 0125967AB

Record Protection Status Public record

Record Status Validated (UNII)

Record Version 2

Tags

Show Definitional References

Definitional Access Public definition

Figure 134 – Substance –Approved

GSRS User Guide (v3.x)

Edit Substances

Substances in any status can be edited.

1. There are several options to find substances:
 - a. Share the link, ex: <https://gsrs.ncats.nih.gov/ginias/app/beta/substances/fa9f99b9-c77f-45c8-ab7fa75b36ae65df>
 - b. [Search](#)
 - c. [Browse](#) and filter
 - d. Select a register option from the [registrars landing page](#)
 2. From the results select the edit pencil

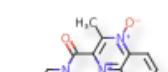
CINOQUIDOX		5743F6U086
ACHIRAL	Names: CINOQUIDOX ✓ CINOQUIDOX [INN]	Inxight Drugs
	Codes: CAS: 64557-97-7	Created: 6/27/21
	EVMPD: SUB06308MIG	Created By: admin
	ChEMBL: CHEMBL2106103	Status: Validated (UNII)
	INN: 4561	Validated By: FDA_SRS
	NCI_THESSAURUS: C76114	Last Modified: 6/27/21
   	Relationships: 1	Last Modified By: admin
	Mol. Weight: 272.2594	Version: 1
	Formula: C ₁₃ H ₁₂ N ₄ O ₃	
Substance Hierarchy		
CINOQUIDOX		5743F6U086 (ACTIVE MOIETY)

Figure 135 – Substance –Edit

- The registration form will be displayed. You can update any of the previously entered data or add data that was not previously entered for perform functions under Advanced Features

Advanced Features

1. After locating the substance, press the Edit pencil
 2. At the top of the registration form, the following buttons will be displayed:
 - a. Show JSON
 - b. Import JSON
 - c. Advanced Features
 - d. Validate and Submit
 - e. Approve – this button is activated if your user account did not register the subject substance and the substance is not already validated
 3. Advanced Features is a drop-down menu with options for administrator level users.

GSRS User Guide (v3.x)

The screenshot shows the GSRS interface for editing a substance. At the top, there is a navigation bar with the GSRS logo, a 'Menu' button, and a search bar labeled 'Search Substances'. On the right side of the top bar, there is a user icon and the word 'admin'. Below the top bar, there are buttons for 'Show JSON' and 'Import JSON' on the left, and 'Validate and Submit' on the right. The main content area has a title 'Editing Chemical' and a 'Preferred Term' field containing 'CINOQUI'. Underneath this, there are dropdown menus for 'Definition Type' (set to 'Primary') and 'Definition Level' (set to 'Complete'). A 'Substance tags' section contains a button for 'INN'. To the right of the main form, there is a redacted ID '5743F6U086' and a 'Record Level Access' link. A large red box highlights the 'Advanced Features' dropdown menu, which contains the following options: 'Change Substance Class', 'Change Status to approved', 'Change Status to pending', 'Set Definition to private', and 'Set Definition to public'. A vertical scroll bar is visible on the right side of this menu.

Figure 136 – Substance – Advanced Features

Change Substance Class

This advanced feature is used to switch a record from one type to another, a common example is to switch a chemical to a protein.

1. In the edit form of the subject substance select Change Substance Class from the Advanced Features drop-down. A second drop-down is displayed for New Class.
2. Select the target class that you want the substance to be updated to from this field

The screenshot shows the GSRS interface for editing a substance, similar to Figure 136. The 'Editing Chemical' section is highlighted with a red box. The 'Advanced Features' dropdown is open, showing the option 'Change Substance C...'. A second dropdown, also highlighted with a red box, is titled 'New Class' and lists the following options: 'concept', 'protein', 'chemical', 'structurallyDiverse', and 'polymer'. A vertical scroll bar is visible on the right side of this second dropdown. To the right of the form, there is a redacted ID 'QL05X0PL6T' and a 'Record Level Access' link. A 'Details page' link is also present.

Figure 137 – Substance – Advanced Features – Change Substance Class

3. Your browser will confirm that that "Substance type switched. Submit changes to save". Press OK.
4. You are returned to the registration form and the substance type is updated, the cards specific to that substance class are not available

GSRS User Guide (v3.x)

The screenshot shows the GSRS User Guide interface for editing a substance record. The top navigation bar includes the GSRS logo, version 3.0, a menu icon, a search bar labeled 'Search Substances', and a user account for 'admin'. Below the header, there are buttons for 'Show JSON', 'Import JSON', 'Advanced Features' (which is currently selected), and 'Validate and Submit'. The main content area is titled 'Editing Protein' (highlighted with a red box) and shows the 'Preferred Term: ASPOXICILLIN TRIHYDRATE'. It includes fields for 'Definition Type' (Primary), 'Definition Level' (Complete), 'Deprecated' status, and 'Record Level Access' (with a lock icon). A 'Substance tags' section contains 'JAN' with a delete icon. There is a text input for entering new tags and a list of suggested tags. Below this is a 'Definitional References' section with 'Create new' and 'Reuse' buttons, and a 'Definition Access' button. The 'Created By' and 'Last Edited By' fields both show 'admin' on April 4, 2019, at 3:49:16 AM. The 'Names' section has an 'Add Names' button. The 'Protein Details' section (highlighted with a red box) includes dropdowns for 'Protein Type' (protein subType), 'Sequence Origin', 'Sequence Type', and 'Access' (with a lock icon). Below this are sections for 'Subunits', 'Other Links', 'Disulfide Links', and 'Glycosylation', each with an 'Add' button. The entire screenshot is framed by a red border.

Figure 138 – Substance – Advanced Features – Change Substance Class Results

Change Status to Pending

In some instances, substances may have an inaccurate status. A common example is a processing or import error that should be reviewed or a mistake that needs to be reverted.

1. In the edit form of the subject substance select Change Status to Pending from the Advanced Features drop-down.
2. Your browser will confirm that that “Status changed to pending”. Press OK.

GSRS User Guide (v3.x)

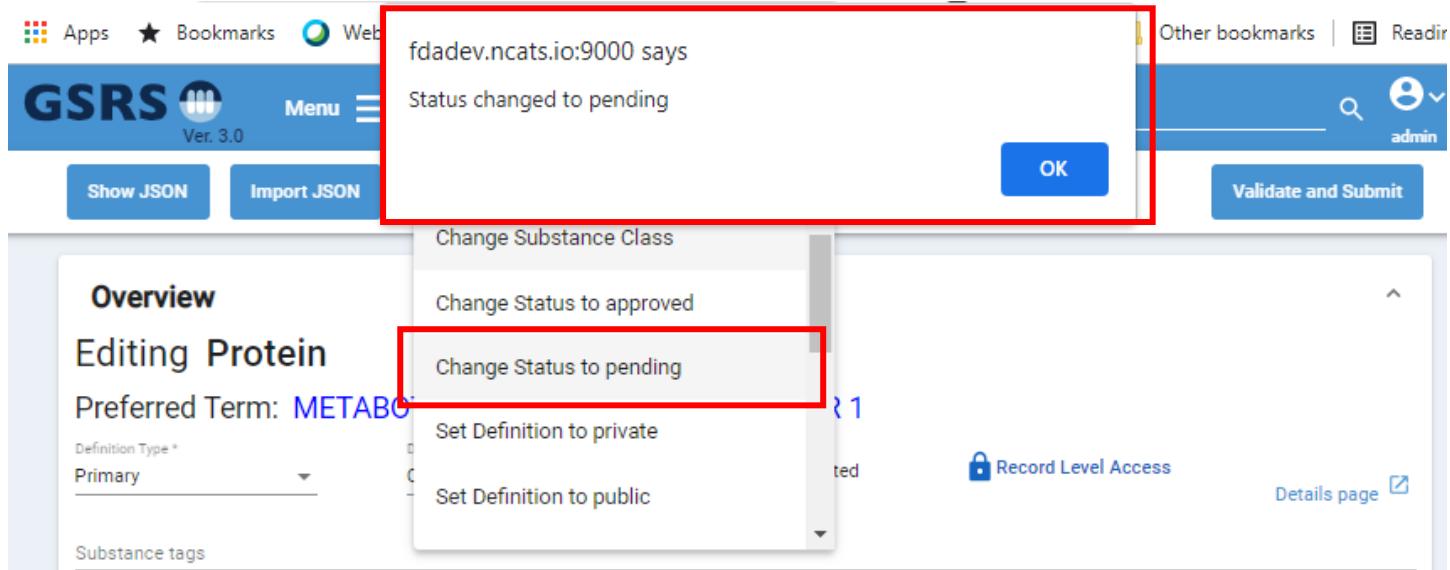


Figure 139 – Substance – Advanced Features – Change Status to Pending

3. The status is not displayed in the registration form, to apply these changes press Validation and Submit.
 - a. If you are prompted with existing Errors or Warning, resolve and dismiss as necessary.
4. At the Success window, press the View Substance button. Verify the status and version was updated.

The screenshot shows the GSRS interface displaying the details for 'METABOTROPIC GLUTAMATE RECEPTOR 1'. On the left is a navigation sidebar with various tabs like Overview, Names, Identifiers, Subunits, Glycosylation, Disulfide Links, Relationships, Relationships Visualization, Notes, and Audit Info. The main content area shows the substance's name and some basic details: Substance Class: Protein, Record UNII, BNUM, Record Protection Status: Not a public record (with a lock icon), Record Status: pending (highlighted with a red box), Protein Type: RECEPTOR, Sequence Type: COMPLETE, Sequence Origin: HUMAN, and Record Version: 9 (highlighted with a red box). To the right of the details are edit and download icons.

Figure 140 – Substance – Advanced Features – Status to Changed to Pending

GSRS User Guide (v3.x)

Change Status to Approved

In some instances, substances may have an inaccurate status. A common example is a processing or import error. If after a bulk transfer or mass import of approved records, you have records in Failed status, but you know are already approved use the Change Status to Approved Advanced Feature.

1. In the edit form of the subject substance select Change Status to Approved from the Advanced Features drop-down.
2. Your browser will confirm that that “Status changed to approved”. Press OK.

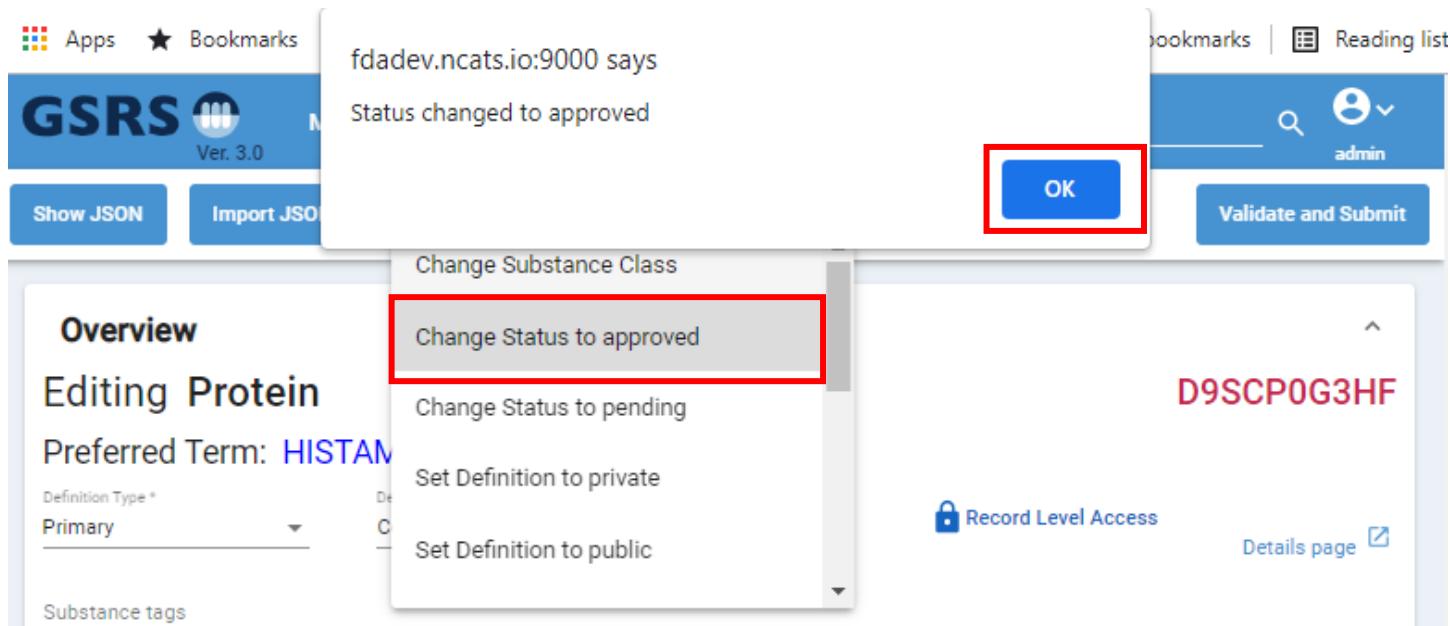


Figure 141 – Substance – Advanced Features – Change Status to Approved

3. The status is not displayed in the registration form, to apply and save your updates, press Validation and Submit.
 - a. If you are prompted with existing Errors or Warnings, resolve and dismiss as necessary.
4. At the Success window, press the View Substance button. Verify the status and version are updated and the approval ID was maintained.

GSRS User Guide (v3.x)

The screenshot shows the GSRS interface for a substance record. The top navigation bar includes the GSRS logo, version 3.0, a menu icon, a search bar labeled "Search Substances", and a user account section for "admin". The main content area displays the substance details for "HISTAMINE H3 RECEPTOR". A red box highlights the Record UNII field, which contains "D9SCP0G3HF". Another red box highlights the "Record Status" field, which is set to "Validated (UNII)". A third red box highlights the "Record Version" dropdown, which is currently set to "17". On the right side of the detail panel, there are edit, download, and delete icons.

Figure 142 – Substance – Advanced Features –Status Changed to Approved

Check for Duplicates

When registering a new substance, the first step is to check for duplicates. Performing these steps prior to starting registration ensures that your new registration is unique. There are a few ways to check for duplicates.

1. Go to the Name card and select Validate and submit and look for errors;

The screenshot shows the "Names" card for the substance "Benzene". At the top, there are buttons for "Show JSON", "Import JSON", "Hide messages", "Advanced Features", "Validate and Submit" (which is highlighted with a red box), and "Approve". A message box indicates that "Substance BENZENE (ID: 1a7d23dc-777d-4bb4-a796-3d36171b50e2) appears to be a full duplicate [J64922108F]BENZENE". Below this, there is a "Dismiss All and Submit" button. The "Definitional References" section has "Create new" and "Reuse" buttons. The "Names" section shows a table with columns for Name*, Type*, and Access. It lists "benzene" as a common name. The "Languages" section shows "English" selected. The "References" section shows one reference entry. Buttons for "Create new" and "Reuse" are also present here.

Figure 143 – Names Card – Sample Benzene

2. Select resolve and see the duplicates in the GSRS system;

GSRS User Guide (v3.x)

The screenshot shows the 'Names' card in the GSRS interface. At the top right, there is a 'Standardize Names' button and a 'Resolve' dropdown menu. Both of these are highlighted with red boxes. Below the dropdown menu is a 'Common Name' field. To the right of the names card, a modal window titled 'Get Structure From Name' is open, showing search results for 'benzene' from various sources like OPSIN, NCI, and PubChem.

Figure 144 – Names Card – Standardize Name and Resolve; Select Structure from Options

1. Look for structure duplicates by clicking on check for duplicates below the Chemical web editorbox

The search options are available for all users, both registrars and research users. There are several options to check for duplicates (using all will ensure an exhaustive search), search by one of the search options below:

The screenshot shows the 'Structure' card in the GSRS interface. It features a chemical editor with a benzene ring structure. Below the editor, there is a button labeled 'Check for duplicates' which is highlighted with a red box. Other buttons visible include 'Import', 'Export', and 'View stereochemistry'.

Figure 145 – Structure – Check for Duplicates