

Food and Drug Administration



FDA GLOBAL SUBSTANCE REGISTRATION SYSTEM (FDA GSRS)

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ENTERPRISE PERFORMANCE LIFECYCLE USER MANUAL

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VERSION HISTORY

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| 1.0 | Frank Switzer | 11/27/2016 | | | Initial Draft |
| 1.1 | Sarah Stemann | 10/20/2017 | | | Updated for v2 |
| 2.1 | Sarah Stemann/Frank Switzer | 4/2/2018 | | | Updated for v2.1 and registration (chemical) |

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1.

PURPOSE AND SCOPE

The purpose of the Global Substance Registration System (GSRS) is to unambiguously and consistently identify all substances which may be present in regulated products or substances produced metabolically from these substances or interacting with these substances in biological systems. To accomplish this, each substance entered into the GSRS is assigned a strong, non-proprietary identifier known as a Unique Ingredient Identifier (UNII) that is permanently associated with the defined substance. GSRS provides UNIs freely for general use and specifically for electronic ingredient listing activities. This data is available to FDA users and systems via a web client and REST and JAVA APIs. The public portion of this data is available for search and download at <https://fdasis.nlm.nih.gov/srs/srs.jsp>

The scope of regulated products covered by GSRS is as follows:

Foods

Specific foods or components of food, regardless of whether the food is in conventional food form or a dietary supplement, such as vitamins, minerals, herbs or other nutritional substances.

Drugs

Both active and inactive ingredients used in drug products, including those for veterinary purposes.

Biologics

Both active and inactive ingredients used in biologics, such as blood products, therapeutic products, vaccines, cellular and gene therapy products, allergenic products and tissues.

Devices

Components of devices including, for example, silicon for implants and chemical reagents for glucose test kits.

Cosmetics

Components of cosmetic products, such as flavors, fragrances, colorants, vitamins, plant and animal derived ingredients and polymers.

Tobacco

Components of tobacco products, such as flavors, fragrances, colorants, vitamins, plant and animal derived ingredients and polymers.

2. CONSIDERATIONS

The process of registering substances in the GSRS is captured by detailed business rules developed by the SRS Project Management Team located in FDA's Office of Health Information with the Office of the Chief Scientist and overseen by the SRS Program Review and Technical Boards. These boards work closely with multiple global stakeholders in the development of these rules.

To use effectively use GSRS, users should understand how GSRS:

Categorizes substances (principles)

Defines substances (identities)

Associates data with substances (metadata)

Links substance information from other FDA systems (interoperability)

2.1. *Principles*

A substance is any matter (has mass and occupies space) that has discrete existence. Substances are defined based on what they are and not how they are made or used. They are defined independent of grade or level of purity.

Broadly, substances can be divided into three major categories. Classifying a substance by category determines which attributes are necessary to fully identify it in GSRS.

- Monodisperse: single molecular connectivity including:
 - Chemicals aka small molecules.
 - Proteins: defined sequence chains of amino acid residues connected by peptide bonds.
 - Nucleic acids: defined sequence chains of nucleotide residues connected by phosphate esters.
- Polydisperse: collection of multiple but related molecular connectivities including:
 - Polymers: chemical entities that are related due to being based on one or more structural repeating units.
 - Structurally-diverse: entities that are related due to originating from a single well-defined biological or mineral source.

Together, monodisperse and polydisperse substances account for all single substances.

- Mixture: limited (<50) set of synthetic or naturally-occurring single substances that are synthesized and/or isolated together (does not include substances synthesized separately and then recombined).

2.2. Identities

The guiding principle of the GSRS is to limit ambiguity, which implies uniqueness and internal consistency of representations.

In the legacy SRS system, a substance was identified using two fields: Structure and an XML Identifying description. In GSRS, a JSON schema is used but the data management principles are the same.

The primary identifying attribute of a chemical substance is a two-dimensional molfile (.mol) format array. This non-proprietary data format is compatible with chemical search engines, may be faithfully rendered as an image showing molecular connectivity and stereochemistry or may be converted to other common chemical data formats.

GSRS uses precise stereochemistry when identifying chemical substances distinguishing ABSOLUTE, RACEMIC, ACHIRAL, UNKNOWN, EPIMERIC, MIXED and other less common isomeric types.

Many substances cannot be described completely or at all as a single molfile structure or sets of molfile structures so other forms of representation are also necessary. Fielded controlled vocabulary is used for substances that are not easily defined using molfile structures. Data captured and organized using the JSON schema is used either to add additional information about a substance or to describe substances for which a structure is not drawn. Different types of substances, such as polymers and proteins have specific attributes in the schema used to describe them.

3. USER MANUAL

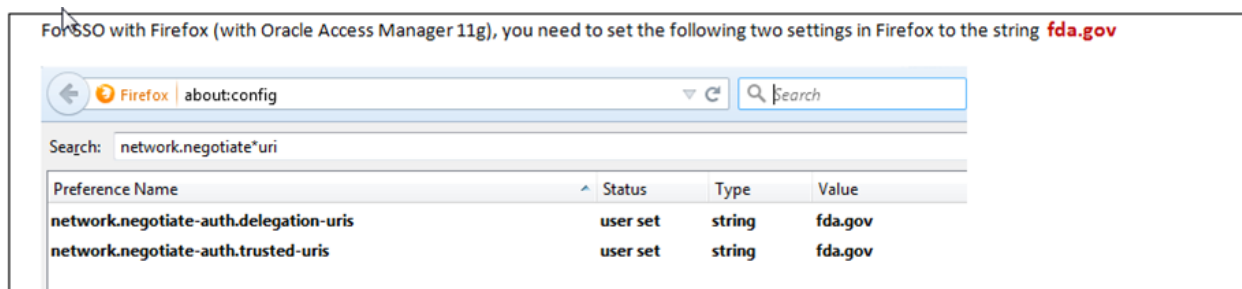
3.1. Access

To access FDA GSRS use an FDA supported browser to navigate to:

Pre-prod (testing and UAT): <http://gsrs.preprod.fda.gov/ginas/app>

Prod: <http://gsrs.fda.gov/ginas/app>

Google Chrome is the preferred browser for use with GRSS. Firefox also works well with the changes below:



3.2. Browse

FDA GSRS supports a browsing interface that provides a high-level overview of all the records contained within the system while still allowing a user to filter and drill down to specific records as desired.

To navigate to the browser interface, click on the Browse Substances tab on the navigation pane at the top of any page on the FDA GSRS website.

Browsing substances in the FDA GSRS is conducted via a dashboard interface. The content of the Browse Substances page looks like this:

Show Deprecated Records ☐

▼ Record Status

Search Record Status...

- ☐ Validated (UNII) 94404
- ☐ pending 67017
- ☐ Concept 9837
- ☐ Approved Subconcept (UNII) 5511
- ☐ FAILED 293
- [More ...](#)

▼ Substance Type

Search Substance Class...

- ☐ Chemical 125917
- ☐ Structurally Diverse 25588
- ☐ Concept 15371
- ☐ Protein 5304
- ☐ Mixture 2650
- [More ...](#)

▼ Source Tag

Search GlnAS Tag...

- ☐ MI 16153
- ☐ WHO-DD 14085
- ☐ INCI 9437
- ☐ INN 9295
- ☐ MART. 5805
- [More ...](#)

► Relationships

► Code System

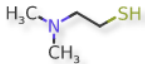
► ATC Level 1

177087 << < 1 2 3 4 5 6 7 8 ... 11067 11068 > >>

Sort By: Sort By

CAPTAMINE UNII:9FS0ENU0GR

ACHIRAL



Names: test 1
CAPTAMINE
ETHANETHIOL, 2-(DIMETHYLAMINO)-
2-(DIMETHYLAMINO)-ETHANETHIOL
CAPTAMINE [INN]

Codes: BDNUM: 00174694A
CAS: 108-02-1
EVMPPD: SUB06079MIG
ChEMBL: ChEMBL1395579

Relationships: 2

Formula: C4H11NS

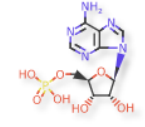
Mol Weight: 105.20

Date approved: 9 years ago
Created: 32 years ago
Last modified: 13 days ago
Status: Validated (UNII)
Version: 5

Product Count: Active: 0 Inactive: 0
Application Count: CDER: 0 SRS: 0
Clinical Trial Count: 0
Adverse Event Count: 0

ADENOSINE PHOSPHATE UNII:415SHH325A

ABSOLUTE



Names: A 5MP
A-5MP
ADENOSINE PHOSPHATE [VANDF]
ADENOSINE PHOSPHATE [WHO-DD]
5'-ADENYLIC ACID [USP-RS]

Codes: BDNUM: 00106394A
CAS: 61-19-8
EVMPPD: SUB05267MIG
ChEMBL: ChEMBL752

Relationships: 6

Formula: C10H14N5O7P

Mol Weight: 347.22

Date approved: 9 years ago
Created: 32 years ago
Last modified: 13 days ago
Status: Validated (UNII)
Version: 3

Product Count: Active: 0
Application Count: CDER: 8
Clinical Trial Count: 5
Adverse Event Count: 17

The dashboard can be divided into three major components:

- Filter/Facets pane
- Display (header/footer) pane
- Results pane

3.2.1. Filter Pane

The filter pane is located on the far left of the dashboard. Here, the user can see the number of substance records stored in the FDA GSRS database based on a select number of facets. This count data is displayed in the pill-shaped field found to the right of each category name.

Under each facet title is the “ Search [Facet name]...” box. Enter the facet name (full or partial) and search for the facet category within the facet. To the left of each facet category name is a checkbox. At the bottom of the displayed list is a link to “More...”. This will expand the list to display the top 20 options. Use the search to filter for options that are not explicitly displayed.

After making your facet selections Boolean options are displayed. Exclude, All Match or Any Match may be selected. By default, the filters are applied as “Any Match”. To display facets that fulfill all criteria, select “All Match”. Click “Apply” to filter based on the selected options (for one or more filters at once). The filtered records are displayed in the results pane located at the center of the dashboard.

The screenshot shows the FDA GSRS dashboard with the following facets expanded:

- Record Status:** Validated (UNII), pending, Concept, Validated Subconcept (UNII), FAILED.
- Substance Type:** Chemical, Structurally Diverse, Concept, Protein, Mixture.
- Source Tag:** USAN, USP, USP-RS, HPLS, USP-PC.
- Relationships:** METABOLITE ACTIVE OF PRODRUG, PRODRUG OF METABOLITE ACTIVE, ACTIVE MOIETY, SALT/SOLVATE OF PARENT, PARENT OF IMPURITY.

The results pane displays two records:

- CAPSELLA BURSA-PASTORIS (UNII: W0X9457M59):** Structurally Diverse. Names: CAPSELLA VIRIDIS WHOLE, CAPSELLA VIRGATA WHOLE, CAPSELLA VIRIDALIS WHOLE, CAPSELLA VIGUERI WHOLE, CAPSELLA VARIUM WHOLE. Codes: BONJUM: 020160544, EVMPD: SUB0225940, ENA ASSESSMENT REPORTS: CAPSELLA [PINAL2013] [PINAL2013] [PINAL2013]. Date approved: 11 years ago. Created: 11 years ago. Last modified: 11 years ago. Status: Validated (UNII). Version: 2.
- PANDANUS TECTORIUS WHOLE (UNII: 06X5QB4BY):** Structurally Diverse. Names: PANDANUS TAPINOS WHOLE, PANDANUS TAMARUENSIS WHOLE, PANDANUS TAKARAENSIS WHOLE, PANDANUS TANTENENS WHOLE, PANDANUS TANAENSIS WHOLE. Codes: BONJUM: 061563444, GRN: 261119, ITS: 564095, MPNS: WICS-265436. Date approved: 7 years ago. Created: 7 years ago. Last modified: 5 years ago. Status: Validated (UNII). Version: 1.

Filter:

Substance Type = Chemicals OR Mixture

Source Tag = USAN AND USP

Relationships do NOT include METABOLITE ACTIVE OF PRODRUG OR PRODRUG OF METABOLITE ACTIVE

The screenshot shows the FDA GSRS dashboard with the following facets expanded:

- Relationships:** METABOLITE ACTIVE OF PRODRUG, PRODRUG OF METABOLITE ACTIVE.
- Source Tag:** USAN, USP.
- Substance Class:** Mixture.

The results pane displays two records:

- HYDROCODONE BITARTRATE (UNII: N070W88KK):** ABSOLUTE. Names: HYDROCODONE TARTRATE, REZIRA COMPONENT HYDROCODONE BITARTRATE, ZUTRIPRO COMPONENT HYDROCODONE BITARTRATE, HYDROCODONE BITARTRATE COMPONENT O, HYDROCODONE BITARTRATE COMPONENT O. Codes: BONJUM: 004609344, CAS: 34195-34-1, EVMPD: SUB0255940, CHEMBL: CHEMBL1457. Date approved: 13 years ago. Created: 14 years ago. Last modified: 5 years ago. Status: Validated (UNII). Version: 1.
- PSEUDOEPHEDRINE HYDROCHLORIDE (UNII: 6V9V2RYJ8N):** ABSOLUTE. Names: CHILDRENS ADVIL COLD COMPONENT PSEUDOEPHEDRINE HYDROCHLORIDE COMP, SEUPREX-O COMPONENT PSEUDOEPHEDRINE HYDROCHLORIDE COMP, PSEUDOEPHEDRINE HYDROCHLORIDE COMP, ALLERFER COMPONENT PSEUDOEPHEDRINE HYDROCHLORIDE COMP. Codes: BONJUM: 004620844, CAS: 34579-9-6, EVMPD: SUB0411940, CFR: 21 CFR 341.20. Date approved: 13 years ago. Created: 14 years ago. Last modified: 5 years ago. Status: Validated (UNII). Version: 1.

The applied facets are at the top of the display pane, and can be removed which will update the data set. Facets with the icon indicate selections that are excluded from the results. Facets with the icon indicate selections where one or more criteria must be met by the substance.

The facets are organized into sections, such as stereochemistry, molecular weight, relationships, etc. The first three facets are fully expanded by default, the remaining facets are collapsed and can be expanded as needed.

3.2.2. Display (Header & Footer) Pane

The display pane has components located at the top and bottom of the dashboard. In both places, the display pane shows the user the total number of records returned by the FDA GSRS database based on any (defaults to none) search criteria specified in the filter pane and includes pagination for the user to navigate to a specific page of results.

At the top portion of the dashboard only, there is a download icon that allows the user to export a summary of each of the records displayed in the results pane to a separate file. The following export formats are supported:

- Codes File
- JSON
- TSV
- CSV
- SDF
- XLSX
- Names File
- SPL Term Validation (xml)
- Legacy SRS Dictionary

The screenshot shows the FDA GSRS dashboard interface. At the top, there is a pagination bar showing 6153 records and a list of page numbers (1, 2, 3, 4, 5, 6, 7, 8, ..., 384, 385). Below this is a 'Sort By' dropdown menu and a toggle switch. A download icon (a square with a downward arrow) is visible, and a menu is open showing the following options:

- Codes File
- CSV (csv) File
- TSV (tab) File
- Excel (xlsx) File
- Names File
- SD (sdf) File
- SPL term validation (xml) File
- Json Export (gsrs) File
- Legacy SRS Dictionary File
- ☐ Include Private Data

Below the menu, there is a table of results. The first row shows the following information:

| UNII: BH3B64OKL9 |
|--|
| 4-AMINOPYRIDINE FAMPRIDINE 4-PYRIDINAMINE NEURELAN EL-970 BDNUM: 0121335AA CAS: 504-24-5 WHO-ATC: N07XX07 EVMPD: SUB07505MIG |
| Date approved: 10 years ago Created: 31 years ago Last modified: a day ago Status: Validated (UNII) Version: 4 |

At the bottom of the dashboard, there is a 'Relationships' section with a count of 3.

After initiating a download, enter a filename (or accept the default date/time) and retrieve the file from My Downloads

Enter Filename

Info

An export was prepared with this criteria **4 minutes ago**. You can retrieve this export, or start a new one by entering a filename below.


View old version

Ok

Cancel

While the download is generated, continue using GSRS for your research.

[export-2017-10-20_17_08_43.xlsx](#)



Processing export ...
(click to cancel)

| | |
|--------------------|---|
| Number of Records: | 502 |
| Original URL: | http://gsrs.preprod.fda.gov/ginas/app/substances?facet=Substance%20Class%2Fprotein |
| Previous versions | See other versions of this export. |


RUNNING


Date started:
a few seconds ago
Date ended:
a few seconds ago


[See all Downloads](#)


To access your download(s), click your user name in the upper right corner, click My Downloads, and View My Downloads

[Home](#)
[Browse Substances](#)
[Search](#)
[Register](#)
[FARM Integration](#)
[Admin](#)
[Help](#)

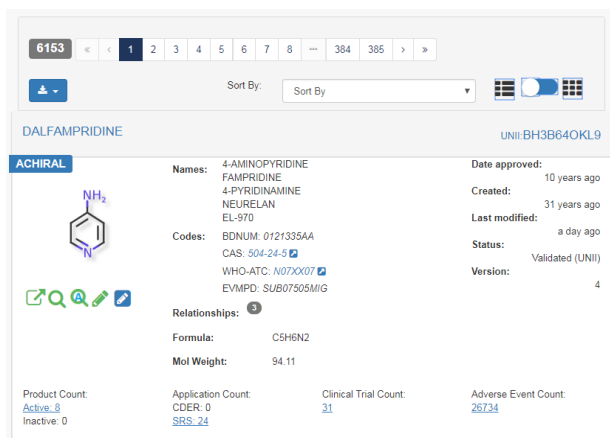
 Sarah.Stemann

 User Info

 My Downloads

 View My Downloads

In addition to the download icon, there is a toggle that allows the user to change the display format of records in the results pane between a summary list and grid format.




6153 < 1 2 3 4 5 6 7 8 ... 384 385 >

Sort By: Sort By

DALFAMPRIDINE UNII: BH3B64OKL9

ACHIRAL



Names: 4-AMINOPYRIDINE
FAMPRIDINE
4-PYRIDINAMINE
NEURELAN
EL-970

Codes: BDNUM: 0121335AA
CAS: 504-24-5
WHO-ATC: N07XX07
EVMPD: SUB07505MIG

Relationships: 3

Formula: C5H6N2

Mol Weight: 94.11

Date approved: 10 years ago

Created: 31 years ago

Last modified: a day ago

Status: Validated (UNII)

Version: 4

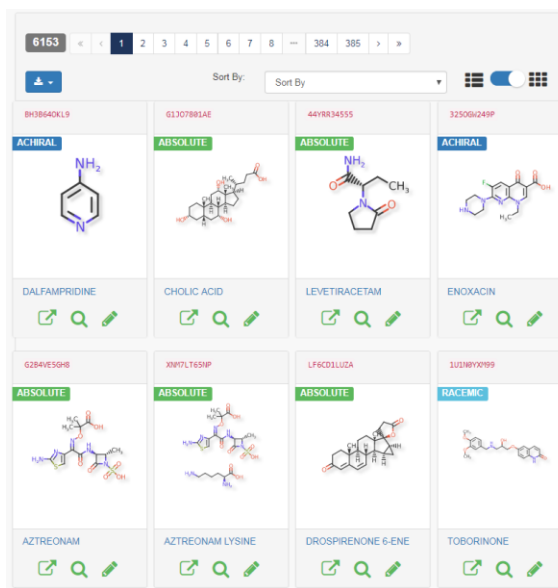
Product Count:
Active: 8
Inactive: 0

Application Count:
CDER: 0
SRS: 24

Clinical Trial Count:
31


Adverse Event Count:
26734


List Format (default)





6153 < 1 2 3 4 5 6 7 8 ... 384 385 >


Sort By: Sort By


BH3B64OKL9 **ACHIRAL**  **DALFAMPRIDINE**


G1307881AE **ABSOLUTE**  **CHOLIC ACID**


44YR34555 **ABSOLUTE**  **LEVETIRACETAM**

3250GQ48P **ACHIRAL**  **ENOXACIN**

G2B4V5G8 **ABSOLUTE**  **AZTREONAM**

X0W7L65NP **ABSOLUTE**  **AZTREONAM LYSINE**

LF6CD1LUZ **ABSOLUTE**  **DROSPIRENONE 6-ENE**

1UD8PY099 **RACEMIC**  **TOBORINONE**

Grid Format

3.2.3. Results Pane

The results pane is located at the center of the dashboard. Here, the substance answers are displayed in either list or grid format depending on which setting is toggled from the display pane at the top.

The list format provides a summary view for each record returned by the FDA GSRS database. Basic information captured in a summary view includes the substance UNII code (if any), names (up to six simultaneously), codes (up to six simultaneously), number of relationships to other substance records, date approved, and time last modified.

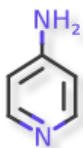
Additional information depending on substance type is also presented; for instance, substance records include the chemical formula, number of moieties, the stereochemistry category and a two-dimensional chemical structure. An example summary view for a chemical substance record is shown below:

6153 << < 1 2 3 4 5 6 7 8 ... 384 385 > >>

Sort By: Sort By

DALFAMPRIDINE UNII: BH3B64OKL9

ACHIRAL



Names: 4-AMINOPYRIDINE
FAMPRIDINE
4-PYRIDINAMINE
NEURELAN
EL-970

Codes: BDNUM: 0121335AA
CAS: 504-24-5
WHO-ATC: N07XX07
EVMPD: SUB07505MIG

Relationships: 3

Formula: C5H6N2

Mol Weight: 94.11

Date approved: 10 years ago

Created: 31 years ago

Last modified: a day ago

Status: Validated (UNII)

Version: 4

Product Count: [Active: 8](#)
Inactive: 0






Application Count: CDER: 0
[SRS: 24](#)

Clinical Trial Count: [31](#)


























Adverse Event Count: [26734](#)

The additional information incorporated into the summary view for each substance type is included below:

- Substance
 - Formula
 - Number of moieties
 - Stereochemistry
 - 2D structure
- Structurally diverse
 - Part
- Mixture
 - Number of components
- Polymer
 - Display structure
- Protein
 - Number of subunits
- Nucleic Acid
 - Number of subunits
- Actions available from the summary view include:

-  Export – options for individual substance export provided in next window
-  Structure (or Sequence) Search – if applicable
-  Structure Search in Advanced Search – if applicable
-  Edit – power users
-  New Form – power users

The grid format solely presents the UNII code (if any), the preferred name of the substance, and the structure (if the substance is either a chemical or a polymer). An example grid view displaying several chemical substance records is shown below:

| | | | |
|---|--|--|--|
| B03B640K19 ACHIRAL  DALFAMPRIDINE    | G1307861AE ABSOLUTE  CHOLIC ACID    | 44YRL34555 ABSOLUTE  LEVETIRACETAM    | J250G249P ACHIRAL  ENOXACIN    |
| G284VESQ4E ABSOLUTE  AZTREONAM    | XN0LT658P ABSOLUTE  AZTREONAM LYISINE    | LP6CD3LJ2A ABSOLUTE  DROSPIRENONE 6-ENE    | J03WYX999 RACEMIC  TOBORINONE    |

For chemical and polymer records in either view, the user can export a chemical table file or SMILES string of the substance record by clicking on the export icon below the structure. The user can also transfer the structure to the Structure Search interface to perform an additional search by clicking on the search icon.

3.3. Search

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

3.3.1. Global Search

Global search is a free-text search box in the upper right of every page. Type the text you are looking for and the type-ahead feature will display the top matches for UNII's and names separated by preferred names and all other name types. You can select from one of the matches, or use the magnifying glass for a wider search. Results are presented in the display pane.

[Advanced Search](#)

UNII

GLY4K2IZ8E
GLY8ABW25V
GLY7G3G72E

Preferred Term

...METHYL)AMINO)ETHYL)-N-((2S)-2-(BIS(CARBOXY...
GLYCERYL 1,2-DINITRATE
... HIS-SER-ASP-ALA-VAL-PHE-THR-ASP-ASN-TYR-T...
GLYCERYL 1,3-DINITRATE
...G-ARG-PRO-HYP-GLY-THI-SER-D-PHE-THI-ARG
1,2-DIOLEOYL-SN-GLYCERO-3-PHOSPHOETHANOL...
...LA-THR-CYS-VAL-THR-HIS-ARG-LEU-ALA-GLY-LEU...
...RG-HIS-ASP-SER-GLY-TYR-GLN-VAL-HIS-HIS-GLN-...
MANGANESE 2-GLYCEROPHOSPHATE
...1,4,5,6-TETRAHYDRO-5-HYDROXY-2-PYRIMIDINYL...

Name

GLYCINE SOJA (SOYBEAN) SEED WATER
GLYCERYL TRI(5-HYDROXYDECANOATE)
GLICYRRHIZA LAEVIS WHOLE
GLYCERYL DISTEARATE [II]
GLICYRRHIZA GLABRA (LICORICE) LEAF EXTRACT

3.3.2. Advanced Search

Not included in the current public-facing site. The advanced search can be reached via the navigation pane, global search results or by selecting the A magnifying glass from a specific substance. The structure search pane within Advanced Search can be used similar to Structure Search described in section 3.4.3.

The Advanced Search criteria is organized by five tabs: Substance, Product, Application, Clinical Trial, and Adverse Event. Within each of the tabs, a structure can be searched (similar to structure search), or criteria specific to each tab can be searched. For the criteria there are three selections:

- Match By: Contains or Exact
- Search By: field name
- Search Text: free text, with type-ahead matches displayed as optional selections

Advanced Search

The screenshot displays the 'Advanced Search' interface with the 'Substance' tab active. The search criteria are set to 'Match By: Contains', 'Search By: Product Name', and 'Search Text: nitro-'. A dropdown menu lists several chemical structures containing the 'nitro-' group, such as '1-(A-HYDROXYETHYL)-2-METHYL-5-NITRO-IMIDAZOLE, A NEW TRICHOMONOCIDE'. Below the search results, there is a 'Substructure' section with a 'Get Structure From Name' button and a 'Resolve Name' button.

After entering the criteria and clicking search, the results are presented in a grid, with details specific to the advanced search type. Results can be exported to Excel or filtered similar to Browse Substances.

Application Search Results [New Search](#) [Export to Excel](#)

Product Name: nitro-
Search Completed

62 << < 1 2 3 4 5 > >>

| Details | Substance Name | Structure | Application Type | Application Number | Product Name | Sponsor Name |
|---|----------------------|-----------|------------------|--------------------|--|----------------------|
| Details | SODIUM NITROPRUSSIDE | | IND | 127579 | NG-NITRO-L-ARGININE (L-NNA) AND EPOPROSTENOL SODIUM | SMITH CAROLINE J PHD |
| Details Update (SRS) | NITAZOXANIDE | | IND | 102896 | ALINIA; NITAZOXANIDE; 2-ACETILOXY-N-(5-NITRO-2-THIAZOLYL)BENZAMIDE; PH 5776 | DICKSON ROLLAND C MD |
| Details | SODIUM NITROPRUSSIDE | | IND | 134950 | ASCORBATE, NG-NITRO-L-ARGININE METHYL ESTER (L-NAME), SODIUM NITROPRUSSIDE, AND 5-METHYL-TETRAHYDROFOLATE (5-MTHF) | KENNEY WILLIAM L PHD |
| Details | SODIUM NITROPRUSSIDE | | IND | 127630 | NG-NITRO-L-ARGININE METHYL ESTER | LANG JAMES A PHD |

Application Type

- IND 47
- NDA 8
- MF 7

Sponsor Name

Search Sponsor Name...

- LANG JAMES A PHD 9
- KEY PHARMACEUTI... INC SUB SCHERING PLOUGH CORP 4
- HOECHST MARION ROUSSEL INC 3
- SMITH CAROLINE J PHD 3
- LANGE MARIANNE MD 2
- [More ...](#)

Application Status

Search Application Status...

- ACTIVE 15
- WDRAWN 11
- TERM 9
- INACTIVE 7
- WDRAWN FREFF 4

3.3.3. Structure Search

FDA GSRS Structure Search is a means for searching for specific chemical and polymer records based on their two-dimensional chemical structure. The interface on the Structure Search page looks like this:


Draw Structure ?

Get Structure From Name ?

Name

There are several ways that a structure can be prepared to perform a search.

- Transfer a structure found during a search or browse session using the results pane search icon.



ANHYDROUS DEXTROSE

UNI: 5SLOG7R00K

ABSOLUTE

Names: NSC-406991
GLUCOSE, ANHYDROUS
D-GLUCOSE
DEXTROROSE (CONSTITUENT OF CRANBERRY ...
GLUCOSE [WHO-DD])

Codes: BDNUM: 01266924A
CAS: 2280-44-8 50-99-7
EVMID: SUB74990 SUB11968MIG
CFR: 21 CFR 862.1342 21 CFR 168.110

Relationships: 0

Formula: C₆H₁₂O₆

Mol Weight: 180.16

Product Count: Active: 10 Inactive: 65

Application Count: CDER: 105 SRS: 9

Clinical Trial Count: 0

Adverse Event Count: 118888

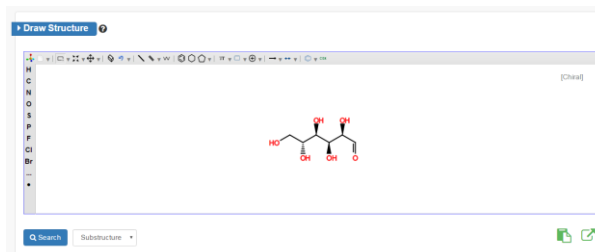
Date approved: 12 years ago

Created: 12 years ago

Last modified: 5 years ago

Status: Validated (UNII)

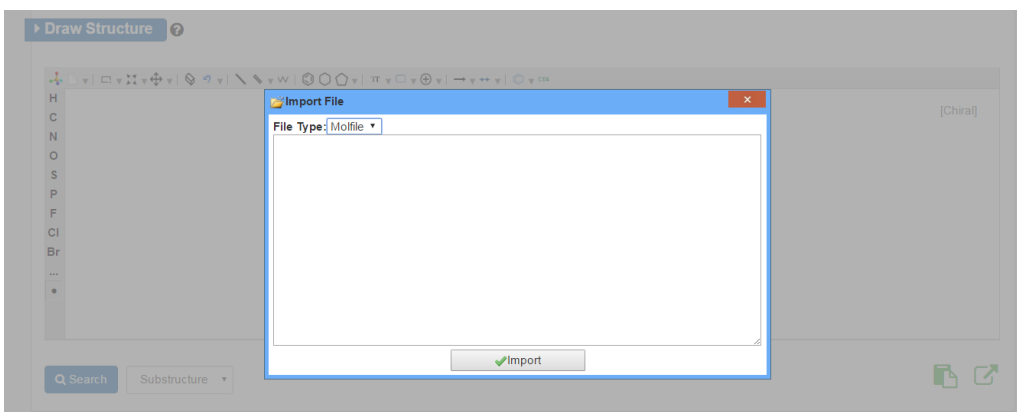
Version: 1



Clicking on the search (magnifying glass) icon below the structure...

Transfers the structure to the Structure Search window.

- Import an external file (supported formats: Molfile, Rxnfile, Html).




Draw Structure

Import File

File Type: Molfile

Import

- Draw a structure by using the included drawing tool. You may use either the default JSDraw editor or more standalone chemical editor. SymyxDraw is the preferred standalone because the molfile is its native format.
- Get structure from its substance name

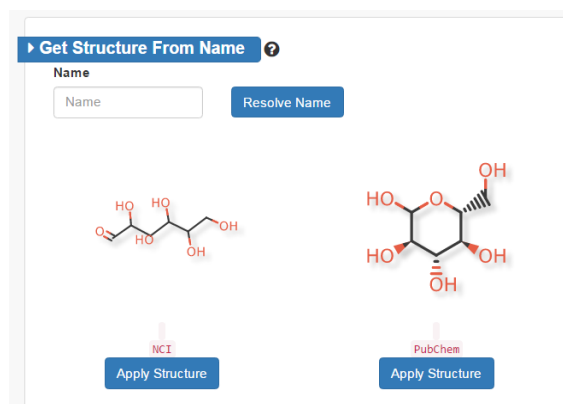


Get Structure From Name

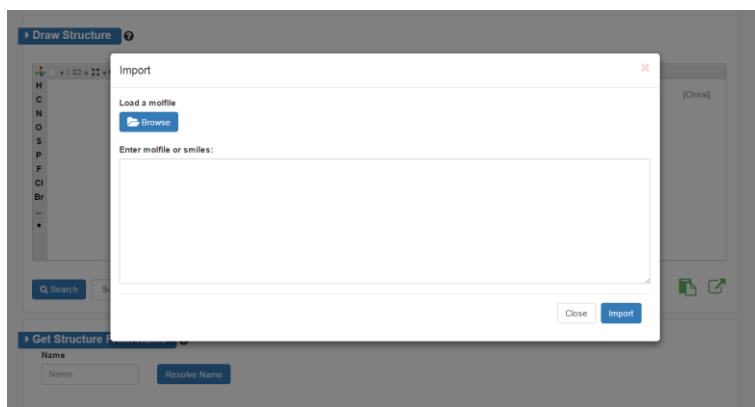
Name

glucose

Resolve Name



- Get structure from its SMILES string representation



With the structure ready, select the search option.

- Substructure: find other compounds that the query structure is embedded in. This is useful for finding a set of compounds that share a common “substructure.”
- Similarity: find other compounds with structural features that are similar to those of the query structure. Similarity percentages between 50% and 100% are returned. Compounds that are related and are relatively close in overall size can be found using this method.
- Exact: find the query structure as a complete entity, where all the structure’s atoms and bonds are identical in the retrieved compound.
- Flex: Find the query structure, with all bonds identical in the retrieved compound including stereochemical and tautomeric bonds. Flex also finds salts, mixtures, hydrates, and polymers of the parent.

3.3.4. Sequence Search

FDA GSRS also supports searching on sequences to locate protein and nucleic acid substance records. Sequence searching can be accessed from the Search menu or from an existing substance, using the magnifying glass which now links to the sequence page.

HUMAN INTERFERON BETA
UNII:V9GU1EM8SF

PROTEIN



Subunit 1 (166) Similarity Search

Names: HUMAN INTERFERON BETA
INTERFERON BETA
INTERFERON BETA [INN]
INTERFERON BETA [JAN]
INTERFERON BETA [MART.]
Codes: BDNUM: 0297927AA
CAS: 74899-71-1
WHO-ATC: L03AB02
EVMPD: SUB02709MIG
Relationships: 1
Subunits: 1

Date approved: a month ago
Created: 2 months ago
Last modified: a month ago
Status: Validated (UNII)
Version: 8

Product Count: Active: 0 Inactive: 0
Application Count: CDER: 0 SRS: 1
Clinical Trial Count: 10
Adverse Event Count: 389

Sequence Search

Search Identity: 0.5

Cutoff Type: Contains Alignment Match

Sequence Type: Protein

Query Sequence:

MSYNLLGFLQRSSNFQCQKLLWQLNGRLEYCLKDRMNFDIPEEIKQLQQFKEDAALTIYEMLQNIFA
LKTVLEEKLEKEDFTRGKLMSSLHLKRYYGRIHLHYLKAKEYSHCAWTIVRVEILRNFYFINRLTGYLE
TIVENLLANVYHQINH

Search


FDA GSRS has three alignment methods with which to search sequence candidates: contains, global, and local alignment matches. There are also two sequence types.





The results display the statistics for the match:

INTERFERON BETA-1B



UNII:TTD90R31WZ

PROTEIN



Names: INTERFERON BETA-1B
17-L-SERINE-2-166-INTERFERON B1 (HUMAN F...
BETASERON
INTERFERON BETA-1B [USAN]
RPROT P01574 (IFNB_HUMAN) INTERFERON B...

Codes: BDNUM: 0215690AA
CAS: [145155-23-3](#) 
WHO-ATC: [L03AB08](#) 
EVMPD: SUB12432MIG SUB39502

Relationships: 1

Subunits: 1

Date approved: 11 years ago

Created: 13 years ago

Last modified: 5 months ago

Status: Validated (UNII)

Version: 3

Subunit 1 [1552cf75-61e1-467d-b732-f1d3d89da8a3](#)

```

identity = 0.988
local   = 0.994
sub     = 0.982
matched = 164
SYNLLGFLQRSSNFQCQKLLWQLNGRLEYCLKDRMNFDIPEEIKQLQQFQKEDAALTIYEMLQNIFAIFRQDSSSTGWNETIVENLLANVYHQINHLKTVLEEKLEKEDFTRGKL
|||||
SYNLLGFLQRSSNFQSQKLLWQLNGRLEYCLKDRMNFDIPEEIKQLQQFQKEDAALTIYEMLQNIFAIFRQDSSSTGWNETIVENLLANVYHQINHLKTVLEEKLEKEDFTRGKL
Target Sites:1_1-165

```

Product Count:
[Active: 1](#)
Inactive: 0

Application Count:
[CDER: 5](#)
[SRS: 6](#)

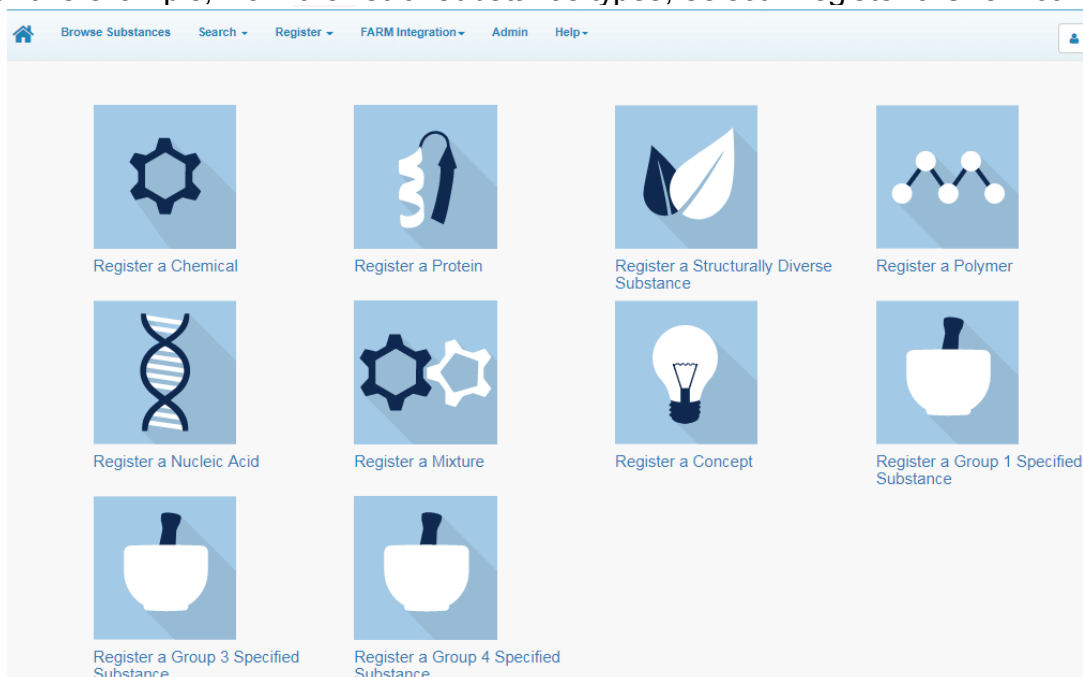
Clinical Trial Count:
[40](#)


Adverse Event Count:
[33967](#)

3.4. Registration

3.4.1. Chemical

1. From the navigation pane, select Register > Register Substance
2. For this example, from the list of substance types, select “Register a Chemical”



3. Definition Level should be set to Complete. Incomplete and Representative definition levels should be avoided. Also avoid generating records with unknown stoichiometry, stereochemistry, or substitution.
4. Add a Definition Reference by clicking the  icon
 - a. Click Apply to ensure the reference is selected after Save
 - b. Update Source Type and Source Text



▼ References 1 + Add reference

| Apply | Source Type * | Source Text / Citation * | Access | Show Details |
|-------------------------------------|-----------------|--------------------------|--------|--------------|
| <input checked="" type="checkbox"/> | STN (SCIFINDER) | STN | Public | |
| | | | | |
| | | | | |
| | | | | |

Save & Close

- c. Click Show Details
- d. Select Public Domain checkbox and add the Public Domain Release tag


e. Click Save & Close

- f. Ensure the Reference is attached to the Definition, the  is replaced with  number will correspond to the number of references added

5. Add a Name by clicking the Add Name button


- Add a Name and Reference, click Show Details. Names should be standardized to ASCII UPPER CASE. Names should be globally unique and most relevant to the specific record.
- Update Display/Priority Name checkbox as necessary. Only one Display name is allowed per record per software instance. Display names should use natural word order EXCEPT for stereochemical attributes which should be preceded by a comma and followed by a dash at the end of the name; i.e. display names should be formatted like the following example: 1,2-DIMETHYLCYCLOHEXANE, (1R,2R)- . **Only ADMIN users should select Preferred/Listing names.**

Languages Display (Priority Name) Preferred (Listing Name)

 ☒ ☐

Created By: LINH.HUYNH On: May 14, 2014 1:55:23 PM - Last Edited By: CALLAHANL On: Apr 2, 2018 12:13:17 PM

c. Click Add Name as many times as needed

6. Add a Structure, as created in ChemDraw or your preferred tool and saved in molfile format, using the Import button .

▼ Structure

Check for duplicates

a. Browse for your file and click Import

Import

Load a molfile

Browse

results (13).mol

Enter molfile or smiles:

```
25 26 0 0 0 0 999 v2000
14.5463 -3.0332 0.0000 N 0 0 0 0 0 0 0 0 0 0 0 0
15.2605 -2.6222 0.0000 C 0 0 0 0 0 0 0 0 0 0 0 0
14.5463 -1.3860 0.0000 S 0 0 0 0 0 0 0 0 0 0 0 0
15.9748 -3.0332 0.0000 C 0 0 0 0 0 0 0 0 0 0 0 0
13.8262 -2.6162 0.0000 C 0 0 0 0 0 0 0 0 0 0 0 0
15.2605 -1.7972 0.0000 C 0 0 0 0 0 0 0 0 0 0 0 0
13.8262 -1.8029 0.0000 C 0 0 0 0 0 0 0 0 0 0 0 0
17.4236 -3.0157 0.0000 S 0 3 0 0 0 0 0 0 0 0 0 0
16.6948 -2.6162 0.0000 C 0 0 0 0 0 0 0 0 0 0 0 0
14.5463 -3.8581 0.0000 C 0 0 0 0 0 0 0 0 0 0 0 0
```

Close

Import

b. The structure and it's details are available for editing via JSDraw

▼ Structure

Check for duplicates

Molecular Formula *
C20H24N2OS2

Molecular Weight
372.547

Stereochemistry
Mixed

Defined Stereocenters
0/2

Optical Activity
(+/-)

EZ Centers
0

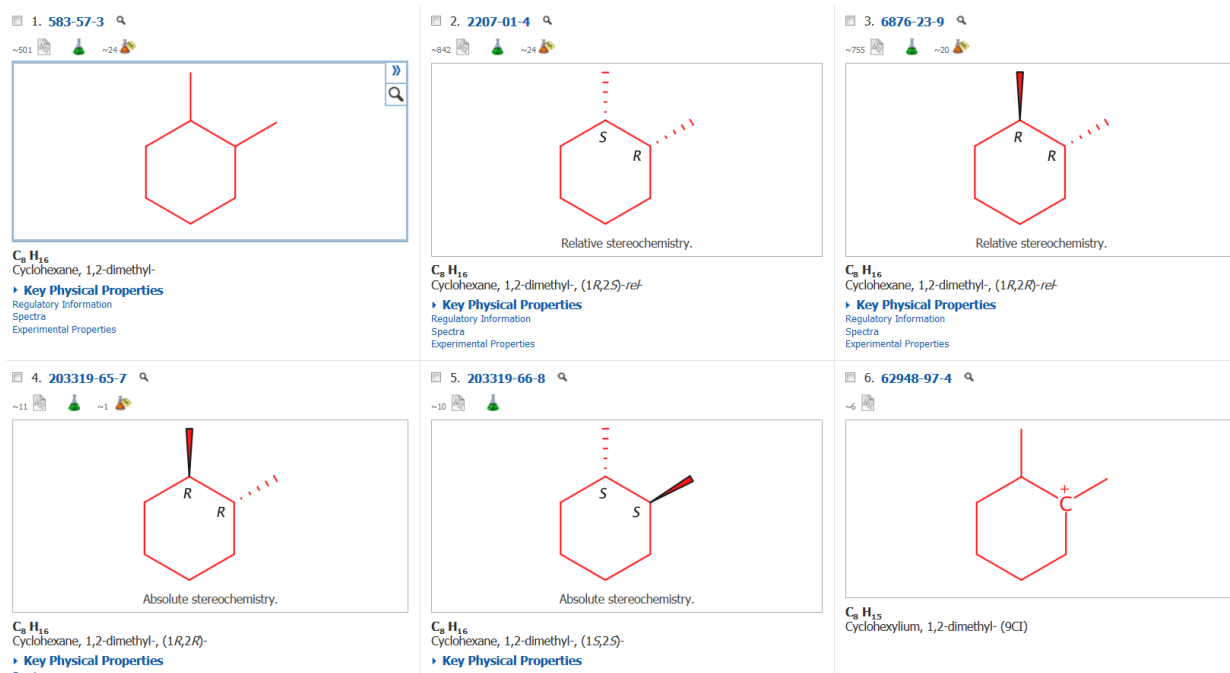
Additional Stereochemistry
Additional Stereochemistry...

Structure Charge
0

Stereo Comments
Stereo Comments

Access
Public



7. Each unique stereochemical option should have its own GSRS record. For the example of 1,2-DIMETHYLCYCLOHEXANE, 5 GSRS records should be created: (1R,2R), (1S,2S), (+/-)-TRANS, CIS (meso), and mixed isomers (with two component CIS/TRANS mixture substance as alternative definition). These are the first five CAS Registry numbers below.





Exact CAS Registry structure searches are equivalent to Flex searches in GSRS.

8. Add Codes as needed, update Access if the code is protected. URLs will be automatically generated for the most common code systems. The first code added for a particular code system should have the PRIMARY Type attribute. Additional codes using the same code system require selection of the most appropriate other attribute. CAS Registry numbers listed by CAS as DELETED are referred to as SUPERCEDED in GSRS.

Codes 2


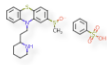


| Delete | Code System * | Code System Type | Type | Code * | References * | Access |
|---|---------------|---------------------|---------|-----------|--------------|---|
|  | BDNUM | Code System Type... | PRIMARY | 0114597AB | 1 |  PROTECTED |
| Url <input type="text" value="url"/> | | | | | | |
| Code Text <input type="text" value="Code Text"/> | | | | | | |

| Delete | Code System * | Code System Type | Type | Code * | References * | Access |
|---|---------------|------------------|---------|------------|--------------|--|
|  | CAS | CHEMICAL | PRIMARY | 14471-95-5 | 1 |  Public |
| Url <input type="text" value="url"/> | | | | | | |
| Code Text <input type="text" value="Code Text"/> | | | | | | |

[+ Add another code](#)

9. Add Relationships, select the substance after searching. Salts and solvates containing multiple discrete molecular entities should always include reference to the organic parent GSRS record.

Relationships 1

| Delete | Related Substance | Type * | References * | Access | Hide Details |
|---|---|--|---|--|---|
|  |  2-METHYLSULFINYL-10-(2-(PIPERIDYL-2)ETHYL-1)PHENOTHIAZINE BESYLATE | SALT/SOLVATE -> PARENT | 1 |  Public | <input type="button" value="Hide Details"/> |
| Qualification <input type="text" value="qualification..."/> | | Mediator Substance <input type="text" value="Search ..."/> <input type="button" value="Q"/> | InteractionType <input type="text" value="interactionType..."/> | Amount  | |
| | | | Comments <input type="text" value="comments"/> | | |

[+ Add another relationship](#)

10. Skip Properties for Chemicals

11. To avoid repeating work, click Submit frequently during the registration process after a structure, a name, and a reference have been added to the record.
 - a. Any Errors (in red) will need to be resolved
 - b. Warnings (in orange) can be dismissed after research has determined there is no need to adjust the registration

The screenshot shows a web form titled "Submit Substance" with a red "X" icon in the top right corner. Below the title, a message states "Errors must be dismissed before final submission". A red button labeled "Dismiss All" is positioned above a yellow warning box. The warning box contains the text "WARNING" followed by "Structure has 1 possible duplicate:" and a blue link "[pending record]2-METHYLSULFINYL-10-(2-(PIPERIDYL-2)ETHYL-1)PHENOTHIAZINE BESYLATE". An orange "Dismiss" button is located at the bottom right of the warning box. Below the warning box, a question asks "Are you sure you'd like to submit this substance?". At the bottom right of the form, there are two buttons: "Go Back" (red) and "Submit" (green).

12. Once a Chemical is submitted, it can be Viewed, Edited, and Edited in New Forms – it's status is Pending
13. A privileged user account will review the registration and approve
 - a. At this point that status will change from Pending to Approved
 - b. A UNII will be assigned

4. Metadata

The attributes included in the schema are briefly summarized below:

Contains GSRS identifier information for the substance such as the BDNUM and the UNII.

Substance Type Specific:

This attribute is shared across all substance types.

This attribute is included in all records.

GSRS prefaces the detail attribute name with the type of substance described (e.g. chemical detail, polymer detail, etc.).

i. Structure

Contains the two-dimensional chemical structure as well as additional metadata such as stereochemistry, optical activity, the molecular formula and weight, number of defined stereocenters and EZ centers, and the charge.

Substance Type Specific:

This attribute is chemical specific.

ii. Moieties

Contains structure information (see Structure) and stoichiometry of moieties contained within the substance.

A moiety is defined as an entity within a substance that has a complete and continuous molecular structure. This includes single substances, ions and solvate molecules.

Substance Type Specific:

This attribute is chemical specific.

iii. Active Moieties

Contains links to the active moieties of the substance.

An active moiety is defined in 21CFR316.3 as the “molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a

complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance.”

Substance Type Specific:

This attribute is shared across all substance types.

iv. Names

Contains Chemical Names, compiled from authoritative and other public sources, associated with the substance.

Chemical Name Types:

- Brand: trade name.
- Code: code name.
- Common: trivial name.
- Official: name given by an official registration authority.
- Systematic: any name constructed using a nomenclature that describes the structure of the substance.

Substance Type Specific:

This attribute is shared across all substance types.

This attribute is included in all records.

v. Codes

Contains numerical identifiers, compiled from authoritative and other public sources, associated with the substance.

Substance Type Specific:

This attribute is shared across all substance types.

This attribute is included in all records.

vi. Relationships

Contains links to substance records related to the substance.

Substance Type Specific:

This attribute is shared across all substance types.

vii. Notes

Contains free-text comments related to the substance and its data.

Substance Type Specific:

This attribute is shared across all substance types.

viii. References

Contains source text/citations for all data presented in the schema.

Substance Type Specific:

This attribute is shared across all substance types.

This attribute is included in all records.

ix. Audit Information

Contains timestamps and identifies the Data Steward associated with approval, creation, and last edit of the substance record.

Substance Type Specific:

This attribute is shared across all substance types.

This attribute is included in all records.

x. Metabolites

Contains links to the metabolites of the substance.

Substance Type Specific:

This attribute is shared by chemical, mixture, protein, concept, and structurally diverse substance types.

xi. Definition

Contains a schema that is used to unambiguously identify a substance that cannot be adequately defined by its structure, sequence, or components.

Substance Type Specific:

This attribute is shared by concept and structurally diverse substance types.

xii. Subunits

Contains sequence information for each subunit in a substance.

Substance Type Specific:

This attribute is shared by protein and nucleic acid substance types.

xiii. Disulfide Bridges

Identifies which pairs of residues are connected by disulfide bridges.

Substance Type Specific:

This attribute is protein specific.

xiv. Modifications

Contains information on structural, physical, and agent modifications to a substance.

Substance Type: Specific:

This attribute is shared by protein, structurally diverse, polymer, and nucleic acid substance types.

xv. Properties

Contains properties information on a substance.

Substance Type Specific:

This attribute is shared by protein, polymer, and nucleic acid substance types.

xvi. Components

Contains links to substance records that are contained within a mixture substance definition and identifies the mixture type.

Mixture Types:

- All of: single substances that are synthesized or isolated together
- One of: used for ambiguous substance classes

Substance Type: Specific:

This attribute is mixture specific.

xvii. Applications, Products, Clinical Trials, Adverse Events

Contains a data table that lists the product, application, clinical trial, and adverse event details associated with the substance and links to the individual records.

Substance Type Specific:

This attribute is shared across all substance types.

xviii. Display Structure

Contains the two-dimensional chemical structure with repeating units shown in brackets.

Substance Type Specific:

This attribute is polymer specific.

xix. Monomers

Contains links to substance records from which repeated units are derived.

Substance Type Specific:

This attribute is polymer specific.

xx. Structural Units

Contains the two-dimensional chemical structure of repeating units.

Substance Type Specific:

This attribute is polymer specific.

xxi. Sugars

Lists the nucleotide sugars contained in a nucleic acid.

Substance Type Specific:

This attribute is nucleic acid specific.

xxii. Linkages

Lists the type of phosphate ester bonds joining nucleotides in a nucleic acid.

Substance Type Specific:

This attribute is nucleic acid specific.

APPENDIX A: USER MANUAL APPROVAL

The undersigned acknowledge that they have reviewed the FDA GSRS **User Manual** and agree with the information presented within this document. Changes to this **User Manual** will be coordinated with, and approved by, the undersigned, or their designated representatives.

Signature: _____ Date: _____
Print Name: _____
Title: _____
Role: Project Manager

APPENDIX B: REFERENCES

The following table summarizes the documents referenced in this document.

| Document Name | Description | Location |
|---------------|-------------|----------|
| | | |
| | | |

APPENDIX C: KEY TERMS

The following table provides definitions and explanations for terms and acronyms relevant to the content presented within this document.

| Term | Definition |
|--------|--|
| CSV | Comma Separated Values |
| GSRS | Global Substance Registration System |
| JSON | JavaScript Object Notation |
| SDF | Structure-data File |
| SMILES | Simplified Molecular Input Line Entry System |
| SRS | Substance Registration System |
| TSV | Tab Separated Values |
| UNII | Unique Ingredient Identifier |
| XML | eXtensible Markup Language |