

Searching for Biosimilars on STN[®]

STN[®]



STN[®]

CAS is a division of the American Chemical Society

Agenda

- What are biosimilars
- Issues with biosimilars
- How to search for biosimilars on STN
 - Text search
 - Sequence search

What are biosimilars?

- Similar to innovator biopharmaceutical products
- Also referred to as follow-on biologics or biogenerics
- Often are protein based, manufactured using microorganisms, plant, or animal cells
- Many are produced using recombinant DNA technology

Biosimilars are more complex than traditional pharmaceuticals

- **Traditional pharmaceuticals**
 - Have well defined chemical structures
 - Manufactured through chemical synthesis
 - Can be analyzed to determine components
- **Biosimilars**
 - Difficult to characterize a complex biologic
 - Changes in the manufacturing process can affect the finished biologic
 - Components of a biologic can be unknown

Biosimilars are not generics

- Generic drugs are equivalent to the reference drug
 - Must contain the same active ingredients, strength, and dosage form
 - Must be therapeutically equivalent
- Manufacturing of biosimilars is less predictable
 - Use of living organisms can affect the final product
 - This can change the therapeutic activity

STN provides useful and up to date information on biosimilars

- Comprehensive collection of patent information
 - CAplusSM, DWPISM, INPADOCDB, PCTFULL, USPAT full text, IFIPAT, IMSPATENTS
- Comprehensive collection of biosequence information
 - CAS REGISTRYSM, DGENE, PCTGEN, and USGENE[®]
- Comprehensive collection of biological and pharmaceutical publications
 - BIOSIS[®], MEDLINE[®], EMBASE, CAplus, and DRUGU

STN clusters help determine which databases have relevant information

- Database clusters
 - BIOSCIENCE
 - BUSINESS
 - FORMULATIONS
 - HEALTH
 - MEDICINE
 - MEETINGS
 - PATENTS
 - PHARMACOLOGY

Database cluster information can be accessed during an online session

=> **DISPLAY CLUSTER**

CLUSTER NAME	COMMENT
ADISBASES	Adis International Limited Database Cluster
AEROTECH	Aerospace and Related Technology Cluster
AGRICULTURE	Agriculture Cluster
ALLBIB	All bibliographic files for
AUTHORS	Files for STNINDEX author
BIOSCIENCE	Bioscience Literature Cluster
BUSINESS	Sci-Tech Business and News Cluster
CASLINK	Linked CAS files (Predefined Search Sequences)
CASRNS	CAS Registry Numbers Cluster
CHEMENG	Chemical Engineering Cluster
CHEMISTRY	Chemical Literature Cluster
COMPANIES	Files for company based searches
COMPUTER	Computer Science Cluster
CONSTRUCTION	Building and Construction Cluster
CORPSOURCE	Files for STNINDEX corporate source based searches

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A list of database clusters can be displayed while using STN.

View the databases included in a specific cluster

```
=> D CLUSTER PHARM
```

CLUSTER NAME	CLUSTER DEFINITION
PHARMACOLOGY	ADISCTI ADISINSIGHT ADISNEWS BABS BIOENG BIOSIS BIOTECHNO CAPLUS CBNB CIN CONFSCI DDFB DDFU DGENE DISSABS DRUGB DRUGU EMBAL EMBASE EPFULL ESBIOBASE IFIPAT IMSPATENTS IMSRESEARCH IPA KOSMET LIFESCI MEDLINE NAPRALERT PASCAL PCTGEN PCTFULL PS RDISCLOSURE SCISEARCH TOXCENTER USAN USGENE USPATFULL USPAT2 Pharmaceutical Science Cluster

To see the databases in the PHARMACOLOGY cluster, enter **D CLUSTER PHARM** at the command prompt.

Customized clusters may be created using the SET CLUSTER command

=> **SET CLUSTER COMMENT**

ENTER CLUSTER NAME OR (?): **.MYBIOCLUSTER**

ENTER COMMENT OR (NONE): **MY BIOSCIENCE CLUSTER**

ENTER LIST OF FILE NAMES OR (?): **CAPLUS AGRICOLA BIOSIS
BIOTECHNO**

MORE FILES, (NONE) OR ?: **NONE**

CLUSTER '**.MYBIOCLUSTER**' DEFINED AS '**CAPLUS, AGRICOLA, BIOSIS,
BIOTECHNO**'

SET COMMAND COMPLETED

=> **D CLUSTER**

CLUSTER NAME	COMMENT
.MYBIOCLUSTER	MY BIOSCIENCE CLUSTER
2ANAVIST	STN AnaVist, Version 2.0, Cluster
2HANAVIST	STN AnaVist, Version 2.0, Cluster (HCAplus)
ADISBASES	Adis International Limited Database Cluster
AEROTECH	Aerospace and Related Technology Cluster

Customized cluster names must start with a period (.)

For example: **.MYBIOCLUSTER**

STNindex is a direct way to identify relevant databases

- Use INDEX to screen STN databases for information of interest
- EXPAND and SEARCH to find which databases cover your search topic and test your search strategy
- Databases can be ranked by the number of hits to identify those with the most information of interest

Use INDEX to screen one or more database clusters

=> **INDEX MEDICINE**

```
INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CAPLUS,
      DDFB, DDFU, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL,
      EMBASE, ESBIODBASE, IFIPAT, IMSDRUGNEWS, IMSPRODUCT, IPA,
      KOSMET, LIFESCI, MEDLINE, NAPRALERT, NLDB, PASCAL, PCTGEN,
      SCISEARCH, ...'
```

Upon entering an INDEX cluster, STN will list the databases within that cluster.

=> **INDEX MEDICINE CONFSCI -IFIPAT**

Databases can be omitted from a cluster by using a minus (-) sign before a database name. To add a database to a cluster, type the database name before or after the cluster name.

Search Example:

The biopharmaceutical drug Neupogen, a granulocyte colony stimulating factor, is used to promote the production of blood cells, mainly neutrophils, *in vivo*.

Retrieve information on biosimilars of granulocyte colony stimulating factor (GCSF).

Determine the appropriate databases

- Use STN clusters to help determine which databases have the relevant information
 - INDEX ALLBIB
 - Use INDEX ALLBIB for comprehensiveness
 - Contains 123 bibliographic databases
 - SEARCH the query
 - DISPLAY RANK the databases
 - Ranks the databases with the highest number of hits first

Use STNindex to see which databases have the desired information

```
=> INDEX ALLBIB
```

```
INDEX '1MOBILITY, 2MOBILITY, ADISCTI, AEROSPACE, AGRICOLA,  
ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, BABS,  
BIBLIODATA, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO,  
CABA, CAPLUS, CASREACT, CBNB, CEABA-VTB, CERAB, CHEMINFORMRX,  
CHEMSAFE, ...'
```

```
ENTERED AT ...
```

There are 123 databases in the ALLBIB cluster.

```
123 FILES IN THE FILE LIST IN STNINDEX
```

```
Enter SET DETAIL ON to see search term postings or to view  
search error messages that display as 0* with SET DETAIL OFF
```

For a full list of the databases included in the ALLBIB cluster, enter **D CLUSTER ALLBIB** at the command prompt.

Search the biosimilar and GCSF concepts in STNindex

```
=> S FOLLOW ON BIOLOGIC OR BIOSIMILAR
```

```
4 FILE ADISCTI
```

```
15 FILE ADISINSIGHT
```

```
18 FILE ADISNEWS
```

```
6 FILE BABS
```

```
• • •
```

```
54 FILES HAVE ONE OR MORE ANSWERS, 123 FILES SEARCHED IN STNINDEX
```

```
L1 QUE FOLLOW ON BIOLOGIC OR BIOSIMILAR
```

```
=> S GRANULOCYTE COLONY STIMULATING FACTOR OR GCSF OR G-CSF
```

```
2963 FILE ADISCTI
```

```
102 FILE ADISINSIGHT
```

```
859 FILE ADISNEWS
```

```
• • •
```

```
86 FILES HAVE ONE OR MORE ANSWERS, 123 FILES SEARCHED IN STNINDEX
```

```
L2 QUE GRANULOCYTE COLONY STIMULATING FACTOR OR GCSF OR G-CSF
```

Searching each concept and retrieving separate L-numbers allows you to easily combine different concepts later on.

RANK the databases to reorder the databases

```

=> S L1 AND L2
      2 FILE ADISCTI
      2 FILE AGRICOLA
      1 FILE BIBLIODATA
      4 FILE BIOENG
     18 FILE BIOSIS
      . . .
  26 FILES HAVE ONE OR MORE ANSWERS,
L3   QUE L1 AND L2

=> D RANK
F1      119   EMBASE
F2       70   CBNB
F3       22   SCISEARCH
F4       18   BIOSIS
F5       14   CAPLUS
. . .

```

Use the AND operator to combine the two concepts to make the initial search a broad search. After determining database specific terms, use more specific proximity operators to narrow the search.

DISPLAY RANK (D RANK) reorders databases in hit occurrence order instead of alphabetical order.

Enter EMBASE to find additional terms

```
=> FILE F1; S L3; D SCAN
```

```
L4          119 L1 AND L2
```

```
L4  119 ANSWERS  EMBASE  COPYRIGHT (c) 2011 Elsevier B.V. All
```

```
TI  [Biodrugs] and biosimilars in oncology: At what point are we?].
```

```
• • •
```

```
L4  119 ANSWERS  EMBASE  COPYRIGHT (c) 2011 Elsevier B.V. All
rights reserved on STN
```

```
TI  Health economics of market access for biopharmaceuticals and
biosimilars.
```

```
• • •
```

```
L4  119 ANSWERS  EMBASE  COPYRIGHT (c)
```

```
TI  [Protein drugs: Biosimilars are co
```

```
• • •
```

```
L4  119 ANSWERS  EMBASE  COPYRIGHT (c)
reserved on STN
```

```
TI  [Similar biological medicinal products] - Legislation
modifications and development].
```

You can enter the command **FILE EMBASE** instead of FILE F1.

The terms *biodrugs*, *biopharmaceuticals*, *protein drugs*, and *similar biological medicinal products* can be added to the search query.

Enter CBNB to find additional terms

=> **FILE CBNB**

=> **S L3**

L5 70 L1(L)L2

=> **D TRIAL TI**

L5 ANSWER 1 OF 70 CBNB COPYRIGHT 2011 EI on STN

TI Hospira Japan to begin development of biosimilars in Japan.

L4 ANSWER 13 OF 70 CBNB COPYRIGHT 2011 EI on STN

TI Hospira begins Phase I US clinical trial of biosimilar erythropoietin in renal patients.

L4 ANSWER 20 OF 70 CBNB COPYRIGHT 2011 EI

TI Teva announces FDA accepts BLA for XM02.

L4 ANSWER 23 OF 70 CBNB COPYRIGHT 2011 EI

TI Intas looks beyond **biogenerics.**

CBNB is a database that focuses on chemical industry news. For more information about this database, please refer to the Database Summary Sheet.

The term *biogeneric* can be added to the search query.

Use Controlled Term Thesauri to find relevant terms

=> FILE MEDLINE

=> E BIOSIMILAR/CT

E#	FREQUENCY	AT	TERM
--	-----	--	----
E1	0	2	BIOSEPT/CT
E2	0	2	BIOSHIK/CT
E3	0	-->	BIOSIMILAR/CT
E4	0	2	BIOSINT/CT
E5	0	2	BIOSTATIST/CT
E6	291	31	BIOSTATISTICS/CT
E7	6		BIOSTATISTICS: HI, HISTORY/CT
E8	126		BIOSTATISTICS: MT, METHODS/CT
E9	0	1	BIOSTIMULATION/CT
E10	0	2	BIOSTIMULATION, LASER/CT
E11	21	38	BIOSURVEILLANCE/CT
E12	14		BIOSURVEILLANCE: MT, METHODS/CT

Use the Controlled Term (/CT) Thesaurus in each database to find database specific terms.

The term *BIOSIMILAR* is not a controlled term for MEDLINE.

A thesaurus is a useful tool to check for database specific terms

=> E BIOPHARMACEUTICAL/CT			
E#	FREQUENCY	AT	T
---	-----	--	-
E13	0	1	B
E14	0	2	B
			DIHYDROCHLORIDE/CT
E15	0	-->	BIOPHARMACEUTICALS/CT
E16	1960	11	BIOPHARMACEUTICS/CT
E17	38		BIOPHARMACEUTICS: CL, CLASSIFICATION/CT
E18	46		BIOPHARMACEUTICS: EC, ECONOMICS/CT
E19	2		BIOPHARMACEUTICS: ED, EDUCATION/CT
E20	1		BIOPHARMACEUTICS: ES, ETHICS/CT
E21	6		BIOPHARMACEUTICS: HI, HISTORY/CT
E22	15		BIOPHARMACEUTICS: IS,
E23	26		BIOPHARMACEUTICS: LJ,
			JURISPRUDENCE/CT
E24	169		BIOPHARMACEUTICS: MT,

The term *Biopharmaceuticals* is not a controlled term in MEDLINE, although the term *Biopharmaceutics* is a controlled term and has 11 associated terms.

Use the **+ALL** relationship code to see related terms.

Check for database specific terms related to Granulocyte Colony Stimulating Factor

```

=> E GRANULOCYTE COLONY STIMULATING FACTOR/CT
E#   FREQUENCY   AT   TERM
--   -
E72      0       2   GRANULOCYTE CHEMOTACTIC PROTEIN 2/CT
E73      0       2   GRANULOCYTE CHEMOTACTIC PROTEIN-2/CT
E74      0       1 --> GRANULOCYTE COLONY STIMULATING FACTOR/CT
E75      0       2   GRANULOCYTE COLONY STIMULATING FACTOR RECEPTORS/CT
E76     926     61   GRANULOCYTE COLONY STIMULATING FACTOR, RECOMBINANT/CT
E77      1       1   GRANULOCYTE COLONY STIMULATING FACTOR, RECOMBINANT:
AA, ANALOGS & DERIVATIVES/CT
E78     221     1   GRANULOCYTE COLONY STIMULATING FACTOR, RECOMBINANT:
AD, ADMINISTRATION & DOSAGE/CT
E79     110     1   GRANULOCYTE COLONY STIMULATING FACTOR, RECOMBINANT:
AE, ADVERSE EFFECTS/CT
E80      5       1   GRANULOCYTE COLONY STIMULATING FACTOR, RECOMBINANT:
AF, ANALOGS & DERIVATIVES/CT
E81      5       1   GRANULOCYTE COLONY STIMULATING FACTOR, RECOMBINANT:
AG, ADMINISTRATION & DOSAGE/CT
E82     15      1   GRANULOCYTE COLONY STIMULATING FACTOR, RECOMBINANT:
BI, BIOSYNTHESIS/CT
  
```

In MEDLINE, the term *Granulocyte Colony Stimulating Factor, Recombinant/CT* might be of interest since it has 61 associated terms (AT).

MEDLINE's MeSH term thesaurus includes the MeSH number

=> E E76+ALL

• • •

E126	4972	BT2	Colony
E127	9703	BT1	Granu
			Facto
E128	926	-->	Gran
			Factor, Recombinant/CT

MeSH headings are arranged in a hierarchical tree structure within broad categories. These categories are further divided into narrower and related topics.

E129	2200	MN	D12.644.276.374.410.240.350.375./CT
E130	2200	MN	D12.644.276.374.410.240.75.350./CT
E131	2200	MN	D12.776.395.240.200.375./CT
E132	2200	MN	D12.776.395.240.75.350./CT
E133	2200	MN	D12.776.467.374.410.240.350.375./CT
E134	2200	MN	D12.776.467.374.410.240.75.350./CT
E135	2200	MN	D12.776.828.75.350./CT
E136	2200	MN	D23.529.374.410.240.350.375./CT
E137	2200	MN	D23.529.374.410.240.75.350./CT

DC an INDEX MEDICUS major descriptor

Additional terms can be found in the MeSH thesaurus

Previous Indexing Note (PNTE) lists the previous index name for the term.

NOTE Granulocyte colony stimulating factors prepared by recombinant DNA technology.
 INDX DF: GCSF RECOMBINANT
 AQ AD AE AG AI AN BI BL CF CH CL CS CT
 DE DU EC GE HI IM IP ME PD PK PO RE
 SDSE ST TO TU UL UR

PNTE Colony-Stimulating Factors (1986-1990)
 PNTE Granulocyte Colony-Stimulating Factor (1991-1996)
 PNTE Recombinant Proteins (1986-1996)

E138 0 UF **G CSF,** Recombinant/CT
 E139 0 UF G-CSF, Recombinant/CT
 F GCSF RECOMBINANT/CT
 F Recombinant G CSF/CT
 F Recombinant G-CSF/CT
 F Recombinant Granulocyte Colony Stimulating Factor/CT
 T1 **Filgrastim/**CT
 ***** END *****

Terms such as G CSF, G-CSF recombinant, recombinant G-CSF, and Colony Stimulating Factors can be useful.

Additional terms found in EMBASE, CBNB, BIOSIS, CAPLUS, and MEDLINE for biosimilars

- Biogenerics
- Biological drugs
- Biopharmaceutical
- Biopharmaceutical based-biosimilar drug
- Follow-on proteins
- Follow-on drug
- Generic biologic drug
- Protein drugs
- Similar biological medicinal products

Additional terms found for Granulocyte Colony Stimulating Factor

- Colony stimulating factor
- Filgrastim
- G CSF
- G-CSF
- GCSF
- GCSF recombinant
- G CSF recombinant
- Recombinant GCSF
- Recombinant G CSF

Several factors should be considered when selecting databases

- Type of database
 - Bibliographic, full-text, news, and substance
- Years and countries covered
- Are the records indexed?
- Does the database include patents?
- Does the database include classifications?

Check the STN Database Summary Sheets at www.cas.org for information on STN database content and coverage.

Enter the databases of interest

```
=> FILE F1-F6
```

```
FILE 'EMBASE' ENTERED ● ● ●
```

```
FILE 'CBNB' ENTERED ● ● ●
```

```
FILE 'SCISEARCH' ENTERED ● ● ●
```

```
FILE 'BIOSIS' ENTERED ● ● ●
```

```
FILE 'CAPLUS' ENTERED ● ● ●
```

```
FILE 'MEDLINE' ENTERED ● ● ●
```

After reviewing the STN Database Summary Sheets, these are the top ranked databases for our search.

For a comprehensive search, use all relevant files.

Modify the original search query

```
=> SET MSTEPS ON
```

```
=> S ((BIOLOGICAL OR GENERIC BIOLOGIC OR PROTEIN OR FOLLOW ON OR
BIOPHARMACEUTICAL BASED BIOSIMILAR) (W) DRUG) OR FOLLOW ON
PROTEIN OR FOLLOW ON BIOLOGIC OR SIMILAR BIOLOGICAL MEDICINAL
PRODUCTS OR BIOPHARMACEUTICAL OR BIOGENERIC OR BIOSIMILAR
```

L9	5002	FILE	EMBASE
L10	32342	FILE	CBNB
L11	4269	FILE	SCISEARCH
L12	4588	FILE	BIOSIS
L13	9810	FILE	CAPLUS
L14	3273	FILE	MEDLINE

Using **SET MSTEPS ON**, each database has its own L-number answer set. This allows you to refine the information from a specific database without having to re-run the search.

```
TOTAL FOR ALL FILES
```

```
L15      59284 ((BIOLOGICAL OR GENERIC BIOLOGIC OR PROTEIN OR FOLLOW
ON OR BIOPHARMACEUTICAL BASED BIOSIMILAR) (W) DRUG)
OR FOLLOW ON PROTEIN OR FOLLOW ON BIOLOGIC OR • • •
```

Modify the original search query (cont.)

```
=> SET MSTEPS OFF
```

```
=> S GRANULOCYTE COLONY STIMULATING FACTOR OR GCSEF OR G CSF OR G-CSF  
OR COLONY STIMULATING FACTOR OR CSF OR FILGRASTIM
```

```
L16      441017 GRANULOCYTE COLONY STIMULATING FACTOR OR GCSEF OR G  
          CSF OR G-CSF OR COLONY STIMULATING FACTOR OR CSF OR  
          FILGRASTIM
```

Using **SET MSTEPS OFF**, only one L-number is shown containing the total for all files.

Duplicate Remove removes duplicates from a multifile search

```
=> SET MSTEPS ON
```

```
=> S L15 (L) L16
```

```
L17          39 FILE EMBASE
L18          228 FILE CBNB
L19          38 FILE SCISEARCH
L20          35 FILE BIOSIS
L21          72 FILE CAPLUS
L22          35 FILE MEDLINE
```

```
TOTAL FOR ALL FILES
```

```
L23          447 L15 (L) L16
```

```
=> DUP REMOVE L18 L21 L22 L17 L20 L19
```

```
L24  327 DUP REMOVE L18 L21 L22 L17 L20 L19 (120 DUPLICATES REMOVED)
```

```
ANSWERS '1-228' FROM FILE CBNB
```

```
ANSWERS '229-300' FROM FILE CAPLUS
```

```
ANSWERS '301-311' FROM FILE MEDLINE
```

```
ANSWERS '312-314' FROM FILE EMBASE
```

```
ANSWERS '315-321' FROM FILE BIOSIS
```

```
ANSWERS '322-327' FROM FILE SCISEARCH
```

MSTEPS ON allows you to select the order of the files that you want to keep during a duplicate remove command.

Display the information

=> **D BIB 1 FROM EACH**

L24 ANSWER 1 OF 327 **CBNB** COPYRIGHT 2011 EI on STN
AN 27(14):18479 CBNB
TI Investigational direct-acting antiviral BMS-790052 plus peg-
interferon alfa and ribavirin achieved up to 92% sustained
virologic response in Phase II dose-ranging study of
treatment-naive hepatitis C patients.
SO (31 Mar 2011), (900 plus words)
Availability: Bristol-Myers Squibb Co, 345 Park Avenue, NY
10154 0037, USA, tel: +1 212 546 4000, website:
<http://www.bms.com>
DT Press Release; (Overview)
LA English
PY 2011

The command **D BIB 1 FROM EACH** allows you to easily display the first record from each database. To display the second record from each database, enter **D BIB 2 FROM EACH**.

Record 1 from CPlus

L24 ANSWER 229 OF 327 **CAPLUS** COPYRIGHT 2011 ACS on STN DUPLICATE 1
AN 2010:1423231 CAPLUS
DN 154:103919
TI Carbon nanotube-assisted enhancement of surface plasmon
resonance signal
AU Lee, Eun Gyo; Park, Kyung Mi; Jeong, Jin Young; Lee, Seung Hui;
Baek, Jung Eun; Lee, Hong Weon; Jung, Joon Ki; Chung, Bong Hyun
CS Korea Research Institute of Bioscience and Biotechnology,
Yuseong, Daejeon, 305-600, S. Korea
SO Analytical Biochemistry (2011), 408(2), 206-211
CODEN: ANBCA2; ISSN: 0003-2697
PB Elsevier B.V.
DT Journal
LA English
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

Record 1 from MEDLINE

L24 ANSWER 301 OF 327 **MEDLINE** on STN DUPLICATE 5
AN 2010848275 MEDLINE
DN PubMed ID: 20706990
TI Biosimilar epoetins and other "follow-on" biologics: update on
the European experiences.
AU Jelkmann Wolfgang
CS Institute of Physiology, University of Luebeck, Ratzeburger
Allee 160, Luebeck, Germany. jelkmann@physio.uni-luebeck.de
SO American journal of hematology, (2010 Oct) Vol. 85, No. 10, pp.
771-80.
• • •
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 201010
ED Entered STN: 28 Sep 2010
Last Updated on STN: 13 Oct 2010
Entered Medline: 12 Oct 2010

Record 1 from EMBASE

```
L24 ANSWER 312 OF 327 EMBASE COPYRIGHT (c) 2011 Elsevier B.V. All
rights reserved on STN DUPLICATE 10
AN 2009017354 EMBASE
TI Neutrophil biology and the next generation of myeloid growth
factors.
AU Dale, David C., Dr. (correspondence)
CS Department of Medicine, University of Washington Medical
Center, 1959 NE Pacific Street, Seattle, WA 98195-6422, United
States.
SO JNCCN Journal of the National Comprehensive Cancer Network,
(January 2009) Vol. 7, No. 1, pp. 92-98.
PB Jones and Bartlett Publishers, 40 Tall Pine Drive, Sudbury, MA
DT Journal; Article
FS 016 Cancer
025 Hematology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
ED Entered STN: 6 Feb 2009
Last Updated on STN: 6 Feb 2009
```

Record 1 from BIOSIS

L24 ANSWER 315 OF 327 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on STN

AN 2010:26023 BIOSIS

DN PREV201000026023

TI Enzymatic techniques for PEGylation of biopharmaceuticals.

AU Sergi, Mauro [Reprint Author]; Caboi, Francesca; Maullu, Carlo; Orsini, Gaetano; Tonon, Giancarlo

CS Bioker Srl, Parco Sci and Tecnol Sardegna, I-09010 Cagliari, Italy mauro.sergi@ablynx.com

SO Veronese, FM [Editor]. (2009) pp. 75-88. PEGylated Protein Drugs: Basic Science and Clinical Applications. Publisher: BIRKHAUSER VERLAG AG, VIADUKSTRASSE 40-44, PO BOX 133, CH-4010 BASEL, SWITZERLAND. Series: Milestones in Drug Therapy. ISBN: 978-3-7643-8678-8 (H).

DT Book; (Book Chapter)

LA English

ED Entered STN: 23 Dec 2009
Last Updated on STN: 23 Dec 2009

Record 1 from SCISEARCH®

L24 ANSWER 322 OF 327 SCISEARCH COPYRIGHT (c) 2011 The Thomson Corporation on STN

AN 2007:1211290 SCISEARCH

GA The Genuine Article (R) Number: 228IE

TI Biologically active human GM-CSF produced in the seeds of transgenic rice plants

AU Dudani, Anil K. (Reprint)

CS Hlth Canada, Biol & Genet Therapies Directorate, Tunneys Pasture, Ottawa, ON K1A 0L2, Canada (Reprint)

• • •

SO TRANSGENIC RESEARCH, (DEC 2007) Vol. 16, No. 6, pp. 713-721. ISSN: 0962-8819.

PB SPRINGER, VAN GODEWIJCKSTRAAT 30, 3311 GZ DORDRECHT, NETHERLANDS.

DT Article; Journal

LA English

REC Reference Count: 46

ED Entered STN: 6 Dec 2007
Last Updated on STN: 6 Dec 2007

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

Search Example

The biopharmaceutical drug Neupogen, a granulocyte colony stimulating factor, is used to promote the production of blood cells, mainly neutrophils, *in vivo*.

Retrieve information on biosimilars of granulocyte colony stimulating factor (GCSF).

Create an alert in CBNB, CAplus, MEDLINE, EMBASE, BIOSIS, and SCISEARCH to monitor information on GCSF biosimilars.

What is a current awareness alert?

- The ALERT command is used to set up an automatic current awareness search
- Alerts run on a user-defined, periodic basis
- Alert queries run only on the segment of a database that has been added/updated since the last run

Why use current awareness alerts?

- Monitor research developments
 - New technology
 - New substances
 - New uses for substances
- Track competitor publications
- Monitor patent portfolios
 - Freedom to operate
 - Validity
 - Infringement

STN offers both single-file and multifile alerts

- Run the query in one or more database
- Run a customized query in each database
- Specify the number of databases
 - Alerts must be allowed in the database of interest
- Duplicates are automatically removed
- Answers are delivered by either e-mail, online, or hardcopy

Different ways to receive alert results

- Online
 - Saved in an answer set with your login ID
 - Retrieve your online session using the `ACTIVATE` command
 - Allows you to perform additional analysis and editing
- E-mail
 - For multifile results, each database's results delivered separately
- Hardcopy
 - Delivered to a specified address via US mail

Update dates are the key for alert retrieval

- Key update field codes
 - Entry Date (/ED)
 - Retrieves records the day they are added to the database
 - Usually does not change unless the database is reloaded
 - Update Date (/UP)
 - Retrieves records when they are added or modified
 - This is the default Alert option

HELP UPDATE lists database-specific update codes

=> **FILE CAPLUS**

=> **HELP UPDATE**

● ● ●

The most frequently used update qualifiers in CAPLUS SDIs or SMARTracker are:

- UP (Update Date); retrieves records when they are added or modified, up to their publication in CA (the default SDI option)
- UPIT (Update by Addition of Registered Substance); retrieves records updated with new CAS Registry Number identifiers after publication of the record in CA
- UPM (Update Date, Maximum); retrieves records meeting the qualifications for UPIT as well as patent records updated with new or significantly modified patent family member information
- UPOG (Update Date, Citing References); retrieves records updated with new citing references

Many databases have specialized Update codes for alerts. Check **HELP UPDATE** when setting up your alert.

Setting up multifile alerts in STN is easy

```
=> FILE CBNB CAPLUS MEDLINE EMBASE SCISEARCH BIOSIS
```

```
=> ALERT MFILE
```

```
MULTIFILE SDI GENERAL PARAMETERS
```

Enter the databases
for the multifile alert.

```
-----  
ENTER MULTIFILE SDI REQUEST NAME ('AA001/S'), OR END: MFILEGCSF/S
```

```
ENTER TITLE (NONE): MULTIFILE GCSF BIOSIMILARS
```

```
ENTER COST CENTER (NONE) OR NONE: NONE
```

```
ENTER METHOD OF DELIVERY (EMAIL), OFFLINE, OR ONLINE: EMAIL
```

```
ENTER EMAIL ID (6485C): JANEDOE@CAS.ORG
```

```
JANEDOE@CAS.ORG
```

```
RECEIVE DELIVERY NOTIFICATION? (Y)/N: Y
```

```
SEND SDI WITH NO ANSWERS? (Y)/N: N
```

```
DISPLAY QUERY INFORMATION? (Y)/N: Y
```

```
ELIMINATE PREVIOUSLY SEEN ANSWERS WITH EACH SDI RUN? Y/(N): N
```

```
HIGHLIGHT HIT TERMS? (Y)/N: Y
```

```
ENTER SDI EXPIRATION DATE 'YYYYMMDD' OR (NONE): 20111231
```

In the first part of the
MFILE ALERT, you can
set general parameters.

Set database specific parameters

MULTIFILE SDI FILE SPECIFIC PARAMETERS: **CBNB**

ENTER COMPONENT SDI REQUEST NAME ('AA001/S') OR END: **GCSFCBNB/S**

ENTER QUERY L# FOR MULTIFILE SDI REQUEST OR END: **L23**

MULTIFILE SDI FILE SPECIFIC PARAMETERS: **EMBASE**

ENTER COMPONENT SDI REQUEST NAME ('AA001/S') OR END: **GCSFEMBASE/S**

ENTER QUERY L# FOR MULTIFILE SDI REQUEST OR END: **L23**

ENTER UPDATE FIELD CODE (ED), UP, EDAL, UPAL OR ?: **UP**

ENTER SDI RUN FREQUENCY - (WEEKLY), BIWEEKLY, OR ?: **WEEKLY**

L-numbers created by the SORT or DUPLICATE commands, or the result of a multifile search, cannot be used as the query in an alert request.

MULTIFILE SDI FILE SPECIFIC PARAMETERS: **SCISEARCH**

ENTER COMPONENT SDI REQUEST NAME ('AA001/S') OR END: **GCSFSICSE/S**

ENTER QUERY L# FOR MULTIFILE SDI REQUEST OR END: **L23**

ENTER UPDATE FIELD CODE (ED), UP, EDAL, UPAL OR ?: **UP**

Set database specific parameters (cont'd)

MULTIFILE SDI FILE SPECIFIC PARAMETERS: **CAPLUS**

ENTER COMPONENT SDI REQUEST NAME ('AA001/S') OR END: **GCSFCAP/S**

ENTER QUERY L# FOR MULTIFILE SDI REQUEST OR END: **L23**

ENTER UPDATE FIELD CODE (UP), UPM, UPIT, UPI, ED, UPP, UPOG OR ?: **UP**

ENTER SDI RUN FREQUENCY - DAILY, (WEEKLY), BIWEEKLY, OR ?: **WEEKLY**

MULTIFILE SDI FILE SPECIFIC PARAMETERS: **MEDLINE**

ENTER COMPONENT SDI REQUEST NAME ('AA001/S') OR END: **GCSFMEDLINE/S**

ENTER QUERY L# FOR MULTIFILE SDI REQUEST OR END: **L23**

ENTER UPDATE FIELD CODE (ED), UP OR ?: **UP**

ENTER SDI RUN FREQUENCY - EVERYUPDATE, (WEEKLY), MONTHLY, OR ?: **WEEKLY**

MULTIFILE SDI FILE SPECIFIC PARAMETERS: **BIOSIS**

ENTER COMPONENT SDI REQUEST NAME ('AA001/S') OR END: **GCSFBIOSIS/S**

ENTER QUERY L# FOR MULTIFILE SDI REQUEST OR END: **L23**

ENTER UPDATE FIELD CODE (ED), UP OR ?: **UP**

ENTER SDI RUN FREQUENCY - (WEEKLY), BIWEEKLY, OR ?: **WEEKLY**

Four links are provided to display your results in email delivery

STN Results: MULTIFILE GCSF BIOSIMILARS

Your STN results are just a click away. STN brings you more electronic delivery options than ever. Delivering sci-tech information as you like it, STN is proud to be your choice for the most current and timely information available.

Click on a link below to retrieve your results:

Title: **MULTIFILE GCSF BIOSIMILARS**
Reference Number: **AFS0097C**
Number of Answers: **2**
File Name: **CAPLUS**
SDI Name: **GCSFCAP/S**
SDI Run Number: **015**
SDI Run Date: **APR 15, 2011**

1. [RTF](#) (Rich Text Format)
2. [PDF](#) (Adobe Portable Document Format)
3. [HTML](#) (Hypertext Markup Language)
4. [Plain Text](#) (ASCII)

Links will expire 90 days from the date this message was sent. Be sure to save your results.

If you have any questions regarding these options or require assistance retrieving your results, please contact the [Help Desk](#).

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SEQLINK EXACT is a quick and easy way to find biosimilars having similar sequences

- For comprehensive retrieval of CAplus references, use Registry Numbers for all records with the same sequence
- SEQLINK EXACT locates additional protein or nucleic acid sequences that have the same sequence backbone as that of a protein or nucleic acid sequence of interest

SEQLINK EXACT

- Use SEQLINK EXACT with
 - A Registry Number
 - An E-number containing the CAS Registry Number
 - A REGISTRY L-number answer set
 - An ANALYZE L-number set containing CAS Registry Numbers

Search Example:

Epex is a biopharmaceutical used to treat anemia in patients with kidney problems or patients receiving chemotherapy. Epex's active ingredient is epoetin alpha. Retrieve all the various glycoforms of epoetin, and find references focusing on epoetin biosimilars.

CAS sequence indexing

- CAS indexes sequences from many sources
- A separate Registry Number is assigned to each reported sequence
 - Chemically modified sequences receive their own CAS Registry Numbers
 - Each GENBANK[®] accession number and each sequence from journals and patents are registered by a separate Registry Number
- The CAS RN for each sequence is linked to the original source of registration or the reference from which it was indexed

Retrieve the sequence information for Eprex

```
=> FILE REGISTRY

=> E EPREX/CN 10
E1          1      EPRAZINONE HYDROCHLORIDE/CN
E2          1      EPREG/CN
E3          1 --> EPREX/CN
E4          1      EPRI 13/CN
E5          1      EPRI P87/CN
E6          1      EPRI-E/CN
E7          1      EPRI-T/CN
E8          1      EPRICORD/CN
E9          1      EPRICORD OPAQUE PRIMER/CN
E10         1      EPRIN/CN

=> S E3;D SQIDE
L1          1 EPREX/CN
```

EXPAND on the chemical name before searching.

Use the semicolon (;) to stack multiple commands onto one command line. SQIDE displays identification information, plus the sequence.

REGISTRY provides detailed sequence information in the CA index name

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2011 ACS on STN

RN 113427-24-0 REGISTRY

CN 1-165-Erythropoietin (human clone λ HEPOFL13 protein moiety),
glycoform α (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Alfaepoetina
CN Binocrit
CN EPIAO
CN EPO
CN Epoade
CN Epoetin alfa
CN Epoetin alfa Hexal
CN Epogen
CN ***Eprex***
CN Erypo
CN Erypo 4000

Information about the type of glycoform (alpha in this example) is listed in the Chemical Name (/CN) field.

Other common names for epoetin alpha, such as Eprex and Erypo are listed in Other Names.



Sequence Notes field (/NTE) provides additional useful information

```
FS    PROTEIN SEQUENCE
SQL  165
```

```
NTE
```

```
----- location -----
type                description
-----
bridge              Cys-7      - Cys-161    disulfide bridge
bridge              Cys-29     - Cys-33     disulfide bridge
-----
```

Modifications, bridges, uncommon residues, etc. are listed in the Sequence Notes field (/NTE).

```
SEQ      1 APPRLICDSR VLERYLLEAK EAE
          51 WKRMEVGQQA VEVWQGLALL SEA
          101 GLRSLTLLR  ALGAQKEAIS PPD
          151 GKLKLYTGEA CRTGD
```

“Related Sequences Available with SEQLINK” indicates that there are related sequences indexed with different RNs.

```
**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
```

```
• • •
```

Use SEQLINK to quickly and easily retrieve other related sequences

```

=> SEQLINK L1; D SQIDE 1
L2          55 SEQLINK EXACT L1
L2  ANSWER 1 OF 55  REGISTRY  COPYRIGHT
RN  1256858-75-9  REGISTRY
CN  Erythropoietin (human)  (CA INDEX NA
OTHER NAMES:
CN  1: PN: US7842661 SEQID: 1 claimed protein
FS  PROTEIN SEQUENCE
SQL  165
PATENT ANNOTATIONS (PNTE):
Sequence Source |Patent Reference
=====+=====
Not Given      |US7842661
                |claimed SEQID 1
SEQ           1 APPRLICDSR VLERYLLEAK EAENITTGCA EHCSLNENIT VPDTKVNFYA
              51 WKRMEVGQQA VEVWQGLALL SEAVLRGQAL LVNSSQPWEP LQLHVDKAVS
                ...
**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

```

Using SEQLINK, a total of 54 additional sequences were retrieved, plus the original RN for Eprex.

This sequence record has the same sequence listing as Eprex, but has a separate Registry Number.

SEQLINK retrieves various glycoforms of epoetin

RN 604802-70-2 REGISTRY
 CN 1-165-Erythropoietin (human clone B03XA01) (CA INDEX NAME)

OTHER NAMES:

CN Epoetin zeta
 CN Retacrit
 CN Silapo

This record is for the zeta glycoform of epoetin.

FS PROTEIN SEQUENCE

SQL 165

NTE

Both Retacrit and Silapo were approved and authorized as biosimilar medicines in the European Union (EU) in 2007.

type	location		description
bridge	Cys-7	- Cys-161	disulfide bridge
bridge	Cys-29	- Cys-33	disulfide bridge


```

SEQ      1 APPRLICDSR VLERYLLEAK EAENITTGCA EHCSLNENIT VPDTKVNIFYA
        51 WKRMEVGQQA VEVWQGLALL SEAVLRGQAL LVNSSQPWEP LQLHVDKAVS
       101 GLRSLTLLR ALGAQKEAIS PPDAASAAPL RTITADTFRK LFRVYSNFLR
       151 GCLKLYTGEA CRTGD
  
```

Enter CAPLUS to retrieve references for biosimilars of epoetin

=> FILE CAPLUS

=> S L2

L3 1148 L2

A total of 1148 references retrieved in CAPLUS for epoetin.

=> S L3 AND (((BIOLOGICAL OR GENERIC BIOLOGIC OR PROTEIN OR FOLLOW ON OR BIOPHARMACEUTICAL BASED BIOSIMILAR) (W) DRUG) OR FOLLOW ON PROTEIN OR FOLLOW ON BIOLOGIC OR SIMILAR BIOLOGICAL MEDICINAL PRODUCTS OR BIOPHARMACEUTICAL OR BIOGENERIC OR BIOSIMILAR)

L4 26 L3 AND (BIOSIMILAR OR BIOGENERIC OR F

Refine the references with terms representing biosimilars.

=> D BIB HITIND

L4 ANSWER 1 OF 26 CAPLUS COPYRIGHT 2011 A

AN 2010:1230317 CAPLUS

DN 154:118974

TI Quality of Original and ***Biosimilar*** Epoetin Products

AU Brinks, Vera; Hawe, Andrea; Basmeh, Abdul H. H.; Joachin-

Rodriguez, Liliana; Haselberg, Rob; Somsen, Govert W.; • • •

HIT indexing in CPlus

CS Department of Pharmaceutics Utrecht Institute for
Pharmaceutical Sciences (UIPS), Utrecht University, • • •

SO Pharmaceutical Research (2011), 28(2), 386-393

ST erythropoietin detn **biosimilar** ELISA electrophoresis chromatog
quality control

IT Structure-activity relationship
(immunogenic; quality of products)

IT High-performance gel-permea
(size-exclusion, high performance size exclusion chromatog.;
quality of original and **biosimilar** epoetin products)

IT **113427-24-0**, Eprex **261356-80-3**, Dynepo
604802-70-2, Retacrit

RL: ANT (Analyte); PAC (Pharmacological activity); PRP
(Properties); THU (Therapeutic use); ANST (Analytical study);
BIOL (Biological study); USES (Uses)
(quality of original and **biosimilar** epoetin products)

This journal record focused on three glycoforms of epoetin: *Eporex* (alpha), *Dynepo* (delta), and *Retacrit* (zeta).

AN 2009:1433050 CAPLUS
 DN 151:537072
 TI Treatment of hearing and balance impairments using compounds
 having erythropoietin activity
 IN Miller, Guy M.
 PA Edison Pharmaceuticals, Inc. USA
 SO PCT Int. Appl., 39 pp.
 DT Patent
 LA English
 FAN.CNT 1

This patent record focuses on the delta form of epoetin. This record might have been missed without SEQLINK.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	WO 2009140382	A2	20091119	WO 2009-US43786	20090513
	WO 2009140382	A3	20100107		
	CA 2723621	A1	20091119	CA 2009-2723621	20090513
PRAI	US 2008-127877P	P	20080515		
	WO 2009-US43786	W	20090513		

IT 11096-26-7D, Erythropoietin, carbamylated **261356-80-3**, Dynepo

• • •

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (hearing and balance impairments treatment using compds.
 having erythropoietin activity)

Summary

- STN has multiple tools for searching biosimilar information
- Find chemical name synonyms in REGISTRY and in thesauri in STN databases
- Use SEQLINK to easily and quickly retrieve related sequences
- Create ALERTs to stay updated about biosimilars

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