Searching for Biosimilars on STN®
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
  – CAplus\textsuperscript{SM}, DWPI\textsuperscript{SM}, INPADOCDB, PCTFULL, USPAT full text, IFIPAT, IMSPATENTS

• Comprehensive collection of biosequence information
  – CAS REGISTRY\textsuperscript{SM}, DGENE, PCTGEN, and USGENE\textsuperscript{®}

• Comprehensive collection of biological and pharmaceutical publications
  – BIOSIS\textsuperscript{®}, MEDLINE\textsuperscript{®}, 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

A list of database clusters can be displayed while using STN.
View the databases included in a specific cluster

=> D CLUSTER PHARM

<table>
<thead>
<tr>
<th>CLUSTER NAME</th>
<th>CLUSTER DEFINITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHARMACOLOGY</td>
<td>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</td>
</tr>
</tbody>
</table>

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, ESBIOBASE, 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
ti Health economics of market access for biopharmaceuticals and

biosimilars.

L4  119 ANSWERS EMBASE COPYRIGHT (c) reserved on STN
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 on STN
TI  Teva announces FDA accepts BLA for XM02.

L4  ANSWER 23 OF 70  CBNB  COPYRIGHT 2011 EI on STN
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

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

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

The term **BIOSIMILAR** is not a controlled term for MEDLINE.
A thesaurus is a useful tool to check for database specific terms

<table>
<thead>
<tr>
<th>E#</th>
<th>FREQUENCY</th>
<th>AT</th>
<th>TERM</th>
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</thead>
<tbody>
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<td>1</td>
<td>BIOPHARMACEUTICAL/CT</td>
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</tr>
<tr>
<td>E15</td>
<td>0</td>
<td>→</td>
<td>BIOPHARMACEUTICALS/CT</td>
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<tr>
<td>E16</td>
<td>1960</td>
<td>11</td>
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<tr>
<td>E17</td>
<td>38</td>
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<td>BIOPHARMACEUTICS: CL, CLASSIFICATION/CT</td>
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<tr>
<td>E18</td>
<td>46</td>
<td></td>
<td>BIOPHARMACEUTICS: EC, ECONOMICS/CT</td>
</tr>
<tr>
<td>E19</td>
<td>2</td>
<td></td>
<td>BIOPHARMACEUTICS: ED, EDUCATION/CT</td>
</tr>
<tr>
<td>E20</td>
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<td></td>
<td>BIOPHARMACEUTICS: ES, ETHICS/CT</td>
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<tr>
<td>E21</td>
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<td></td>
<td>BIOPHARMACEUTICS: HI, HISTORY/CT</td>
</tr>
<tr>
<td>E22</td>
<td>15</td>
<td></td>
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<td>E23</td>
<td>26</td>
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<td>BIOPHARMACEUTICS: LJ,</td>
</tr>
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<td></td>
<td>JURISPRUDENCE/CT</td>
</tr>
<tr>
<td>E24</td>
<td>169</td>
<td></td>
<td>BIOPHARMACEUTICS: MT,</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>E#</th>
<th>FREQUENCY</th>
<th>AT</th>
<th>TERM</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>----------</td>
<td>----</td>
<td>--------------------------------------------------------</td>
</tr>
<tr>
<td>E72</td>
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<td>2</td>
<td>GRANULOCYTE CHEMOTACTIC PROTEIN 2/CT</td>
</tr>
<tr>
<td>E73</td>
<td>0</td>
<td>2</td>
<td>GRANULOCYTE CHEMOTACTIC PROTEIN-2/CT</td>
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<tr>
<td>E74</td>
<td>0</td>
<td>1</td>
<td>GRANULOCYTE COLONY STIMULATING FACTOR/CT --&gt;</td>
</tr>
<tr>
<td>E75</td>
<td>0</td>
<td>2</td>
<td>GRANULOCYTE COLONY STIMULATING FACTOR RECEPTORS/CT</td>
</tr>
<tr>
<td>E76</td>
<td>926</td>
<td>61</td>
<td>GRANULOCYTE COLONY STIMULATING FACTOR, RECOMBINANT/CT</td>
</tr>
<tr>
<td>E77</td>
<td>1</td>
<td></td>
<td>GRANULOCYTE COLONY STIMULATING FACTOR, RECOMBINANT:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>AA, ANALOGS &amp; DERIVATIVES/CT</td>
</tr>
<tr>
<td>E78</td>
<td>221</td>
<td></td>
<td>GRANULOCYTE COLONY STIMULATING FACTOR, RECOMBINANT:</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>AD, ADMINISTRATION &amp; DOSAGE/CT</td>
</tr>
<tr>
<td>E79</td>
<td>110</td>
<td></td>
<td>GRANULOCYTE COLONY STIMULATING FACTOR, RECOMBINANT:</td>
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<tr>
<td></td>
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<td>AE, ADVERSE EFFECTS/CT</td>
</tr>
<tr>
<td>E80</td>
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<tr>
<td>E81</td>
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<tr>
<td>E82</td>
<td>15</td>
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<td>GRANULOCYTE COLONY STIMULATING FACTOR, RECOMBINANT:</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>BI, BIOSYNTHESIS/CT</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>MeSH number</th>
<th>BT/CT</th>
<th>MeSH heading</th>
</tr>
</thead>
<tbody>
<tr>
<td>E126</td>
<td>4972</td>
<td>Colony</td>
</tr>
<tr>
<td>E127</td>
<td>9703</td>
<td>Granulocyte</td>
</tr>
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<td>E128</td>
<td>926</td>
<td>Granulocyte</td>
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<tr>
<td></td>
<td></td>
<td>Factor, Recombinant</td>
</tr>
<tr>
<td>E135</td>
<td>2200</td>
<td>D12.776.828.75.350.</td>
</tr>
<tr>
<td>E137</td>
<td>2200</td>
<td>D23.529.374.410.240.75.350.</td>
</tr>
</tbody>
</table>

DC: an INDEX MEDICUS major descriptor
Additional terms can be found in the MeSH thesaurus

NOTE Granulocyte colony stimulating factors prepared by recombinant DNA technology.

INDX DF: GCSF RECOMBINANT

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

********** END **********
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 MSTEMPS OFF

=> S GRANULOCYTE COLONY STIMULATING FACTOR OR GCSF OR G CSF OR G–CSF OR COLONY STIMULATING FACTOR OR CSF OR FILGRASTIM

Using SET MSTEMPS 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 CAplus

<table>
<thead>
<tr>
<th>L24</th>
<th>ANSWER 229 OF 327</th>
<th>CAPLUS COPYRIGHT 2011 ACS on STN DUPLICATE 1</th>
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<tbody>
<tr>
<td>AN</td>
<td>2010:1423231</td>
<td>CAPLUS</td>
</tr>
<tr>
<td>DN</td>
<td>154:103919</td>
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<tr>
<td>TI</td>
<td>Carbon nanotube-assisted enhancement of surface plasmon resonance signal</td>
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<tr>
<td>AU</td>
<td>Lee, Eun Gyo; Park, Kyung Mi; Jeong, Jin Young; Lee, Seung Hui; Baek, Jung Eun; Lee, Hong Weon; Jung, Joon Ki; Chung, Bong Hyun</td>
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<tr>
<td>CS</td>
<td>Korea Research Institute of Bioscience and Biotechnology, Yuseong, Daejeon, 305-600, S. Korea</td>
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<tr>
<td>SO</td>
<td>Analytical Biochemistry (2011), 408(2), 206-211</td>
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<td>CODEN</td>
<td>ANBCA2; ISSN: 0003-2697</td>
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<tr>
<td>LA</td>
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</tbody>
</table>

RE_CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
Biosimilar epoetins and other "follow-on" biologics: update on the European experiences.

Jelkmann Wolfgang

Institute of Physiology, University of Luebeck, Ratzeburger Allee 160, Luebeck, Germany. jelkmann@physio.uni-luebeck.de


Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

English

Priority Journals

201010

Entered STN: 28 Sep 2010
Last Updated on STN: 13 Oct 2010
Entered Medline: 12 Oct 2010
## Neutrophil biology and the next generation of myeloid growth factors.

Dale, David C., Dr. (correspondence)

Department of Medicine, University of Washington Medical Center, 1959 NE Pacific Street, Seattle, WA 98195-6422, United States.


Entered STN: 6 Feb 2009

Last Updated on STN: 6 Feb 2009
Enzymatic techniques for PEGylation of **biopharmaceuticals**.

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

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


Book; (Book Chapter)

English

Entered STN: 23 Dec 2009

Last Updated on STN: 23 Dec 2009
Biologically active human GM-CSF produced in the seeds of transgenic rice plants

Dudani, Anil K. (Reprint)

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


ISSN: 0962-8819.

SPRINGER, VAN GODEWIJKSTRAAT 30, 3311 GZ DORDRECHT, NETHERLANDS.

Article; Journal

English

Reference Count: 46

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

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

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
Setting up multifile alerts in STN is easy

=> FILE CBNB CAPLUS MEDLINE EMBASE SCISEARCH BIOSIS

=> ALERT MFILE

MULTIFILE SDI GENERAL PARAMETERS

-----------------------------------------------

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.

Enter the databases for the multifile alert.
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
-----------------------------------------------

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
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.
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: AF50097C
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.

STN® - Your Connection to Science and Technology
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:
Eprex is a biopharmaceutical used to treat anemia in patients with kidney problems or patients receiving chemotherapy. Eprex’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

```sh
=> 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 λHEPOFL13 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

<table>
<thead>
<tr>
<th>type</th>
<th>location</th>
<th>description</th>
</tr>
</thead>
<tbody>
<tr>
<td>bridge</td>
<td>Cys-7</td>
<td>disulfide bridge</td>
</tr>
<tr>
<td>bridge</td>
<td>Cys-29</td>
<td>disulfide bridge</td>
</tr>
<tr>
<td></td>
<td>Cys-161</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cys-33</td>
<td></td>
</tr>
</tbody>
</table>

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

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

- **SEQ**
  - APPRLICDSR VLERYLLEAK EAENITTGCA EHCSLNENIT VPDTKVNFYA
  - WKRMEVGQQA VEVWQGLALL SEAVLRGQAL LVNSSQPWEP LQLHVDKAVS
  - GKLKLYTGEA CRTGD

- **Additional useful information**
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 NAME)

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**
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
FS  PROTEIN SEQUENCE
SQL  165
NTE

This record is for the zeta glycoform of epoetin.

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 VPDTKVNFYA
     51 WKRMEVQGQA VEVVQGLALL SEAVLRSQGAL LVNSSQPWEP LQLHVDKANS
     101 GLRLSLLTLLR ALGAQKEAIS PPDAASAAPL RTITADTFRK LFRVYSNFLR
     151 GKLKLYTGEA CRTGD
Enter CAplus to retrieve references for biosimilars of epoetin

=> FILE CAPLUS

=> S L2

L3 1148 L2

=> 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 FOLLOW ON BIOLOGIC •••

=> D BIB HITIND

L4 ANSWER 1 OF 26 CAPLUS COPYRIGHT 2011 AN
AN 2010:1230317 CAPLUS
DN 154:118974
TI Quality of Original and Biosimilar Epoetin Products
AU Brinks, Vera; Hawe, Andrea; Basmelekh, Abdul H. H.; Joachin-Rodriguez, Liliana; Haselberg, Rob; Somsen, Govert W.; • • •
HIT indexing in CAplus

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 original and biosimilar epoetin products)

IT High-performance gel-permeation chromatography (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: Eprex (alpha), Dynepo (delta), and Retacrit (zeta).
This patent record focuses on the delta form of epoetin. This record might have been missed without SEQLINK.

**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
learningsolutions.cas.org - Register today!

Welcome to your personal resource center for CAS learning events and materials.

Locate upcoming training, find STN documentation, recorded seminars, and interactive tutorials.
For more information ...

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Phone: 800-753-4227 or 614-447-3700
Training: www.cas.org
E-mail: help@cas.org

www.cas.org