Pharmacovigilance is defined as…

The science of collecting, monitoring, researching, assessing and evaluating information from healthcare providers and patients on the adverse effects of medicines, biological products, herbals and traditional medicines*

The intent is …

• Identifying information about potential new hazards
• Preventing harm to patients

The word is derived from…

• Greek “pharmakon” - drug
• Latin “vigilare” - to be awake or alert, to keep watch

* - The Importance of Pharmacovigilance, WHO 2002
Quick map of pharmacovigilance process

**External Reports**
- Alerts (every 10 to 15 days depending on regulatory body)
- Periodic reports (required by regulators at various times/intervals)

**PV tech curates information from up to 8 sources**

**Information is analyzed, then sent to PV manager**

**PV Manager reviews, summarizes, and formats information**

**Internal Reports**
- Therapeutic area
- Overall company

**Risk managers roll up information and create risk portfolios**
Common terminology and acronyms

- **PV** - Pharmacovigilance
- **MAH** (Market Authorisation Holder) – the company or person who has been given market authorisation. They are fully responsible for all aspects of the product and are subject to legislation in the country of issuance of the authorisation
- **EMA** – European Medicines Agency
- **MHRA** – Medicines and Healthcare products Regulatory Authority
- **FDA** – Food and Drug Administration
- **ADR** – Adverse Drug Reaction
- **API** – Active Pharmaceutical Ingredient
Primary regulatory authorities

• Europe
  – Regulated by European Medicines Agency in accordance with EU Directive 2010/20/EC (new July 2012)
  – Enforced in European countries by national authorities such as the MHRA in the United Kingdom

• United States
  – Regulated by the FDA in compliance with key regulations
    • US-IND Annual Reporting 21CFR 312.33
    • Post-marketing Reporting of ADRs 21CFR 314.80
Regulation of PV Activity

- Regulatory Authorities undertake routine inspections of the Market Authorisation Holder pharmacovigilance procedures in accordance with the appropriate country guidelines.

- Market Authorisation Holder prepares SPS (Summary of Pharmacovigilance Systems) outlining operations and procedures which includes database searches for Adverse Effect information for all types of pharmacovigilance searches.

- Failure to comply with the regulations can be a result of “Inadequacies in the construction of, or process used for literature searching (sources used, adequacy of scope of search with respect to search objective, local literature scanning, language restrictions, lack of Quality Control).”
Types of PV searches

• Weekly Alerts
  – The structure of a search query will vary from one customer to another
  – Used to monitor global medical literature for reports of suspected adverse reactions to medicinal products (MPs) containing certain active pharmaceutical ingredients (APIs)

• Signal Detection Searches
  – Looks for documentation linking a particular adverse effect to a drug. Usually picked up from weekly alerts or medical reporting on patient observations
  – A signal search will often involve preclinical as well as clinical cases

• Implied signal usually extracted from data tables held by regulatory authorities such as FDA and Medicines and Healthcare products Regulatory Authority (MHRA) and usually entails a previously unknown adverse reaction for a given drug
Types of PV searches (continued)

• Periodic Safety Update Report (PSUR)
  – The PSUR provides an overview of the safety of the product, and includes all Adverse Drug Reactions reported in the period since the last PSUR, together with a summary of the registration status of the product worldwide, actions taken for safety reasons, the worldwide usage of the product and an analysis of safety.
  – Required in the EU and the US at differing time intervals
  – (Change in EU regulations will see the PSUR renamed the PBRER – Periodic Benefit Risk Evaluation Report)

• Periodic Adverse Drug Experience Reports (PADER)
  – Required in the US only and do not cover adverse effects or events reported in the scientific literature
Focus is on the **drug name**, the **CAS RN** and the **trademarked names** held by the Market Authorisation Holder.

- Will include other trademark names (sometimes).
- Limit to human (sometimes).
- Limit with keyword and controlled terms for adverse event terms, neonatal/gestation terms, drug abuse terms (sometimes).
STN Enhancements For Weekly Alerts

The following enhancements have been made at the request of PV searchers

- Package Delivery is now available weekly
- RSS feeds for alerts are now available
- Ahead of Print, Articles in Press
Signal Detection Searches

- **CAS RN** and **Drug name(s)** including those not owned by the Market Authorisation Holder are combined with

- **Keyword terms** and **controlled terminology** for a particular medical indication or adverse effect (*hypertension, asthma, hallucination, etc.*)

- Disease link and drug link terms (*Embase*)

- Allowable Qualifiers/Subheadings (*Medline*)

- No limitation to human – preclinical and clinical are all acceptable sources for signal indication
Periodic Safety Update Report (PSUR) Searches

- Extensive global based search on all reported serious adverse effects or events within the designated time period
  - CAS RN and Drug name(s) including those not owned by the Market Authorisation Holder are combined with
  - All keyword based terminology and controlled terms for adverse incidents, safety, adverse effects
  - Link terms (Embase) and Qualifiers (Medline) also included
Four primary elements drive investment and diligence in pharmacovigilance

- Need to Build a Sustainable Business
- Threat of Litigation & Damages
- Responsibility to Public Health
- Threat of Non-Compliance Fees & Ramifications

Used to generate mandatory alerts & periodic reports for and support audits of pharmaceuticals, biologicals, vaccines, and devices
STN hosts a robust portfolio of pharmacological and medical databases with impressive currency

In addition to industry-best currency, ahead-of-print and articles-in-press are also available on STN
STN enables the pharmacovigilance needs and process

STN provides…

- **Delivery of results in user friendly formats**: De-duplicated, weekly results from single or multiple databases are available via RSS feeds in addition to email alerts

- **Archiving and sharing within the company**: Maximize information dissemination and content archiving utilizing keep and share functionality

- **Tools to analyze data and aid workflow**: Post processing tools convert search results into table or report formats with enhanced formatting functionality

- **Commitment to highest security standards**: Encrypted transmissions, activity is confidential, unique login and usage reporting

*Note: Usage of Derwent databases must be covered under a separate Derwent Open Access license.*
STN is the partner you need; supporting your short term needs and investing in your long term needs

Best-in-class pharmacovigilance training and resources, specific to your company’s needs

Guidance from our knowledgeable helpdesk and sales agents for developing, troubleshooting, or transitioning of alerts as well as any other questions or guidance needed along the way

Partnership with ScienceIP® for expert strategy development, search, and analysis

Development of new STN platform to support the evolving needs of your searchers and your business
Pharmacovigilance Alerts with SDI Package on STN®
Agenda

- Lookup drug names in CAS REGISTRY™
- STNIndex for query development
- Different queries in different databases
- Alert options
- Set up an alert with package delivery
Begin in CAS REGISTRY

- Largest public substance collection in the world
  - More than 75M organic and inorganic substances
  - More than 65M sequences
- Substances from journal articles, patents, chemical catalogs, and reputable web sources from the early 1800s to present
- Updated daily with ~12,000 substances
- Produced by CAS
Lookup drug name in CAS REGISTRY

=> FILE REGISTRY

=> E TOCILIZUMAB/CN 5
E1 1 TOCHUINOL ACETATE/CN
E2 1 TOCHUINYL ACETATE/CN
E3 1 --> TOCILIZUMAB/CN
E4 1 TOCINAMIDE/CN
E5 1 TOCINAMIDE, DEAMINO-/CN

=> S TOCILIZUMAB/CN
L1 1 TOCILIZUMAB/CN

=> D
RN 375823-41-9 REGISTRY
CN Immunoglobulin G1, anti-(human interleukin 6 receptor) (human-mouse monoclonal MRA heavy chain), disulfide with human-mouse monoclonal MRA κ-chain, dimer (CA INDEX NAME)
REGISTRY records contain Other Names and CAS Registry Number® Locator

OTHER NAMES:
CN  Actemra
CN  Actemra 200
CN  Atlizumab
CN  MRA
CN  R 1569
CN  RoActemra
CN  Tocilizumab
FS  PROTEIN SEQUENCE
DR  339528-87-9
MF  Unspecified
CI  MAN
SR  US Adopted Names Council (USAN)
LC  STN Files: ADISINSIGHT, ANABSTR, CA, CAPLUS, CBNB, CHEMCATS,
     CHEMLIST, EMBASE, IMSPATENTS, IMSRESEARCH, IPA, MRCK*,
     PATDPASPC, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
     (*File contains numerically searchable property data)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
USAN records have additional information about monoclonal antibodies

<table>
<thead>
<tr>
<th>Accession Number</th>
<th>2011:9950 USAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Publication Year</td>
<td>2004</td>
</tr>
<tr>
<td>US Adopted Name</td>
<td>Tocilizumab</td>
</tr>
<tr>
<td>OTHER NAMES:</td>
<td></td>
</tr>
<tr>
<td>Chemical Name</td>
<td>Immunoglobulin G1, anti-(human interleukin 6 receptor) (human-mouse monoclonal MRA heavy chain), disulfide with human-mouse monoclonal K-chain, dimer. Molecular weight is approximately 144,986 daltons.</td>
</tr>
<tr>
<td>Code Designation</td>
<td>MRA</td>
</tr>
<tr>
<td>CAS Registry No.</td>
<td>375823-41-9</td>
</tr>
<tr>
<td>Molecular Formula</td>
<td>C6428 H9976 N1720 O2018 S42</td>
</tr>
</tbody>
</table>
USAN records include Treatment Classification Codes

Lin. Str. Formula (LSF): C6428 H9976 N1720 O2018 S42
Reference (RE): International Nonproprietary Name
Classification (CC): Treatment of Castelman's disease; treatment of multiple myeloma; treatment of systemic lupus erythematosus; treatment of Crohn's disease; treatment of rheumatoid arthritis; treatment of systemic juvenile idiopathic arthritis.

STRUCTURE DIAGRAM IS NOT AVAILABLE

Because this is a Monoclonal Antibody, no structure diagram is available
Use SELECT CHEM to extract chemical names and Registry Numbers for a query

| => FILE REGISTRY |
| => SEL CHEM L1 |
| E6 THROUGH E15 ASSIGNED |
| => D SEL E6-E15 |
| E6   | 1  | ACTEMRA 200/BI |
| E7   | 1  | ACTEMRA/BI     |
| E8   | 1  | ATLIZUMAB/BI   |
| E9   | 1  | IMMUNOGLOBULIN G1, ANTI-(HUMAN INTERLEUKIN 6 RECEPTOR) (HUMAN-MOUSE MONOCLONAL MRA HEAVY CHAIN), DISULFIDE WITH HUMAN-MOUSE MONOCLONAL MRA K-CHAIN, DIMER/BI |
| E10  | 1  | MRA/BI         |
| E11  | 1  | R 1569/BI      |
| E12  | 1  | ROACTEMRA/BI   |
| E13  | 1  | TOCILIZUMAB/BI |
| E14  | 1  | 339528-87-9/BI |
| E15  | 1  | 375823-41-9/BI |
Use SELECT CHEM to extract chemical names and Registry Numbers for a query (cont.)

=> QUE E7,E8,E11-E15 OR R1569
L3 QUE (ACTEMRA/BI OR ATLIZUMAB/BI OR "R 1569"/BI OR ROACTEMRA/BI OR TOCILIZUMAB/BI OR 339528-87-9/BI OR 375823-41-9/BI) OR R1569

=> FILE HCAPLUS

=> S MRA
L4 5100 MRA

=> D HIT 1 50 100 250 300
TI The role of mineralocorticoid receptor antagonists (MRAs)
AB ● ● ● marrow repopulating ability (MRA)
AB ● ● ● utilizing multiple regression anal. (MRA)
AB ● ● ● magnetic resonance angiog. (MRA)
AB ● ● ● two clusters of genes, mra and mrb,

=> DELETE L4 Y
STNIndex for query development

=> INDEX PHARMACOLOGY -PNTTEXT
INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOENG, BIOSIS, BIOTECHNO, CAPLUS, CBNB, CIN, CONFSCI, DDFB, DDFU, DGENE, DISSABS, DRUGB, DRUGU, EMBAL, EMBASE, ESBIIOBASE, IFIPAT, IMSPATENTS, IMSRESEARCH, IPA, KOSMET, LIFESCI, MEDLINE, NAPRALERT, PASCAL, PCTGEN, ...' ENTERED
35 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.

- Use STNIndex to test different search strategies and compare numbers of answers.
- L-numbers are packaged queries, not answer sets.
=> S L3 AND (((ADVERSE OR SIDE OR UNWANT? OR UNINTEN? OR UNDESIR?) (2A) (INTERACTION OR RESPONSE OR REACTION OR EFFECT OR EVENT OR OUTCOME)) OR (TOLER? OR HARM### OR ?TOXIC?) OR (POSTMARKET SURVE? OR POST MARKET SURVE?))

L3 = chemical name and RN query.

L4 QUE L3 AND (((ADVERSE OR SIDE OR UNWANT? OR UNINTEN? OR })
D RANK reorders files by number of hits

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>910</td>
<td>EMBASE</td>
</tr>
<tr>
<td>F2</td>
<td>281</td>
<td>TOXCENTER</td>
</tr>
<tr>
<td>F3</td>
<td>228</td>
<td>ADISCTI</td>
</tr>
<tr>
<td>F4</td>
<td>205</td>
<td>MEDLINE</td>
</tr>
<tr>
<td>F5</td>
<td>169</td>
<td>CAPLUS</td>
</tr>
<tr>
<td>F6</td>
<td>153</td>
<td>DRUGU</td>
</tr>
<tr>
<td>F7</td>
<td>136</td>
<td>DDFU</td>
</tr>
<tr>
<td>F8</td>
<td>135</td>
<td>BIOSIS</td>
</tr>
<tr>
<td>F9</td>
<td>121</td>
<td>SCISEARCH</td>
</tr>
<tr>
<td>F10</td>
<td>53*</td>
<td>ADISNEWS</td>
</tr>
<tr>
<td>F11</td>
<td>50</td>
<td>ESBIOBASE</td>
</tr>
<tr>
<td>F12</td>
<td>50*</td>
<td>IPA</td>
</tr>
<tr>
<td>F13</td>
<td>48</td>
<td>PASCAL</td>
</tr>
<tr>
<td>F14</td>
<td>39</td>
<td>CBNB</td>
</tr>
<tr>
<td>F15</td>
<td>31</td>
<td>PQSCITECH</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

• An asterisk (*) next to a file name generally means some part of the search did not work in that file

• Use Database Summary Sheets to find out more information about a specific database
HELP commands

• The master HELP command in any database is HELP DIRECTORY
  – Lists all HELP for an individual file
• For HELP in a multifile environment, use a specific database name, e.g.,
  => FILE MEDLINE, EMBASE
  => HELP THESAURUS FILE=EMBASE
  => HELP LLIMIT FILE=MEDLINE
STN multifile alerts can use different queries in different databases

- Many databases have unique search features that can be leveraged for relevant results, e.g.,
  - CAS roles in CApplus databases
  - MeSH indexing, limiters, and subheadings in MEDLINE
  - Indexing, limiters, and Link terms in Ebase™

- Multifile alerts with individual frequency settings, or single package alert delivery

- Query can be different in each database
CAplus\textsuperscript{SM}/HCAplus

- More than 35M records from Chemical Abstracts\textsuperscript{TM} between 1907 – present, from
  - Worldwide scientific journals (more than 10,000)
  - Patent publications from 63 patent authorities
- All areas of chemistry, biochemistry, chemical engineering, and life sciences
- Contains CAS Roles (\textit{e.g.} ADV: Adverse Effect, Including Toxicity)
- Updated daily with \(~\)4500 records
- Produced by CAS
Use RNs and roles in CAplus alerts

• SMARTTracker alerts (XFILE) are typically used for RN crossover between REGISTRY and CA files
  – Cannot be used with any other multifile alert

• Search RNs in /IT field if you want to include just a few known Registry Numbers

• Use CAS Roles as synonyms for words
**EXPAND** Keyword Terms

---

**=> FILE HCAPLUS**

**=> E ADVERSE+KT/CT**

<table>
<thead>
<tr>
<th>Code</th>
<th>Count</th>
<th>Type</th>
<th>Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>E1</td>
<td>0</td>
<td></td>
<td>--&gt; Adverse/CT</td>
</tr>
<tr>
<td>E2</td>
<td>0</td>
<td>KT</td>
<td>Adverse drug effects/CT</td>
</tr>
<tr>
<td>E3</td>
<td>0</td>
<td>KT</td>
<td>Adverse drug interactions/CT</td>
</tr>
<tr>
<td>E4</td>
<td>0</td>
<td>KT</td>
<td>Adverse interactions/CT</td>
</tr>
<tr>
<td>E5</td>
<td>0</td>
<td>KT</td>
<td>Adverse interactions (drug)/CT</td>
</tr>
<tr>
<td>E6</td>
<td>0</td>
<td>KT</td>
<td>Drug interactions (adverse)/CT</td>
</tr>
<tr>
<td>E7</td>
<td>0</td>
<td>KT</td>
<td>Drug interactions</td>
</tr>
<tr>
<td>E8</td>
<td>0</td>
<td>KT</td>
<td>Drug interactions (L) adverse/CT</td>
</tr>
<tr>
<td>E9</td>
<td>0</td>
<td>KT</td>
<td>Torsadogenic adverse effects/CT</td>
</tr>
</tbody>
</table>

********** END **********

**=> E E2+ALL**

<table>
<thead>
<tr>
<th>Code</th>
<th>Count</th>
<th>Type</th>
<th>Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>E10</td>
<td>0</td>
<td></td>
<td>--&gt; Adverse drug effects/CT</td>
</tr>
<tr>
<td>E11</td>
<td>26649</td>
<td>USE</td>
<td>Drug toxicity/CT</td>
</tr>
</tbody>
</table>

********** END **********

---

- **EXPAND** Keyword Terms (+KT) in the Controlled Terminology field to find headings that can be explored further.
- Type **HELP RCODES** for relationship codes.
Explore the CAS Lexicon for terminology

<table>
<thead>
<tr>
<th>=&gt; E E11+ALL</th>
</tr>
</thead>
<tbody>
<tr>
<td>E12 0 BT2 Biological processes and phenomena (non-CA heading)/CT</td>
</tr>
<tr>
<td>E13 0 BT1 Pharmaceutical phenomena (non-CA heading)/CT</td>
</tr>
<tr>
<td>E14 0 BT2 Biological processes and phenomena (non-CA heading)/CT</td>
</tr>
<tr>
<td>E15 84226 BT1 Toxicity/CT</td>
</tr>
<tr>
<td>E16 26649 --&gt; Drug toxicity/CT</td>
</tr>
<tr>
<td>HNTE Valid heading during volume 136 (2002) to present.</td>
</tr>
<tr>
<td>E17 OLD Toxicity (L) drug/CT</td>
</tr>
<tr>
<td>E18 UF Adverse drug effects/CT</td>
</tr>
<tr>
<td>E19 UF Drug adverse effect/CT</td>
</tr>
<tr>
<td>E20 UF Drug adverse effects/CT</td>
</tr>
<tr>
<td>E21 UF Drug overdose/CT</td>
</tr>
<tr>
<td>E22 UF Drug side effect/CT</td>
</tr>
<tr>
<td>E23 UF Drug side effects/CT</td>
</tr>
<tr>
<td>E24 UF Drug toxicities/CT</td>
</tr>
<tr>
<td>E25 996 NT1 Drug allergy/CT</td>
</tr>
<tr>
<td>E26 48627 RT Drugs/CT</td>
</tr>
<tr>
<td>E27 213 RT Erythema nodosum/CT</td>
</tr>
<tr>
<td>E28 2267 RT Therapeutic drug monitoring/CT</td>
</tr>
</tbody>
</table>
Search individual RNs in the Index Term (IT) field

=> S (ACTEMRA/BI OR ATLIZUMAB/BI OR "R 1569"/BI OR ROACTEMRA/BI OR TOCILIZUMAB/BI OR 339528-87-9/IT OR 375823-41-9/IT) OR R1569
L5  544 (ACTEMRA/BI OR ATLIZUMAB/BI OR "R 1569"/BI OR ● ● ●

Search the RNs in the IT field to prevent automatic Registry crossover during an alert run.

=> S L5 AND ((ADVERSE OR SIDE OR UNWANT? OR UNINTEN? OR UNDESI?) (2A) (INTERACTION OR RESPONSE OR REACTION OR EFFECT OR EVENT OR OUTCOME)) OR (TOLERATE? OR HARM### OR E16-E25) OR (POSTMARKET SURVEY? OR POST MARKET SURVEY?)
L6  128 L5 AND ((ADVERSE OR SIDE OR UNWANT? OR UNINTEN? ● ● ●

=> S (ACTEMRA/IT OR ATLIZUMAB/IT OR R 1569/IT OR R1569/IT OR ROACTEMRA/IT OR TOCILIZUMAB/IT OR 339528-87-9/IT OR 375823-41-9/IT) (L) (ADV OR DMA OR PAC OR PKT)/RL
L7  272 (ACTEMRA/IT

=> S L6 OR L7
L8  315 L6 OR L7

Link (L) roles to terms to find them together in a single index field. Use roles as a synonym for keywords.
Set up HCAplus Alert

=> ALERT
ENTER QUERY L# FOR SDI REQUEST OR (END): L8
ENTER UPDATE FIELD CODE (UP), UPM, UPIT, UPI, ED, UPP, UPOG OR ?: UPM
ENTER SDI REQUEST NAME, (AA052/S), OR END: TOCILHCA/S
ENTER COST CENTER (NONE) OR NONE: NONE
ENTER TITLE (NONE): TOCILIZUMAB MONITORING HCAPLUS
ENTER METHOD OF DELIVERY (EMAIL), ONLINE OR RSS: EMAIL
ENTER EMAIL ID (5584C): R...@ABC.COM
RECEIVE DELIVERY NOTIFICATION? (Y)/N: N
ELIMINATE PREVIOUSLY SEEN ANSWERS WITH EACH SDI RUN? Y/(N): Y
ENTER PRINT FORMAT (BIB) OR ?: BIB ABS
HIGHLIGHT HIT TERMS? (Y)/N: Y
ARCHIVE ANSWERS? Y/(N): N
REDISTRIBUTE ANSWERS? Y/(N): N
ENTER MAXIMUM NUMBER OF HITS TO BE DELIVERED PER RUN (100):.
SORT SDI ANSWER SET (N)/Y?: N
SEND SDI WITH NO ANSWERS? (Y)/N: N
DISPLAY CURRENCY INFORMATION? (Y)/N: Y
ENTER SDI RUN FREQUENCY – DAILY, (WEEKLY), BIWEEKLY, OR ?: WEEKLY
ENTER SDI EXPIRATION DATE 'YYYYMMDD' OR (NONE): NONE
QUERY L8 HAS BEEN SAVED AS SDI REQUEST 'ACTEMRAHCA/S'
MEDLINE®

• Bibliographic database covering biomedical literature (1946 – present), including articles in press
• Contains Registry Numbers
• Medical Subject Headings (MeSH) Thesaurus 2013
  – MeSH vocabulary and tree numbers
• Updated five times per week, annual reload
• Produced by the US National Library of Medicine
You can quickly restrict the search to one or more of the areas by adding a slash (/) and the desired area to the L-number of an answer set created in this file. Only L-numbers may be limited, i.e., search terms may not be directly limited. The L-number must represent an answer set.

LIMIT codes can be used to focus an answer set to indexed documents, e.g., => S L10/MAJ,HUMAN.
EXPAND Keyword Terms (KT) in the MeSH thesaurus

=> FILE MEDLINE

=> E ADVERSE+KT/CT

E1  0  -->  Adverse/CT
E2  0  KT  Adverse Drug/CT
E3  0  KT  Adverse Drug Event/CT
E4  0  KT  Adverse Drug Events/CT
E5  0  KT  Adverse Drug Reaction/CT
E6  4904  KT  Adverse Drug Reaction Reporting Systems/CT
E7  0  KT  Adverse Drug Reactions/CT
E8  1236117  KT  Adverse Effects/CT
E9  0  KT  Drug Event, Adverse/CT
E10  0  KT  Drug Events, Adverse/CT
E11  0  KT  Drug Reaction Reporting Systems, Adverse/CT
E12  0  KT  Drug Reaction, Adverse/CT
E13  0  KT  Drug Reactions, Adverse/CT
E14  0  KT  No Observed Adverse Effect Level/CT

********** END **********
Subheading qualifier definitions are part of MeSH

=> E E8+ALL
E15 1236117 --> Adverse Effects/CT
E16 1236117 QLF adverse effects/CT
E17 1236117 QA AE/CT
QNOTE Used with drugs, chemicals, or biological agents in accepted dosage - or with physical agents or manufactured products in normal usage - when intended for diagnostic, therapeutic, prophylactic, or anesthetic ● ● ●

=> E E4+ALL
E19 0 --> Adverse Drug Events/CT
E20 5216 USE Drug Toxicity/CT
************ END ************

=> E E20+ALL
● ● ●
MeSH headings can be qualified with subheading hierarchies

=> S L3
L9  582 L3 (ACTEMRA/BI OR ATLIZUMAB/BI OR "R 1569"/BI OR ● ● ●

=> D SCAN
L9  ANSWERS 582 MEDLINE® on STN
TI  A case of peripheral neuropathy and skin ulcer in a patient with rheumatoid arthritis after a single infusion of tocilizumab.
CT  Check Tags: Female
   Antibodies, Monoclonal: AD, administration & dosage
   *Antibodies, Monoclonal: AE, adverse effects
   Antibodies, Monoclonal: BL, blood
   Antibodies, Monoclonal, Humanized
   *Arthritis, Rheumatoid: DT, drug therapy

● ● ●
RN  9001-32-5 (Fibrinogen); 9007-41-4 (C-Reactive Protein)
CN  Antibodies, Monoclonal; Antibodies, Monoclonal, Humanized; Interleukin-6; Vascular Endothelial Growth Factor A; tocilizumab

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1): 1
Onset of inflammatory eye disease under tocilizumab treatment for rheumatologic conditions: a paradoxical effect?

**Check Tags:** Male

- Adult
- Aged

*Antibodies, Monoclonal, Humanized: AE, adverse effects
- Antibodies, Monoclonal, Humanized: TU, therapeutic use

*Antirheumatic Agents: AE, adverse effects
- Antirheumatic Agents: TU, therapeutic use

*Arthritis, Rheumatoid: DT, drug therapy

*Eye Diseases: CI, chemically induced
- Humans
- Inflammation: CI, chemically induced
- Receptors, Interleukin-6: AI, antagonists & inhibitors

**CN**

- Antibodies, Monoclonal, Humanized; Antirheumatic Agents;
- Receptors, Interleukin-6; tocilizumab
Search indexed subheading hierarchies and free text

=> S ANTIBODIES, MONOCLONAL?/CT (L) (AE OR TO OR PO OR CT)/CT
L10 9902 S ANTIBODIES, MONOCLONAL?/CT (L) (AE OR TO OR PO OR CT)/CT

=> S L9 AND L10
L11 113 L9 AND L10

Alternatively, you can search a related subheading group together by adding a period to a 2-letter code, e.g., AE./CT, which searches (AE OR TO OR PO)/CT.

=> S L9 AND ((ADVERSE OR SIDE OR UNWANT? OR UNINTEN? OR UNDESIR?) (2A) (INTERACTION OR RESPONSE OR REACTION OR EFFECT OR EVENT OR OUTCOME)) OR (TOLERA? OR HARM### OR ?TOXIC?) OR (POSTMARKET SURVE? OR POST MARKET SURVE?)
L12 205 L9 AND ((ADVERSE OR SIDE OR UNWANT? OR UNINTEN? OR UNDESIR?)

=> S L11 OR L12
L13 206 L11 OR L12

AE: ADVERSE EFFECTS
TO: toxicity
PO: poisoning
Embase

- Bibliographic database covering medical and pharmaceutical information from non-patent literature (1947 – present)
- Approximately 700K conference papers added
- Contains Registry Numbers
- Embase Emtree Thesaurus
- Updated daily
- Produced by Elsevier B.V.
## LIMIT codes in Embase

**=> HELP LLIMIT**

Search results may be restricted to the following search areas in the EMBASE file.

<table>
<thead>
<tr>
<th>SEARCH AREA</th>
<th>CODE</th>
<th>EXAMPLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal subject</td>
<td>/NONHUMAN</td>
<td>S L4/NON</td>
</tr>
<tr>
<td>English-language records</td>
<td>/ENGLISH</td>
<td>S L1/MAJ,ENG</td>
</tr>
<tr>
<td>Female subject</td>
<td>/FEMALE</td>
<td>S L3/FEM</td>
</tr>
<tr>
<td>Human subject</td>
<td>/HUMAN</td>
<td>S L1/HUM</td>
</tr>
<tr>
<td>Major descriptor</td>
<td>/MAJOR</td>
<td>S L1/MAJ</td>
</tr>
<tr>
<td>Male subject</td>
<td>/MALE</td>
<td>S L2/MAL</td>
</tr>
</tbody>
</table>

You can quickly restrict the search to one or more of the areas by adding a slash (/) and the desired area to the L-number of an answer set created in this file. Only L-numbers may be limited, i.e., search terms may not be directly limited.

You can also search for major terms in the Controlled Term (/CT) field by preceding the search term with an asterisk (*), e.g., S *LUNG EMBOLISM/CT.
Embase indexing includes Link Terms

=> FILE EMBASE

=> S L3

L14  1615 (ACTEMRA/BI OR ATLIZUMAB/BI OR "R 1569"/BI OR
ROACTEMRA/BI OR TOCILIZUMAB/BI OR 339528-87-9/BI OR
375823-41-9/BI) OR R1569

=> S L14 AND (((ADVERSE OR SIDE OR UNWANT? OR UNINTEN? OR UNDESIR?)
(2A) (INTERACTION OR RESPONSE OR REACTION OR EFFECT OR EVENT OR
OUTCOME)) OR (TOLERA? OR HARM##### OR ?TOXIC?) OR (POSTMARKET
SURVE? OR POST MARKET SURVE?)

L15  910 L14 AND (((ADVERSE OR SIDE OR UNWANT? OR UNINTEN? ● ● ●

=> S (TOCILIZUMAB/CT (L) (AE OR TO)/CT)

L16  233 (TOCILIZUMAB/CT (P) (AE OR TO)/CT)

=> S L15 OR L16

L17  910 L15 OR L16

- Embase has controlled term subheadings called Link Terms, e.g., AE, adverse effects: S TOCILIZUMAB (L) AE/CT.
- Type HELP LTERMS for more information.
EMBAL – Embase Alerts

• Alert file for Embase content
• Contains the most recent 8 weeks of Embase coverage
• Not indexed
• Updated daily
• Produced by Elsevier B.V.
EMBAL contains Embase records before they are indexed

=> FILE EMBAL

Use the broad, free text query since there is no indexing in EMBAL.

=> S L15

L18 4 L14 AND (((ADVERSE OR SIDE OR UNWANT? OR UNINTEN? OR UNDESIR?) (2A) (INTERACTION OR RESPONSE OR REACTION OR EFFECT OR EVENT OR OUTCOME)) OR (TOLERA? OR HARM### OR ?TOXIC?) OR (POSTMARKET SURVE? OR POST MARKET SURVE?))
There are two delivery options for multifile (MFILE) alerts

• Package delivery
  – Weekly or monthly delivery, regardless of file update
  – All results in a single, de-duplicated package

• Separate results for each file
  – Individual file update frequency, e.g., can mix daily and weekly delivery
  – De-duplicated between databases

Type HELP ALERT or HELP SDPACKAGE for more information.
Set up an ALERT PACKAGE for weekly delivery

=> FILE HCAPPLUS MEDLINE EMBAL EMBASE

=> ALERT PACKAGE

General parameters are set up first.

ENTER MULTIFILE SDI TYPE (MFILE) OR END: MFILE
MULTIFILE SDI GENERAL PARAMETERS
--------------------------------
ENTER MULTIFILE SDI REQUEST NAME ('AA052/S'), OR END: TOCIL2/S
ENTER TITLE (NONE): TOCILIZUMAB ADVERSE EFFECTS
ENTER COST CENTER (NONE) OR NONE:.
ENTER METHOD OF DELIVERY (EMAIL), ONLINE OR RSS: EMAIL
ENTER EMAIL ID (5584C): R...@ABC.COM
RECEIVE DELIVERY NOTIFICATION? (Y)/N: N
ELIMINATE PREVIOUSLY SEEN ANSWERS WITH EACH SDI RUN? Y/(N): Y
SET FILE ANSWER PREFERENCE FOR DUPLICATE REMOVAL? (N)/Y: Y
CURRENT FILE PREFERENCE: 1) HCAPPLUS
2) MEDLINE
3) EMBAL
4) EMBASE
ENTER THE NUMBER OF THE FIRST PREFERRED FILE (OR END): 2

● ● ●
Display formats must work in all files for package delivery

<table>
<thead>
<tr>
<th>CURRENT FILE PREFERENCE:</th>
<th>1) MEDLINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>2) HCAPLUS</td>
<td>&lt;---</td>
</tr>
<tr>
<td>3) EMBAL</td>
<td></td>
</tr>
<tr>
<td>4) EMBASE</td>
<td></td>
</tr>
</tbody>
</table>

ENTER THE NUMBER OF THE NEXT PREFERRED FILE (OR END): **END**

<table>
<thead>
<tr>
<th>FILE PREFERENCE:</th>
<th>1) MEDLINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>2) HCAPLUS</td>
<td></td>
</tr>
<tr>
<td>3) EMBAL</td>
<td></td>
</tr>
<tr>
<td>4) EMBASE</td>
<td></td>
</tr>
</tbody>
</table>

ENTER PRINT FORMAT (FILEDEFAULT) OR ?: **BIB ABS**

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

ARCHIVE ANSWERS? Y/(N): **N**

REDISTRIBUTE ANSWERS? Y/(N): **N**

ENTER MAXIMUM NUMBER OF HITS TO BE DELIVERED PER FILE (100): **.**

SORT SDI ANSWER SET (N)/Y?: **N**

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

DISPLAY CURRENCY INFORMATION? (Y)/N: **Y**

ENTER FREQUENCY OF UPDATE (MONTHLY) OR WEEKLY: **WEEKLY**

ENTER SDI EXPIRATION DATE 'YYYYMMDD' OR (NONE): **NONE**

---

File preference can be re-ordered.
MULTIFILE SDI FILE SPECIFIC PARAMETERS: MEDLINE

ENTER COMPONENT SDI REQUEST NAME ('AA052/S') OR END: TOCILMED/S
ENTER QUERY L# FOR MULTIFILE SDI REQUEST OR END: L13
ENTER UPDATE FIELD CODE (ED), UP OR ?: UP

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

MULTIFILE SDI FILE SPECIFIC PARAMETERS: HCAPLUS

ENTER COMPONENT SDI REQUEST NAME ('AA052/S') OR END: TOCILHCA/S
‘TOCILHCA/S’ IN USE AS A SINGLE FILE SDI
MOVE ‘TOCILHCA/S’ TO THIS MULTIFILE SDI? (Y)/N: Y
CHANGE FILE SPECIFIC PARAMETERS? (N)/Y: N

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

MULTIFILE SDI FILE SPECIFIC PARAMETERS: EMBAL

ENTER COMPONENT SDI REQUEST NAME ('AA052/S') OR END: TOCILEMBAL/S
ENTER QUERY L# FOR MULTIFILE SDI REQUEST OR END: L18
ENTER UPDATE FIELD CODE (ED), UP OR ?: UP
MULTIFILE SDI FILE SPECIFIC PARAMETERS: EMBASE

ENTER COMPONENT SDI REQUEST NAME ('AA052/S') OR END: TOCILEMB/S

ENTER QUERY L# FOR MULTIFILE SDI REQUEST OR END: L17

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

MULTIFILE SDI HAS BEEN SAVED AS SDI REQUEST 'TOCIL2/S'
QUERY L13 HAS BEEN SAVED AS SDI REQUEST 'TOCILMED/S' FOR FILE MEDLINE
QUERY TOCILHCA/S HAS BEEN SAVED AS SDI REQUEST 'TOCILHCA/S' FOR FILE HCAPLUS
QUERY L18 HAS BEEN SAVED AS SDI REQUEST 'TOCILEMBAL/S' FOR FILE EMBAL
QUERY L17 HAS BEEN SAVED AS SDI REQUEST 'TOCILEMB/S' FOR FILE EMBASE
Results delivery

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: TOCILIZUMAB ADVERSE EFFECTS
Reference Number: AJ80071C
Number of Answers: 15
File Names: MEDLINE HCAPLUS EMBASE
SDI Name: TOCIL2/S
SDI Run Number: 31
SDI Run Date: AUG 6, 2012
1. RTF (Rich Text Format)
2. PDF (Adobe Portable Document Format)
3. Self-extracting or Zipped HTML (Hypertext Markup Language)
4. Plain Text (ASCII)

All formats except Plain Text include images.
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
Other files to consider for drug alerts

- ADISNEWS (REACTIONS file segment)
  - Updated daily
  - Queries can be limited to the REACTIONS file segment, e.g., => S L18 AND REACTIONS/FS

- BIOSIS
  - Updated weekly

- Derwent Drug File (DDFU)
  - See next page
Other files to consider for drug alerts

- Derwent Drug File (DDFU)
  - Pharmaceutical substances
  - Substance based indexing using linked-terms and roles
  - Abstracts rewritten / value added by Thomson R.
  - Updated weekly
  - Drug roles – type HELP ROLES
    => S TOCILIZUMAB *AE
Resources

• For more information about purchasing archive and redistribution rights, visit the STN Keep & Share website
  www.cas.org/legal/keepshare

• Additional reference documents available in CAS Learning Solutions
  – Find a comprehensive list of drug names
  – Create a search term command file
    learningsolutions.cas.org
Appendix: Conferences and Groups
PV Conferences - Core

Pharmacovigilance & Risk Management Strategies 2014

Date: January 13-15, 2014

Location: Washington, DC, United States

The annual DIA Pharmacovigilance and Risk Management Strategies Meeting provides a forum to discuss current complexities, controversies, global regulatory updates and hot topics in the area of drug safety and risk management.
PV Conferences - Europe

**PIPA 2013 8th Annual Conference**

Date: 4th-5th July 2013
Location: Latimer Place, The Grove, Latimer, Chesham, Buckinghamshire

Our conference programme this year will include a range of presentations and workshops from expert speakers addressing topical matters of particular significance to MI and PV professionals.

**13th ISoP Annual Meeting "The Renaissance of Pharmacovigilance"**

Date: 1st – 4th October 2013
Location: Pisa, Italy

This meeting will be mostly dedicated to an integrated approach to drug risk management with a particular focus on clinical issues related to adverse drug reactions. Focus will also be given to the young generations of healthcare professionals and scientists dedicated to Pharmacovigilance.
PV Conferences

World Drug Safety Congress – Americas 2013
Date: April 24 & 25, 2013
Location: Boston, USA
The 5th annual World Drug Safety Congress provides you with key insights into the drug safety challenges affecting you and gives you an excellent opportunity to discuss these diverse issues in a conference format.

World Drug Safety Congress – Europe 2013
Date: September 10 - 12, 2013
Location: London, UK
The 7th annual World Drug Safety Congress is a large meeting with the top pharma, biotech and regulatory representatives in attendance. The event’s unique strategic focus provides an insightful look at the detection, analysis and prevention of adverse drug reactions with case studies, industry experiences and global regulatory coverage of developments.
Pharmacovigilance Professionals

We deal with all walks of the pharmacovigilance sector including clinical trials, and drug safety within early and latter phase environments.

This group has been created as a means for all those involved in pharmacovigilance to network and discuss these areas. We strive to help maintain these important links, and allow our members to communicate and ultimately help each other in relation to drug safety.

We are a premier resource for those wishing to interlink to Europe, Asia, America and India, with strong ties to the global pharmaceutical and biotechnology communities.

Pharmacovigilance & Drug Safety Network

The Pharmacovigilance & Drug Safety Network is intended for Professionals in Pharmacovigilance & Drug Safety to share best practices and to expand our network of people and ideas.
PV LinkedIn Groups

Visionaries in Pharmacovigilance

In this group industry professionals and leaders come together to network, share opinions, best practices, and visions in pharmacovigilance, drug safety, and risk management.

We encourage dialog regarding the ever changing regulations in the arena of pharmacovigilance.

No job postings please, only topics and discussion regarding our visions.