

**INSTITUTIONAL REVIEW BOARD,
MOUNT SINAI SCHOOL OF MEDICINE**

**GUIDELINES FOR DETERMINING AN ADEQUATE
AND COMPREHENSIVE LITERATURE SEARCH OF DRUG
AND DEVICE SAFETY FOR USE BY INVESTIGATOR
AND INSTITUTIONAL REVIEW BOARDS**

An adequate and comprehensive literature search for drug and device safety shall be defined as one that produces sufficient information for the investigator and the Institutional Review Board (IRB) to determine if the drug/device is sufficiently safe for use in the subjects of the study

The adequacy and comprehensiveness of the literature search for drug/device safety will vary considerably depending on the status of the drug/device. The adequacy and comprehensiveness spectrum extends from the simplest (for a marketed drug/device used in a manner approved by the FDA) to the most complex (for a drug/device that is not approved by the FDA for any condition). The latter situation places the entire responsibility for adequacy and comprehensiveness on the investigator and the IRB.

These Guidelines will apply to the most complex situation (i.e., for the use of a drug/device that has not been approved by the FDA for any use in humans). In all less complex situations the judgment of adequacy and comprehensiveness will be made by the Pharmacy & Therapeutics (P & T) Committee representative to the IRB.

The investigator will have the initial responsibility of meeting these guidelines. The IRB will have the responsibility of assessing whether it believes the guidelines have been followed and either approving or disapproving the adequacy and comprehensiveness of the literature search by the investigator.

As with all searches for prior information about a drug/device, the process can be divided into two parts: 1) the search for the primary references, and 2) the critical evaluation of information contained in primary sources.

It is assumed that the search must lead to primary peer reviewed publications in reputable medical or scientific journals as opposed to reviews, textbooks (though the reviews and/or textbooks may well lead to the primary publications), abstracts (though if this is the only evidence available abstracts should be taken into account¹), meeting notes, meeting synopses, or advertisements.

Written standards for adequacy and comprehensiveness of literature searches of drug safety are not currently published. Preliminary guidelines are provided in the Appendix.

The investigator must construct a log of the information sources used as well as the search paths that have led to that information to document their review of the primary literature. This will be on the form entitled "Literature Search Log, Summary, and Bibliography."

A model process listing the databases to be considered in the literature search and a template for documenting the search path have been supplied as an Appendix. There may be other relevant databases depending on the proposed research question.

The investigator must summarize his/her evaluation of the information that he/she has used to demonstrate their critical review of identified primary references on the form entitled "Literature Search Log, Summary, and Bibliography."

¹ There is considerable evidence to suggest that a significant proportion of reports of trials published in conference abstracts do not reach full publication (see Scherer RW, Langenberg P. Full publication of results initially presented in abstracts [Cochrane Methodology Review]. In: The Cochrane Library, Issue 3, 2001. Oxford: Update Software.

LITERATURE SEARCH LOG, SUMMARY, AND BIBLIOGRAPHY

For each source searched include the following information:

Date Search Conducted:

Name of Database:

Latest update available:

Years Searched:

Please attach a printout of your search strategy (do **NOT** re-type your search terms on this form – print off the original strategy and attach it to this form).

LITERATURE SUMMARY

BIBLIOGRAPHY

(At least one source must be a peer review journal)

APPENDIX A

PRELIMINARY GUIDELINES FOR A LITERATURE SEARCH FOR DRUG/DEVICE SAFETY (A Model for the Process)

I) THE SEARCH FOR EVIDENCE OF SAFETY/ADVERSE EVENTS

- A) Identify the drug/device.
- B) Check for alternate names of the drug/device.
- C) Define the research setting in which the drug/device will be used.
- D) Consult reference or tertiary sources as a starting point.
 - 1) See “Examples of Reference or Tertiary Drug Information Sources” below*.
- E) Consult secondary sources (abstracting and indexing services) for comprehensiveness and quality assurance.
 - 1) See “Examples of Secondary Sources [Abstracting and Indexing Services aka Databases] for Drug and Chemical Information” below*.
 - 2) See “Suggestions for Search Techniques” below**.
- F) Choose the most appropriate sources of evidence of safety/adverse effects.
- G) Create a bibliography.

* Snow, B. *Drug Information: A Guide to Current Resources*, 2nd edition. Lanham, MD and London: Medical Library Association and Scarecrow Press, 1999.
(This reference guide to the drug literature describes many of the resource listed here in greater detail, and offers a detailed and annotated guide to drug and chemical information.)

** Adapted from “Tips for online database comprehensive searching” in McGibbon A. *PDQ: Evidence-Based Principles and Practice*. Hamilton, London, St. Louis: B.C. Decker, 1999. p. 208; and, from comments by reviewer, Carol Lefebvre.

Examples of Reference or Tertiary Drug Information Sources

The following are available from the **Levy Library**. A complete list of the Library's electronic and print resources can be found at <http://www.mssm.edu/library>. For further information please phone the Reference Desk at 212-241-7793 (x47793) or the Reference Department at 212-241-7204 (x47204).

AHFS Drug information. American Hospital Formulary Service Drug Information

Source of comparative, unbiased and evaluative drug information containing monographs on a comprehensive array of drug entities available in the U.S.

Print:	Electronic:	http://www.mssm.edu/library
QV 740 AA1A51 2002 (<i>Reference</i>)	Databases	
	<ul style="list-style-type: none">• Full Text Books<ul style="list-style-type: none">◦ STAT!Ref	

Basic & Clinical Pharmacology. Katzung, Bertram G., ed.

Includes sections that specifically address the clinical choice and use of drugs in patients and the monitoring of their effects. Lists of the commercial preparations, including the trade and generic names and dosage formulations, are provided at the end of each chapter for easy reference.

Print:	Electronic:	http://www.mssm.edu/library
QV 55 B311 2001 (<i>Reserve Desk</i>)	Databases	
	<ul style="list-style-type: none">• Full Text Books<ul style="list-style-type: none">◦ STAT!Ref	

CenterWatch Directory of Drugs

A comprehensive resource offering detailed profiles of new, cutting-edge medications in phase I through III with a special section on pediatric clinical trials. Provides information on more than 1,200 drugs for more than 400 indications worldwide. Detailed profile information is provided for each drug listed.

Print only:	QV 722 C397 2000 (<i>Reference</i>)
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Drug Facts and Comparisons

A comprehensive drug information compendium. Organized by therapeutic drug classes, the format is designed to provide a wide scope of drug information in a manner that facilitates comparisons among drugs.

Print only:	QV 772 D794 2002 (<i>Reference</i>)
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Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. Ellenhorn, Matthew J., et al., eds.

Contains five major sections: principles of poison management, drugs, the home, chemicals and natural toxins. Appendices include OSHA recommendations and a glossary of terminology.

Print:	Electronic:	http://www.mssm.edu/library
QV 600 E45 1997	Databases	
	<ul style="list-style-type: none">• MD Consult• Full Text Books<ul style="list-style-type: none">◦ STAT!Ref	

Goodman and Gilman's the Pharmacological Basis of Therapeutics. Hardman, Joel G. et al., eds.

Describes the drugs most useful in preventing, diagnosing, and treating disease. It details how and why drugs affect different body systems, the chemical properties of drugs, dosage information, drug interactions and toxic effects.

Print only:	QV 4 G653 2001 (<i>Reserve Desk</i>)
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The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals

A collection of over 10,000 monographs, each a concise description of a single substance or a small group of closely related compounds.

Print: QV 744 M55 2001 (<i>Reference</i>)	Electronic: Databases	http://www.mssm.edu/library
	<ul style="list-style-type: none">• Drug Information<ul style="list-style-type: none">◦ Merck Index Online, 12th Ed. (1996)	

Micromedex

Contains full text information from AltMedDex™ System, DRUGDEX, EMERGINDEX, TOMES and REPRORISK Systems, POISINDEX Managements, MARTINDALE, PDR, MSDS from United States Pharmacopoeia, and other databases.

Electronic: Databases	http://www.mssm.edu/library
<ul style="list-style-type: none">• Drug Information<ul style="list-style-type: none">◦ Micromedex	

Mosby Drug Consult

A comprehensive reference for generic and brand prescription drugs.

Print: QV 722 M894 2002 (<i>Reference</i>)	Electronic: Databases	http://www.mssm.edu/library
	<ul style="list-style-type: none">• MD Consult• Full Text Books<ul style="list-style-type: none">◦ STAT!Ref	

USP DI. United States Pharmacopoeia Dispensing Information

Drug information reference book. Coverage includes both labeled and off-label uses of more than 11,000 generic and brand name drugs.

Print: QV 740 AA1U86 2002 (<i>Reference</i>)	Electronic: Databases	http://www.mssm.edu/library
	<ul style="list-style-type: none">• Full Text Books<ul style="list-style-type: none">◦ STAT!Ref	

Consider also the following sites:

Center for Drug Evaluation and Research. U.S. Food and Drug Administration
Includes FDA approvals, drug codes, drug shortages and registration status information.

<http://www.fda.gov/cder/index.html>

Material Safety Data Sheets Collection

Provides the electronic world's largest freely accessible MSDS archive, and links to many new MSDS archives provided by manufacturers concerned with the safe use of their products.

<http://siri.uvm.edu/msds/>

Internet Search Engines:

- **Google** <http://www.google.com>
- **Scirus** <http://www.scirus.com>

This is a search engine from Elsevier that searches only scientific information on the Internet.

[**Caveat:** Information retrieved through Internet search engines should be evaluated and meet criteria for primary publications (i.e., they should be peer reviewed, and published in reputable medical or scientific journals)].

A full list of online and print resources available from the Levy Library can be found at:
<http://www.mssm.edu/library>

Examples of Secondary Sources

[Abstracting and Indexing Services *aka* Databases] for Drug and Chemical Information

Many of the following databases are licensed by the **Levy Library** and access is restricted to faculty, students and staff of the Mount Sinai School of Medicine and Mount Sinai Hospital.

Access the following Databases through the **Levy Library's** web site at:

<http://www.mssm.edu/library> to ensure proper authentication and linking to full text articles if available (e.g., LinkOut from PubMed).

PubMed

PubMed Medline is the National Library of Medicine's premier search service that provides access to over 11 million citations in Medline, Premedline, and other related databases to journal articles in the life sciences with a concentration on biomedicine. *Coverage: 1966-present*

OldMedline via NLM Gateway (<http://gateway.nlm.nih.gov>)

Contains citations published in the 1958-1965 *Cumulated Index Medicus* and covers the fields of medicine, pre-clinical sciences, and allied health sciences. OldMedline is available through the NLM Gateway. *Coverage: 1958-1965*

Science Citation Index Expanded via Web of Science.

Produced by the Institute for Scientific Information. Provides a citation index of more than 5,700 major journals covering more than 164 disciplines. Some of the disciplines include medicine, biology, chemistry, zoology, and computer science. Includes cited references. *Coverage: 1945 – present*

Toxnet (<http://toxnet.nlm.nih.gov/>)

National Library of Medicine's Toxicology Data Network (Toxnet) offers a grouping of databases on toxicology, hazardous chemicals, and related areas. The toxicology data group has factual information on toxicity and other hazards of chemicals; the toxicology literature group contains scientific studies, reports, and other bibliographic material; and the chemical information group contains nomenclature, identification, and structures. Includes: ChemIDPlus, Toxline, Hazardous Substances Data Bank, Genetic Toxicology, and more.

Micromedex

Contains full text information from AltMedDex™ System, DRUGDEX, EMERGINDEX, TOMES and REPRORISK Systems, POISINDEX Managements, MARTINDALE, PDR, MSDS from United States Pharmacopoeia, and other databases.

Cochrane Library

Includes the Cochrane Database of Systematic Reviews, a collection of structured, systematic reviews of health care interventions including adverse affect information. The Cochrane Controlled Trials Register, also in the Cochrane Library, contains 300,000 reports of randomized controlled trials in health care.

Please contact the **Levy Library** reference staff for additional information or to schedule a consultation (241-7793 or 241-7204).

Suggestions for Search Technique*

- Use multiple bibliographic databases [secondary sources] and reference [tertiary] resources.
- Use databases or secondary sources of different kinds (e.g., citation, theses, National Library of Medicine's catalog called LocatorPlus, PubMed's **related articles** feature).
- Extend the years of searching.
- Have more than one set of searchers do your main searching independently – each searcher will retrieve relevant, unique citations.
- Find out how the articles that you already have are indexed and work backwards using the index terms from the original articles. Bibliographies and personal files are often good places to find relevant citations to start with.
- Avoid “major emphasis” tags available in many databases.
- Avoid, or use the logical operators ‘AND NOT’ carefully. The ‘NOT’ can eliminate references that you are truly interested in.
- Ensure that your synonyms are combined with a logical ‘OR’ and not ‘AND’.
- Avoid the use of *subheadings* [see PubMed's MESH Browser for examples of subheadings] as limiters on main concepts. Use other methods of limiting information such as HUMAN.
- Make sure you know the definitions of the terms you are using e.g. in MEDLINE adults are anyone who is from 19 to 44 years old – anyone over 45 years old is considered to be middle aged.
- When constructing search strategies, remember that indexers of the journal literature are instructed to use the most specific term available to them [e.g. definition of *nutrition* may need many terms or groupings of terms (vitamin deficiency, protein restriction, and so on)].
- Use a combination of textwords and index words (subject headings – e.g., MeSH).
- For index terms expand more general terms to include specific terms (e.g., called *exploding a term*) or check to see that *smart* search engines have done this. In PubMed click on **Details** to examine how the system has performed your search.
- For textwords remember:
 - Appropriate truncation
 - Alternative spellings
 - Differences in terminology across disciplines (bed sores and decubitus ulcers)
 - Differences across national boundaries (SIDS and Cot Death)
 - Differences in historical naming (unwed mothers, *Campylobacter pylori*)
 - Short forms for terms (AIDS and acquired immunodeficiency syndrome)
 - Brand and generic names (Viagra and sildenafil)
- Make sure you use terms that are somewhat related (mortality and survival analysis).
- Use author searching, study names (GISSI, GUSTO, SOLVD), locations/affiliations (Mount Sinai), manufacturers of drugs or products.
- Search using opposites for some topics (e.g. if you are interested in *tallness* make sure you search for being *short* too).
- Keep track of what you have done.

* Adapted from “Tips for online database comprehensive searching” in McGibbon A. *PDQ: Evidence-Based Principles and Practice*. Hamilton, London, St. Louis: B.C. Decker, 1999. p. 208; and, from comments by reviewer, Carol Lefebvre.

Other models for a comprehensive search process can be found in:

JAMA series: *Users Guides to the Medical Literature*. For a link to the citations go to www.mssm.edu/library, click on **Library Services** and **Users' Guides to the Medical Literature**.