

# Literature Search Strategy for Preparing the Report on Carcinogens Monograph on Cobalt and Certain Cobalt Compounds

## Introduction and objective

The objective of the literature search strategy is to identify the published literature that is relevant for evaluating the potential carcinogenicity of cobalt and certain cobalt compounds. This section discusses the general approach for the literature search; specific details, such as search terms and inclusion/exclusion criteria, are described in relevant sections for the following topics:

- Properties
- Human Exposure (focusing on the U.S. population)
- Disposition (ADME) and Toxicokinetics
- Human Cancer Studies
- Studies of Cancer in Experimental Animals
- Mechanistic Data and Other Relevant Effects
  - Genotoxicity and Related Effects
  - Mechanistic Considerations

The methods for identifying the relevant literature, including the literature search strategy. (Section 1) and the review of citations using web-based systematic review software (Section 2), are discussed below.

## 1 Literature search strategy

Relevant literature is identified using multiple approaches (see Figure B-1) including: Database searches (typically PubMed, Scopus, and Web of Science). This is the major source for identifying relevant paper on the relevant topics (see above) and is described in detail below.

- **General data search (see Section 3):** Examples include authoritative reviews and exposure-related data searches (see Part B), which cover a broad range of general data sources for information relevant to many candidate substances.
- **Exposure-related data search:** This search covers a broad range of potential sources for exposure-related information and physical-chemical properties (see Table 2).
- **Focused searches for specific scientific issues**
- **Secondary citations:** Citations identified from authoritative reviews or from primary references located by literature search.
- **Quosa library:** Full text searches of library of specific type of studies. These searches are performed to identify studies where the candidate substance may not be identified in the title or abstract. Currently, a library created by the ORoC for

occupational case- control studies of cancer using QUOSA scientific literature management software is used to identify human epidemiologic studies of specific occupational exposures and cancer.

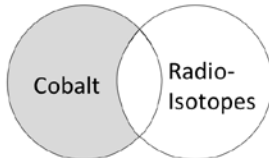
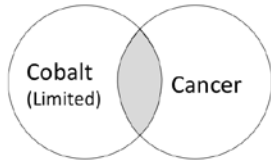
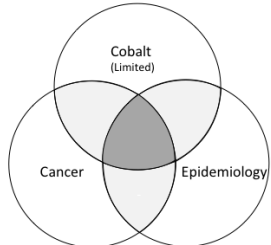
### Database searches

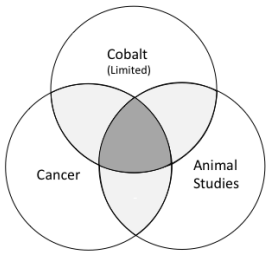
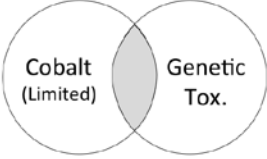
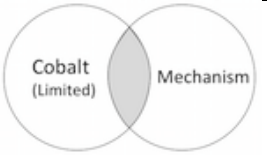
Database searching involves selecting search terms and databases used in the searches and conducting the searches.

Literature searches of several databases are generally conducted using search terms for cobalt and certain cobalt compounds, combined with search terms for cancer and/or specific topics, such as human exposure, cancer studies in animals, epidemiological studies, mechanistic studies, etc. Titles, abstracts, and key words are searched in these databases. For example, in Part C, literature searches for exposure scenarios or settings are also used when cobalt exposure could occur in a specific occupational setting or through use of a specific consumer product.

A critical step in the process involves consultation with an information specialist to develop cancer- and topic-specific search terms for cobalt. These terms are used to search databases such as PubMed, Scopus, and Web of Science. Literature searches are updated by creating monthly alerts in the appropriate databases. The searched concepts for cobalt and monograph topics are listed in the table below.

**Table 1. Topics and Searched Concepts for: Cobalt (7440-48-4)**

Topic	Searched Concepts	Combinations
Cobalt	Cobalt, 7440-48-4	
Cobalt radioisotopes	Cobalt-60 Radiation treatment Radioactive Gamma rays	 <p>Result=Cobalt (Limited)</p>
Cancer	Cancers Neoplasms Tumors Carcinogenicity Malignant Oncogenic	
Epidemiology/ Human studies	Epidemiology Epidemiologic methods/studies Epidemiologic factors Publication and study types (e.g. case-control, cohort, case-report, case-series, follow-up) Occupational Exposure Workers Mortality Incidence Prevalence	

Topic	Searched Concepts	Combinations
Animal Studies	Animals Mice Rats Rabbits Hamsters Guinea pigs Dogs	
Gene Tox	Genetic toxicology Genomic Instability Gene expression Oncogenes DNA Damage/Repair Unscheduled DNA synthesis DNA Adducts Chromosome Breakage/Aberrations Sister Chromatid Exchange Mutation Mutagenicity Tests (e.g., Ames test, Comet assay etc.)	
Mechanism	Lung toxicity Cytotoxicity Cytogenetic Analysis Cell Transformation/Proliferation Neoplastic Aneuploidy/polyploidy Crosslinks Document Type (Review)	

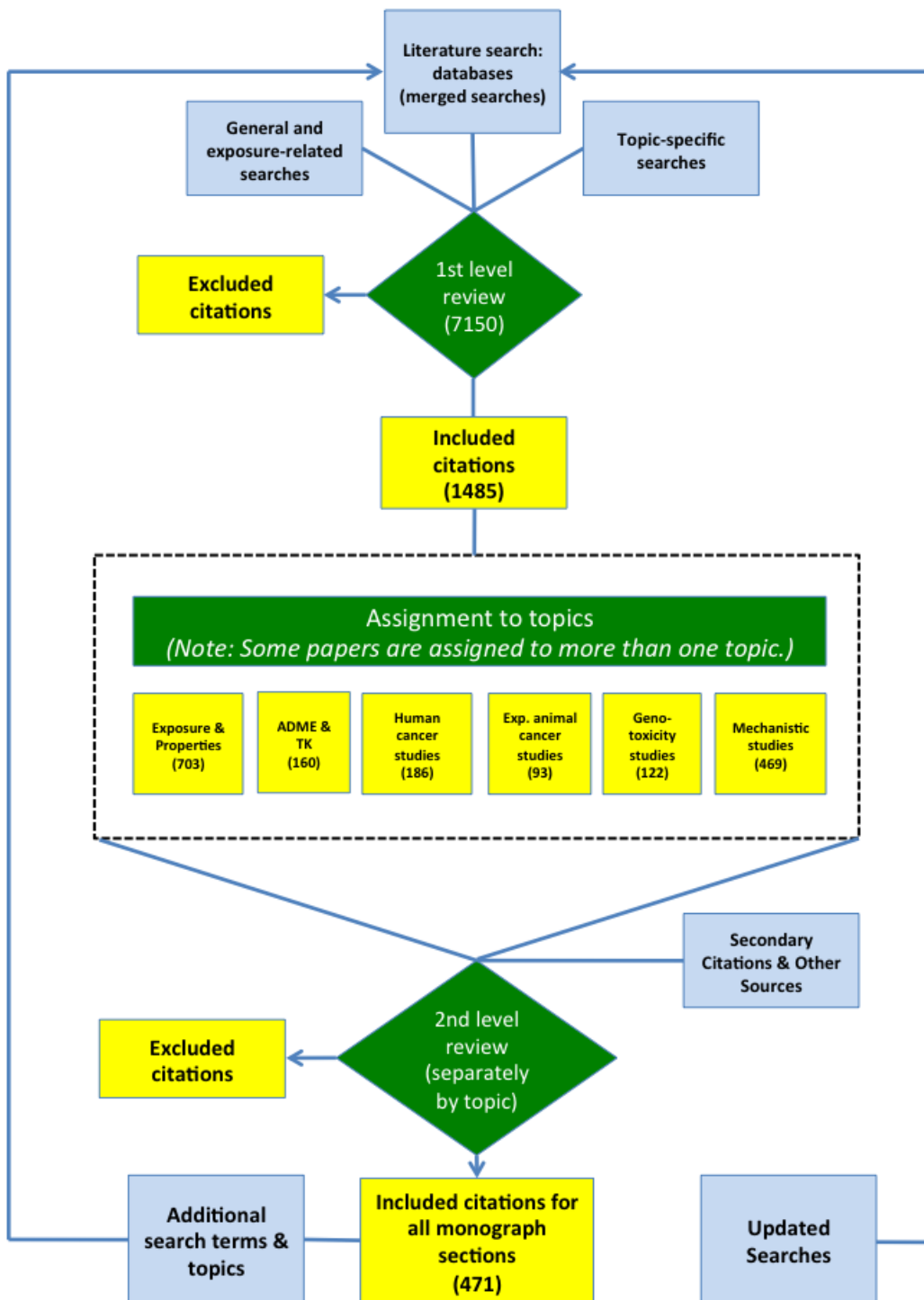
## 2 Screening and selecting literature

Citations retrieved from literature searches (and other sources) are uploaded to an EndNote library and any duplicates removed. Next, the EndNote library is uploaded to web-based systematic review software DistillerSR for multi-level screening using inclusion and exclusion criteria. Each level of screening is done by two scientists (ideally at least one NTP staff person).

The citations are first screened (Level 1) using the title and abstract (where available) by two screeners to eliminate papers that do not contain information on the candidate substance or on any of the key topics or questions (exposure, cancer studies in humans and animals, toxicokinetics, genotoxicity, toxicity, and mechanisms of action) covered by a RoC monograph.

The initial screen is designated as “liberal,” i.e., it is intended to retrieve a PDF if there is any reasonable possibility that it contains information that could be useful for the review process; a positive response by only one of the reviewers is sufficient to pass a publication on to the next review level. The initial reviewers assign (or tag) the citation to one or more of the topic(s) covered by a RoC (see above).

PDFs are obtained for all citations not excluded at Level 1 for Level 2 screening. Topic-specific experts (e.g., writers for each monograph section) screen the citations using inclusion/exclusion criteria. Similar to Level 1, two scientists screen the literature (the 2nd screening is typically by a topic-specific expert who is the reviewer of the section). In general, these exclusion and inclusion criteria are somewhat similar to the first level (e.g., information on the candidate substance and topic); however, Level 2 can make a more informed judgment about the citations than the Level 1 screeners because they have the full text (PDF). Depending on the topic, more specific inclusion and exclusion criteria may be developed, which will be delineated in the protocol, which can be part of the Level 2 screening or a Level 3 screening. Third level reviews are generally limited to the human cancer and animal tumor studies sections, and should identify all studies included in the monograph sections on those topics. Examples of third level screening may be to exclude case reports (human cancer) or studies with very poor reporting. Citations can also be redistributed to other topics (writers) if that topic(s) was not identified by the reviewer at Level 1. The flowchart for review of citations for cobalt is illustrated below.



Flowchart for review of cobalt citations

### 3 Data sources

The following is a list of general data sources that are searched for information on a specific candidate substance. The list includes authoritative reviews or study reports and web-based resources and/or databases. The tables below list the sources searched for general sources (Table 2) and exposure-related sources (Table 3) and the files downloaded from those sources.

**Table 2. General Sources Checklist for: Cobalt (7440-48-4)**

Source	Name of File (ROC)	Name of document (Publisher)
<b>A) Comprehensive Sources for Reviews</b>		
1) NTP technical reports	NTP1998 NTP2013 NTP2014b	TR 471 TR 581 (draft) TR 581
2) NTP nomination for toxicological evaluation documents		
3) NTP RoC Background Documents	NTP2002b NTP2009	
4) NTP RoC Profiles	NTP2011 NTP2014	12 <sup>th</sup> ROC (CS) 13 <sup>th</sup> ROC (CTC)
5) OHAT (formerly CERHR)		
6) IARC monographs	IARC1989 IARC1991 IARC2006	Vol. 45 Vol. 52 Vol. 86
7) ATSDR Toxicological Profiles	ATSDR2004	TP33
8) EPA IRIS		
9) NAS Reports and Publications		
10) WHO (IPCS) INCHEM-related documents (a-k below)	ICPS1997	IARC Vol. 52
a) CICADS	WHO2006	CICAD 69
b) EHC		
c) HSGs		
d) ICSCs	COBALT OXIDE 1308-04-9	ICSC 0785
e) JECFA		
f) JMPR		
g) KemI-Riskline		
h) PDs		
i) PIMS		
j) SIDS	HeCaSAC2011	
k) UKPID	UKPID52	
11) California EPA Prop 65 hazard identification documents		
12) Health Canada	See SIDS	
13) New York State Department of Health- Health Topics A-Z		
<b>B) General Information Sources</b>		
1) U.S. National Library of Medicine (NLM)		
a) HSDB	HSDB2006a Cobalt elemental HSDB2006b Cobalt compounds HSDB2004 Cobalt Chloride HSDB2003 Cobalt Bis 2 Ethylhexanoate	DOCNO:519 DOCNO:7141 DOCNO:1000 DOCNO:5621

Source	Name of File (ROC)	Name of document (Publisher)
b) CCRIS		
c) GENETOX		
d) ITER		
e) LactMed		
f) CPD		
g) CTD		
h) EPA SRS	Cobalt Sulfide 12013-10-4	
2) PubChem	Cobalt 7440-48-4 Cobalt Chloride 7646-79-9 Cobalt (II) nitrate 10141-05-6 Cobalt Propionate 1560-69-6 Cobalt Stearate 1002-88-6	CID:104730 CID:24288 CID:25000 CID:62409 CID:6451168
3) Kirk-Othmer Encyclopedia		
4) USGS (Minerals)	Shedd2013 Shedd2014b Shedd2014c	2011 Yearbook 2012 Yearbook Survey 2-2014
<b>C) European Union – Sources to Search</b>		
1) International Uniform Chemical Information Database (IUCLID)		
2) European Chemicals Agency	ECHA2011	
3) The International Portal on Food Safety, Animal and Plant Health (IPFSAPH)		
4) The European Food Safety Authority	EFSA2012	EFSA Journal 10(7):2791
5) European Centre for Disease Prevention and Control (ECDC)		
6) European Monitoring Centre for Drugs and Drug Addiction		

**Table 3. Exposure-related Sources Checklist for: Cobalt (7440-48-4)**

Source	Name of File (ROC)	Name of document (Publisher)
1) U.S. National Library of Medicine (NLM)- TOXNET		
a) ChemIDplus	Cobalt 7440-48-4	7440-48-4
b) Haz-Map		
c) HPD	HPD2014	
d) TOXMAP		
2) Akron database		
3) SciFinder (American Chemical Society) <i>*Name of File (ROC) begins with Cobalt II</i>	Cobalt 7440-48-4 *Sulfate monohydrate 13455-34-0 *Sulfate 10124-43-3 *Sulfate Heptahydrate 10026-24-1 *Chloride 7646-79-9 *Chloride, hexahydrate 7791-13-1 *Nitrate 10141-05-6 Cobalt III acetate 917-69-1 *Acetate 71-48-7 *Oxide 1307-96-6 Cobalt II III oxide 1308-06-1 Cobalt trioxide 1308-04-9 Cobalt Bis 2-ethyl hexanoate 136-52-7 Cobalt Carbonate 513-79-1 Cobalt Naphthenate 61789-51-3 *Hydroxide 21041-93-0 Cobalt III hydroxide 1307-86-4 Cobalt monosulfide 1317-42-6 *Sulfide 12013-10-4 Cobalt III sulfide 1332-71-4 *Oxalate 814-89-1 Cobalt Tallate 61789-52-4 tall oils Cobalt Propionate 1560-69-6 *Stearate 1002-88-6	7440-48-4 13455-34-0 10124-43-3 10026-24-1 7646-79-9 7791-13-1 10141-05-6 917-69-1 71-48-7 1307-96-6 1308-06-1 1308-04-9 136-52-7 513-79-1 61789-51-3 21041-93-0 1307-86-4 1317-42-6 12013-10-4 1332-71-4 814-89-1 61789-52-4 1560-69-6 1002-88-6
4) Chem Sources Suppliers		
5) National Health and Nutrition Examination Survey (NHANES) data studies	CDC2014	
6) National Occupational Exposure Survey (NOES) (1981-1983)	C.Co.W, Cobalt Tungsten Carbide-Van Carbonic Acid, Cobalt Salt (CH2O3XCO) Cobalt 2-Ethylhexoate Cobalt Ammonium Sulfate Cobalt Carbide Cobalt Carbonate Cobalt Chloride (COCL2), Hexahydrate Cobalt Chloride (COCL2) Cobalt Chloride Cobalt Drier Cobalt Hydroxide Cobalt Monoamyl Acetate Cobalt Naphthenate Cobalt Oxide (CO3O4) Cobalt Oxide (COO) Cobalt Oxide Cobalt Powder	X6225 X2966 83434 X5827 X5708 X4497 X4499 84329 X3243 M0642 M2954 W0094 80347 X4824 A1638 M2576 X5978



Source	Name of File (ROC)	Name of document (Publisher)
	Cobalt Sulfide (COS2) Cobalt Tallate Cobalt, 2-Ethylhexanoate Isononanoate Complexes Cobalt, Borate Neodecanoate Complexes Cobalt Cobaltous Acetate Cobaltous Carbonate	X4498 M2703 X2365  E0222 19770 82777 81240
7) National Institute for Occupational Safety and Health (NIOSH) - Health Hazard Evaluations	NIOSH1977 NIOSH1981 NIOSH1987a NIOSH1987b NIOSH1988	
8) National Response Center (NRC) Database		
9) U.S. International Trade Commission (USITC) Import/Export data	USITC2014	
10) EPA Toxics Release Inventory (TRI)	TRI2014a TRI2014b TRI2014c TRI2014d TRI2014e	
11) EPA AP-42, Compilation of Air Pollutant Emission Factors		
12) EPA EJView Database		
13) EPA HPV Challenge Program Chemical List	EPA2012	
14) EPA Inventory Update Rule (IUR)		
15) EPA Locating and Estimating (L&E) documents		
16) EPA/Office of Pesticide Programs (OPP) Chemical Ingredients Database		
17) Food and Drug Administration (FDA) Pesticide Monitoring Database		
18) FDA Orange Book		
19) FDA Total Diet Study		
20) Medline Plus		
21) United States Patent Office		
22) Trademark Electronic Search System (TESS)		
23) Material Safety Data Sheets (MSDS)		
24) Dow Chemical Product Safety Assessments		