

Abstract Sifter User Guide, Version 1.0

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Availability: The Abstract Sifter and documentation is freely available for download at ftp://newftp.epa.gov/COMPTOX/Sustainable_Chemistry_Data/Chemistry_Dashboard/Abstract_Sifter/.

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Abstract Sifter User Guide – Version 1.0

This user guide describes the functionality of the PubMed Abstract Sifter version 1.0. The reader is invited to download the tool from the freely accessible ftp site and follow along:

ftp://newftp.epa.gov/COMPTOX/Sustainable_Chemistry_Data/Chemistry_Dashboard/Abstract_Sifter/

This document provides guidance on the use of the Abstract Sifter through a series of screen shots showing the most common tasks in the tool followed by some helpful tips.

First open the Abstract Sifter file AbstractSifter_v1.xlsm. A security warning may appear. If so, be sure to enable content as shown in Figure 1.

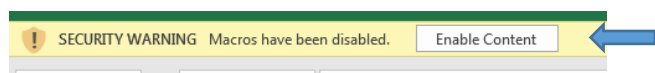


Figure 1. Enable macros upon opening

Once open you will see that the Abstract Sifter Excel file consists of seven sheets. Each sheet is described briefly in the table below.

Sheet name	Sheet Function
ReadMe	Basic information on the sifter with links to more documentation
Main	Starting point for PubMed queries and for sifting
Abstract	The sheet where the citation abstract is shown
Notes	Notes and tags are inserted here
Log	Log of every query run on Main sheet
SampleQueries	Repository of sample queries to use as starting points
Landscape	High level view of literature for entities

Main Sheet

The Main sheet is where the basic functionality of Abstract Shifter occurs, including functions we call “sifting”. To begin using the Abstract Sifter, the end-user clicks on the *Query PubMed* button at the top of the screen in the Main sheet. A form is displayed in which the end-user types a PubMed query of interest (Figure 2). In the example, we are showing a very simple query: “chlorpyrifos”, but these queries can be more complex. The text that the user enters into the box is sent to PubMed, so all PubMed syntax rules apply. (For a review of this syntax, visit

<https://www.ncbi.nlm.nih.gov/books/NBK3827/>)

The screenshot displays the 'Abstract Sifter v1.0' spreadsheet interface. At the top, there is a 'Query PubMed' button. Below it, a section titled 'Your sifter terms and frequency counts' contains three input fields: 'My sifter term 1', 'My sifter term 2', and 'My sifter term 3'. To the right of these fields are columns for 'Total', 'Pub', 'Yr', and 'Title'. A modal window titled 'UserForm1' is overlaid on the spreadsheet, prompting the user to 'Enter your PubMed query and click on Submit.' The text 'chlorpyrifos' is entered into the query box. A 'Submit' button is located in the top right corner of the modal. At the bottom of the modal, a small note reads: 'When this form goes away, your query is done.'

Figure 2. Running a PubMed query

When finished entering the query, the user clicks on *Submit* and the query is packaged by a Visual Basic Application (VBA) into an e-utility command that is passed to the NCBI (National Center for Biotechnology Information) web services. (Note that using Sifter Query PubMed capability requires internet access.) The first response returned by the utility is the number of articles found. (Figure 3) This number is displayed, and the user is asked if he/she want to continue. If the number of articles is over 5,000, the query will not be run and the user is encouraged to refine the query to return fewer records.

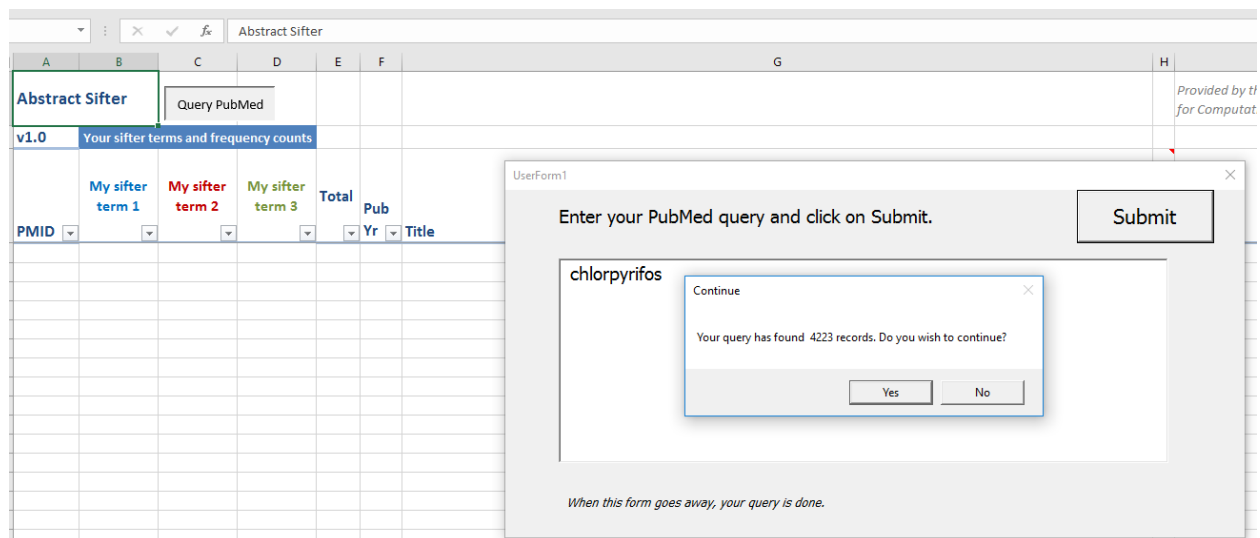


Figure 3. Responding to PubMed

If the returned results are fewer than 5,000 and the user indicates he/she wants to continue, the articles are downloaded from NCBI by Excel, and regular expressions are used to parse the citations for title, abstract, authors, publication year, journal, and PubMed identifier. Each record returned is inserted into a row in the Main sheet. Any rows in the Main sheet from a previous query are deleted.

Abstract Sifter										
Query PubMed										
v1.0 Your sifter terms and frequency counts										
PMID	My sifter term 1	My sifter term 2	My sifter term 3	Total	Pub	Title				
2831109	0	0	0	0	0	2017 Exposure to agricultural pesticide impairs visual lateralization in a larval coral reef fish.				
28311307	0	0	0	0	0	2017 Determination of Residues of Diazinon and Chlorpyrifos in Lavender and Rosemary Leaves by Gas Chromatography.				
28320005	0	0	0	0	0	2017 Inhibition of Endocannabinoid-Metabolizing Enzymes in Peripheral Tissues Following Developmental Chlorpyrifos Expos				
28802139	0	0	0	0	0	2017 Analysis of neurobehavioural data by chemometric methods in ecotoxicological studies.				
28791107	0	0	0	0	0	2017 Determination of selected neurotoxic insecticides in small amounts of animal tissue utilizing a newly constructed mini-e				
28791702	0	0	0	0	0	2017 Developmental neurotoxicity of the organophosphorus insecticide chlorpyrifos: from clinical findings to preclinical mode				
28782362	0	0	0	0	0	2017 Emission Factors for Selected Semivolatile Organic Chemicals from Burning of Tropical Biomass Fuels and Estimation of A				
28780760	0	0	0	0	0	2017 Pesticide dissipation and microbial community changes in a biopurification system: influence of the rhizosphere.				
28780449	0	0	0	0	0	2017 The impact of six insecticides commonly used in control of agricultural pests on the generalist predator Hippodamia conv				
28778749	0	0	0	0	0	2017 Exposure of amateur gardeners to pesticides via the non-gloved skin per day.				
28778031	0	0	0	0	0	2017 Transformation from gold nanoclusters to plasmonic nanoparticles: A general strategy towards selective detection of org				
28774551	0	0	0	0	0	2017 24-Epibrassinolide alleviates organic pollutants-retarded root elongation by promoting redox homeostasis and secondar				
28772184	0	0	0	0	0	2017 Assessing the ecotoxicity of potentially neurotoxic substances - Evaluation of a behavioural parameter in the embryogen				
28769805	0	0	0	0	0	2017 The Mechanism by Which Dodecyl Dimethyl Benzyl Ammonium Chloride Increased the Toxicity of Chlorpyrifos to Spodop				
28768160	0	0	0	0	0	2017 Cytochrome P450 genes from the aquatic midge Chironomus tentans: Atrazine-induced up-regulation of CYP6E3 enha				
28766927	0	0	0	0	0	2017 Combining Hyperspectral Imaging and Chemometrics to Assess and Interpret the Effects of Environmental Stressors on tr				
28757570	0	0	0	0	0	2017 Monitoring of Pesticide Residues in Commonly Used Fruits and Vegetables in Kuwait.				
28756254	0	0	0	0	0	2017 Evaluation of chlorpyrifos effects, alone and combined with lipopolysaccharide stress, on DNA integrity and immune res				
28754986	0	0	0	0	0	2017 Effects of Deltamethrin, Dimethoate, and Chlorpyrifos on Survival and Reproduction of the Collembolan Folsomia candid				
28753233	0	0	0	0	0	2017 Knockout of a P-glycoprotein gene increases susceptibility to abamectin and emamectin benzoate in Spodoptera exigua.				
28748436	0	0	0	0	0	2017 Organophosphorus pesticide mixture removal from environmental matrices by a soil Streptomyces mixed culture.				
28747242	0	0	0	0	0	2017 Identification and characterization of ace1-type acetylcholinesterase in insecticide-resistant and -susceptible Propylaea				
28745304	0	0	0	0	0	2017 Multi-class chemical exposure in rural Peru using silicone wristbands.				
28741215	0	0	0	0	0	2017 Acute toxicity of chlorpyrifos and carbofuran to glochidia of the freshwater mussel Hyriopsis bialata Simpson, 1900.				

Figure 4. Results from PubMed query - before sifting

At this point the results of the query are stored in the Main sheet and can be browsed like any other data in a spreadsheet (Figure 4); however, the most effective way to find articles of interest is to use the innovative sifter functionality. To demonstrate this functionality, we will continue to use our example of chlorpyrifos.

Let us suppose at this point that we are looking for dose-response data for chlorpyrifos in rat studies that focused on brain effects. We type the term “mg/kg” in cell B3, “rat” in C3, and “brain” in D3. As we finish typing and move to the next cell, the Abstract Sifter will count the occurrences of the terms in the title and abstract combined. The citations can then be sorted by these counts, either individually or by the total. Figure 5 shows what the Sifter looks like when these terms have been entered into cells B3, C3, and D3 and then the entries sorted by occurrence counts of “mg/kg” in descending order. PubMed 16472551 has 12 occurrences of “mg/kg”, 22 of “rat”, and two of “brain”. This article indeed describes a dose-response study in rats.

	A	B	C	D	E	F	G	H	I	L	M	
1	Abstract Sifter		Query PubMed			Query run: chlorpyrifos		Provided by the USEPA's National Center for Computational Toxicology				
2	v1.0	Your sifter terms and frequency counts						Take Group Notes	Highlight Noted			
		mg/kg	rat	brain	Total	Pub			Review			
3	PMID					Yr	Title		Authors	Journal		
4	16472551	12	22	2	36	2006	Effect of chlorpyrifos-methyl on steroid and thyroid hormones in rat F0- and F1-generations.		Jeong, Kim, Kang, Ku, Cho	Toxicology		
5	10653531	11	9	3	23	2000	Lack of carcinogenicity of chlorpyrifos insecticide in a high-dose, 2-year dietary toxicity study in Fischer 344 rats.		Yano, Young, Mattsson	Toxicological sciences : an official journal of the Society of Toxicologists		
6	94259	11	10	0	21	1979	Efficiency and safety of methidathion applied as a pour-on systemic insecticide for control of cattle lice.		Hart, Cavey, Moore, Strong	Australian veterinary journal		
7	28269887	10	7	0	17	2017	Temperature influences the toxicity of deltamethrin, chlorpyrifos and dimethoate to the predatory mite Hypoaspis aculeator.		Jegede, Owojori, Römke	Ecotoxicology and environmental safety		
8	12521673	9	6	0	15	2003	Influence of gender on thermoregulation and cholinesterase inhibition in the long-evans rat exposed to diazinon.		Gordon, Mack	Journal of toxicology and environmental health		
9	11829414	9	0	0	9	2001	Striatal dopaminergic pathways as a target for the insecticides permethrin and chlorpyrifos.		Karen, L, Harp, Gillette, Bloomquist	Neurotoxicology		
10	3989223	9	1	0	10	1985	Toxicity of organophosphorus esters to laying hens after oral and dermal administration.		Francis, Metcalf, Hansen	Journal of environmental science and technology		
11	17454568	8	8	0	16	2007	Differential sensitivity to anticholinesterase insecticides in the juvenile rat: effects on thermoregulation.		Mack, Gordon	Journal of toxicology and environmental health		
12	12830919	8	5	0	13	2003	Rapid multi-residue method for the determination of azinphos methyl, bromopropylate, chlorpyrifos, dimethoate, para		Liapis, Aplada-Sarlis, Kyriakidis	Journal of chromatography. A		
13	9588346	8	9	0	17	1998	Effects of the pesticides carbofuran, chlorpyrifos, dimethoate, lindane, triallate, trifluralin, 2,4-D, and pentachloropheno		Rawlings, Cook, Waldbillig	Journal of toxicology and environmental health		
14	2017753	8	1	0	9	1991	Promotion of organophosphate-induced delayed polyneuropathy by phenylmethanesulfonyl fluoride.		Lotti, Caroli, Capodicasa, Moretto	Toxicology and applied pharmacology		
15	6201092	8	0	0	8	1984	Oral intubation of dogs with combinations of fertilizer, herbicide, and insecticide chemicals commonly used on lawns.		Yeary	American journal of veterinary research		
16	28280510	7	3	0	10	2017	Determination of Levels of Organochlorine, Organophosphorus, and Pyrethroid Pesticide Residues in Vegetables from Ma		Mahugija, Khamis, Lugwisha	International journal of analytical chemistry		
17	26642910	7	7	1	15	2017	Decreased anxiety in juvenile rats following exposure to low levels of chlorpyrifos during development.		Carr, Armstrong, Buchanan, Eells, Moham	Neurotoxicology		
18	24809615	7	1	0	8	2014	Organophosphorus pesticide residues in vegetables from farms, markets, and a supermarket around Kwan Phayao Lake c		Sapbamrer, Hongsilboong	Archives of environmental contamination		
19	22504667	7	5	0	12	2012	Cholinesterase inhibition and toxicokinetics in immature and adult rats after acute or repeated exposures to chlorpyrifos		Marty, Andrus, Bell, Passage, Perala, Brzak	Regulatory toxicology and pharmacology		
20	16777161	7	5	1	13	2006	Effects of acute chlorpyrifos exposure on in vivo acetylcholine accumulation in rat striatum.		Karanth, Liu, Mirajkar, Pope	Toxicology and applied pharmacology		
21	10543028	7	6	7	20	1999	Changes in rat brain cholinesterase activity and muscarinic receptor density during and after repeated oral exposure to d		Tang, Carr, Chambers	Toxicological sciences : an official journal of the Society of Toxicologists		
22	28373059	6	6	4	16	2017	Protective properties of 6-gingerol-rich fraction from Zingiber officinale (Ginger) on chlorpyrifos-induced oxidative dama		Abolaji, Ojo, Afolabi, Arowoogun, Nwawo	Chemo-biological interactions		
23	25182558	6	10	3	19	2014	Effects of melatonin on changes in cognitive performances and brain malondialdehyde concentration induced by sub-chr		Bankte, Folorunsho, Mohammed, Musa, Ch	Asian Pacific journal of tropical biome		
24	24394474	6	7	2	15	2014	Taurine mitigates cognitive impairment induced by chronic co-exposure of male Wistar rats to chlorpyrifos and lead acet		Akande, Alliu, Ambali, Ayo	Environmental toxicology and pharma		
25	23624372	6	3	0	9	2013	Oxidative damage induced by chlorpyrifos in the hepatic and renal tissue of Kunming mice and the antioxidant role of vit		Ma, Wu, Zeng, Gan, Chen, Ye, Yang	Food and chemical toxicology : an inte		
26	11687644	6	11	0	17	2011	Ameliorative effect of vitamin C on alterations in thyroid hormones concentrations induced by subchronic coadministrat		Ambali, Orijei, Abubakar, Shittu, Kawu	Journal of thyroid research		
27	20691718	6	3	4	13	2010	Dose-related gene expression changes in forebrain following acute, low-level chlorpyrifos exposure in neonatal rats.		Ray, Liu, Ayoubi, Pope	Toxicology and applied pharmacology		
28	20524109	6	1	0	7	2010	Studies on relative toxicities of six insecticides on epigeic earthworm, Perionyx excavatus.		Das Gupta, Chakravorty, Kaviraj	Bulletin of environmental contaminat		
29	20162264	6	8	0	14	2010	Multipesticide residue assessment of agricultural soil and water in major farming areas in Benguet, Philippines.		Del Prado Lu	Archives of environmental contaminat		
30	19850121	6	2	2	10	2010	Chlorpyrifos induced reproductive toxicity in male mice.		Farag, Radwan, Sorour, El Okazy, El-Agamy	Reproductive toxicology (Elmsford, N.		

Figure 5. After sifter terms were entered into cells B3, C3, D3 and sorting on B3

Abstract Sheet

To see the abstract for any of the retrieved articles, we can either click on the PubMed ID hyperlink to be taken to PubMed, or we can double-click on any other cell in the row for this article. This action brings us to the Abstract sheet where the abstract is displayed along with other article meta-data like title and authors (Figure 6).

A		B		D	E	F
<div><div>Abstract with highlights</div><div><div><- Main</div><div>Add Note</div><div>See Notes >></div></div></div>						
1					PubYr	Authors
2	Article: 16472551					Journal
3	Title: Effect of chlorpyrifos-methyl on steroid and thyroid hormones in rat F0- and F1-generations.				2006	Jeong, Kim, Kang, Ku, Cho
4						Toxicology
5	Title and Abstract: Effect of chlorpyrifos-methyl on steroid and thyroid hormones in rat F0- and F1-generations. Abstract: Chlorpyrifos-methyl (CPM) suppressed androgenic activity in Hershberger assay using castrated rats . Acute oral lowest-observed-adverse-effect-level (LOAEL) and no-observed-adverse-effect-level (NOAEL) was evaluated as 12 and 0.1 mg/kg bw, respectively, based on its major effect of cholinesterase inhibition. Also, repeated oral NOAEL was 0.1 mg/kg bw/day based on adrenal damage in rats . We investigated one-generation reproductive toxicity of CPM focusing on endocrine-disrupting effects by the administration of 1, 10 and 100 mg/kg bw/day CPM to mature SD rats (F0) through pre-mating, mating, gestation and lactation period and to their offspring (F1) until 13 weeks age via gavage. A group treated with corn oil served as vehicle control. In F0 rats , the most affected organs were adrenal glands as increased in weight at all doses of CPM in males and at 10 and 100 mg/kg CPM in females and adrenal vacuolation at CPM 10 and 100 mg/kg . The relative and absolute ovaries and the absolute seminal vesicle weights were decreased but the weights of liver, spleen or kidneys were increased at 100 mg/kg CPM. Parameters representing reproductive performances as mating ratio , gestation length and delivery index were not affected, except for decreased fertility index and numbers of implantation and born pups and a higher male sex ratio of pups at CPM 100 mg/kg . F1 pups exposed to CPM 100 mg/kg in utero and via maternal milk showed lower body weight with changes of absolute or relative weights of brain , ovary, liver, spleen and epididymis and decreased absolute not relative anogenital distance at weaning time. The time of vaginal patency and preputial separation and estrous cycling pattern of F1 rats were not impacted by CPM. After further 10 weeks oral administration until 13 weeks old, adrenal glands, brain , liver, spleen or kidneys tended to be increased, while thyroid gland, testes and ventral prostate of F1 male rats were decreased at CPM 10 or 100 mg/kg . Histopathologically, necrosis or vacuolation of thyroid follicular epithelial cells and adrenal cortical cells were observed at all doses of CPM. Serum levels of estradiol, testosterone, T4 and T3 were significantly lower while TSH and cholesterol were higher in both F1 female and male rats treated with CPM though dose-responsiveness was not clear in F1 females. Decreased sperm were counted in F1 rats at CPM 100 mg/kg . As a whole, LOAEL and NOAEL was evaluated as 10 and 1 mg/kg bw, respectively, based on decreased estradiol and T4 and increased TSH in serum of F1 male rats , and when considering histopathological alteration of adrenal and thyroid glands, LOAEL assumed to be lower than 1 mg/kg bw. This study elucidates that CPM exhibit weak					
6						

Figure 6. An abstract with highlighted sifter terms.

There are several aspects of the Abstract sheet that are important to note. First, the sifter terms in the abstract are highlighted. The font colors reflect the colors of the fonts in cells B3, C3, and D3 entered into the Main Sheet. This highlighting makes the reading the abstract easier by drawing attention to sentences that might be of more interest. It is also interesting to note that the counts and highlighting for “rat” also picked up “administr**ation**”. Putting a spaces before or after search terms (e.g., “ rat ”) would eliminate some of these occurrences.

Sifting the results through specifying sifter terms in B3, C3, and D3 can be repeated as many times as the user wishes. Similarly, new PubMed queries can be run, altered, rerun. There are no restrictions on either of these activities other than the 5000 record return limit.

Notes Sheet:

Given the dynamic nature of the sifter, many users find it helpful to be able to make notes on articles that they want to track. There are two ways using the Sifter to take notes: one way is through the Main page, and the other way starts with the Abstract page. To return to our case study, let us say that we have found a set of articles on the Main page that we know we need to read in depth. We can select these articles and then click on the *Take Group Notes* button. A form appears where we can enter information into fields called Tag and Notes. These elements are self-defined. We can also click on *yes*, *no*, or *maybe*. This set of variables is a quick way to associate articles with a note. Notice that these choices each come with a color (yes-green, no-red, and maybe-yellow). Entering any of these fields is optional. (Figures 7 and 8.) When we click on the *OK* button, each article selected will be inserted into the Notes page with the corresponding information. (Figure 9)

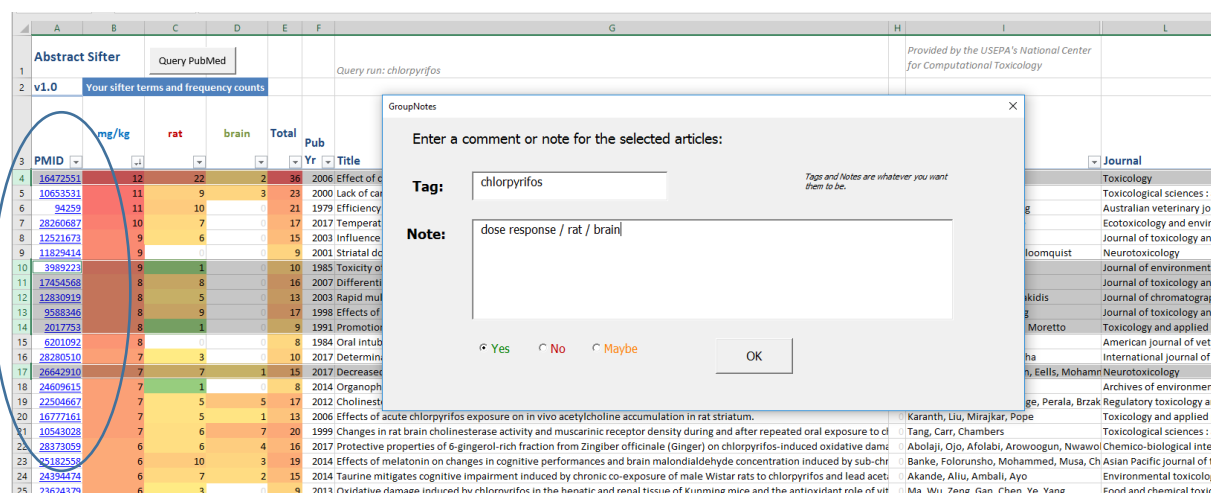


Figure 7. Taking group notes.

Abstract with highlights

Article: 22504667

Title: Cholinesterase inhibition and toxicokinetics in immature and adult rats after acute or repeated exposures to chlorpyrifos or chlorpyrifos-oxon.

Author: Marty, 2012, Passage, Bartels,

Take Notes

Enter a comment or note:

Tag: chlorpyrifos

Note: Acute and repeated dose / rat / cholinesterase inhibition

Yes No Maybe OK

Tags and Notes are whatever you want them to be.

Figure 8. Taking group notes - another example.

PMID	Tag	Note	PubYr	Title	Authors	Journal
22504667	chlorpyrifos	Acute and repeated dose / rat	2012	Cholinesterase inhibition and toxicokinetics in immature and adult rats after acute or repeat	Marty, Andrus, Bell, Passage, Perala, Brzak,	Regulatory toxicology
2017753	chlorpyrifos	dose response / rat / brain	1991	Promotion of organophosphate-induced delayed polyneuropathy by phenylmethanesulfonyl	Lotti, Carolodi, Capodicasa, Moretto	Toxicology and appl
9588346	chlorpyrifos	dose response / rat / brain	1998	Effects of the pesticides carbofuran, chlorpyrifos, dimethoate, lindane, triallate, trifluralin,	2 Rawlings, Cook, Waldbillig	Journal of toxicology
12830919	chlorpyrifos	dose response / rat / brain	2003	Rapid multi-residue method for the determination of azinphos methyl, bromopropylate, chl	Liapis, Aplada-Sarlis, Kyriakidis	Journal of chromatography
17454568	chlorpyrifos	dose response / rat / brain	2007	Differential sensitivity to anticholinesterase insecticides in the juvenile rat: effects on therm	Mack, Gordon	Journal of toxicology
3989223	chlorpyrifos	dose response / rat / brain	1985	Toxicity of organophosphorus esters to laying hens after oral and dermal administration.	Francis, Metcalf, Hansen	Journal of environmental
26642910	chlorpyrifos	dose response / rat / brain	2017	Decreased anxiety in juvenile rats following exposure to low levels of chlorpyrifos during de	Carr, Armstrong, Buchanan, Eells, Mohamm	Neurotoxicology
16472551	chlorpyrifos	dose response / rat / brain	2006	Effect of chlorpyrifos-methyl on steroid and thyroid hormones in rat F0- and F1-generations.	Jeong, Kim, Kang, Ku, Cho	Toxicology

Figure 9. The Notes page. Remember to save your workbook.

The second option for note taking starts with the Abstract Sheet. The “Add Note” button in the top row allows notes to be inserted into the Notes Sheet using the same form used to add Group Notes described above.

The note-taking can be used to help keep track of which citations have been read and evaluated and which have not. By clicking on the *Highlight Noted* button on the Main page or on the Notes page, the color of each noted PubMed ID will be modified as shown in Figure 10.

The user can make changes to the notes sheet by editing, adding or deleting rows below row 2.

Abstract Sifter		Query PubMed		Query run: chlorpyrifos		Provided by the USEPA's National Center for Computational Toxicology	
v1.0		Your sifter terms and frequency counts					
	mg/kg	rat	brain	Total	Pub	Take Group Notes	Highlight Noted
PMID				Yr	Title	Review	Authors
16472551	12	22	2	36	2006 Effect of chlorpyrifos-methyl on steroid and thyroid hormones in rat F0- and F1-generations.		Jeong, Kim, Kang, Ku, Cho
3989223	9	1	0	10	1985 Toxicity of organophosphorus esters to laying hens after oral and dermal administration.		Francis, Metcalf, Hansen
17454568	8	8	0	16	2007 Differential sensitivity to anticholinesterase insecticides in the juvenile rat: effects on thermoregulation.		Clark, Gordon
12830919	8	5	0	13	2003 Rapid multi-residue method for the determination of azinphos methyl, bromopropylate, chlorpyrifos, dimethoate, parathion, and diazinon in rat urine.		Aplada-Sarlis, Kyriakidis, Cook, Waldbillig
9588346	8	9	0	17	1998 Effects of the pesticides carbofuran, chlorpyrifos, dimethoate, lindane, triallate, trifluralin, 2,4-D, and pentachlorophenol on the development of the rat.		Lotti, Maroldi, Capodicasa, Mc
2017753	8	1	0	9	1991 Promotion of organophosphate-induced delayed polyneuropathy by phenylmethanesulfonyl fluoride.		Carr, Armstrong, Buchanan, E
26642910	7	7	1	15	2017 Decreased anxiety in juvenile rats following exposure to low levels of chlorpyrifos during development.		Yano, Young, Mattsson
10653531	11	9	3	23	2000 Lack of carcinogenicity of chlorpyrifos insecticide in a high-dose, 2-year dietary toxicity study in Fischer 344 rats.		Hart, Cavey, Moore, Strong
94259	11	10	0	21	1979 Efficiency and safety of methidathion applied as a pour-on systemic insecticide for control of cattle lice.		Jegade, Owojori, Römcke
2826087	10	7	0	17	2017 Temperature influences the toxicity of deltamethrin, chlorpyrifos and dimethoate to the predatory mite Hypoaspis aculeator.		Gordon, Mack
12521673	9	6	0	15	2003 Influence of gender on thermoregulation and cholinesterase inhibition in the long-evans rat exposed to diazinon.		Karen, Li, Harp, Gillette, Blooi
11829414	9	0	0	9	2001 Striatal dopaminergic pathways as a target for the insecticides permethrin and chlorpyrifos.		Yeary
6201092	8	0	0	8	1984 Oral Intubation of dogs with combinations of fertilizer, herbicide, and insecticide chemicals commonly used on lawns.		Mahugija, Khamis, Lugwisha
28280510	7	3	0	10	2017 Determination of Levels of Organochlorine, Organophosphorus, and Pyrethroid Pesticide Residues in Vegetables from Markets and a Supermarket around Kwan Phayao Lake.		Sapbamrer, Hongsiabong
24609615	7	1	0	8	2014 Organophosphorus pesticide residues in vegetables from farms, markets, and a supermarket around Kwan Phayao Lake.		Marty, Andrus, Bell, Passage,
22504667	7	5	5	17	2012 Cholinesterase inhibition and toxicokinetics in immature and adult rats after acute or repeated exposures to chlorpyrifos.		Karanth, Liu, Mirajkar, Pope
16777161	7	5	1	13	2006 Effects of acute chlorpyrifos exposure on in vivo acetylcholine accumulation in rat striatum.		Tang, Carr, Chambers
10543028	7	6	7	20	1999 Changes in rat brain cholinesterase activity and muscarinic receptor density during and after repeated oral exposure to diazinon.		

Figure 10. After clicking on Highlight Notes and then sorting by color

Log sheet

The Log sheet keeps track of the queries you have run. The Abstract Sifter routines insert a row into the sheet every time you complete a query. These queries can be viewed and rerun. To rerun a query, simply double-click on it. (Figure 11.) Delete any or all rows after Row 2 if you want to clear old entries.

Log of activity		Log of activity		Note: Feel free to delete rows, but not	
Date	Returned	Query Used (double-click on query to rerun)			
7/6/2017 16:46	80	(pfoa OR pfos) AND carolina			
7/6/2017 16:45	24	atrazine AND soybeans			
7/6/2017 16:45	231	oecd AND skin			
7/6/2017 16:25	4187	chlorpyrifos			

Figure 11. View of the Log sheet

Landscape sheet

The Landscape sheet provides an overview of the literature to the user for a set of entities, for example, a list of chemicals or genes. Figure 12 shows an example of a Landscape sheet built by a researcher interested in the toxicity of a particular set of chemicals. Let's take a look at that first. Queries designed to find the chemicals of interest are entered into Column C and in this case, a short version of the chemical name is in Column A. The queries in Row 3 are typical ones used in searching for articles about different kinds of chemical toxicity. We will refer to these queries as subject matter queries.

The premise behind the design of the Landscape sheet is very simple: PubMed queries will be built by taking the values in Column C (in this example chemical names and corresponding CAS numbers) and appending this query text to the subject matter query text in Row 3 with an " AND " in between the two query parts.

B		C		E	F	G	H	I	J	K
1	Landscape View	Feel free to delete columns after Column D and rows after Row 4.								
2		Update Article Counts	View / hide queries	Heat Map by column	Heat Map by row					
3							(dna/drug effects OR DNA Damage OR chromosome aberrations OR	(reproduction AND (toxicity OR abnormal OR adverse effects))	ment OR embryo OR morphogenesis OR congenital abnormal	* OR neurolog* OR behavior OR intelligence OR cognition OR brain
4	Preferred Name		Chemical / entity query	Cancer	Chronic	Dermatitis	Genetox	Repro Tox	DevTox	Neuro Tox
5	Tetrahydrocurcumin	Tetrahydrocurcumin OR 36062-04-1		42	1	5	9	0	22	15
6	(6)-Gingerol	(6)-Gingerol OR 23513-14-6		116	1	13	110	3	52	31
7	Curcumin	Curcumin OR 458-37-7		4115	93	424	627	30	1738	1547
8	Doxorubicin	Doxorubicin OR 23214-92-8		51542	584	9368	16654	275	5890	4031
9	Hydroquinone	Hydroquinone OR 123-31-9		518	49	515	1808	22	449	291
10	Coumarin	Coumarin OR 91-64-5		1066	37	307	255	105	999	781
11	PFOA	Perfluorooctanoic acid OR PFOA OR 335-67-1		106	40	14	63	167	386	181

Figure 12. Example of Landscape sheet use

To illustrate, we will double-click on the cell with the arrow pointer in Figure 13. When we double-click on this cell this tells the Abstract Sifter to take the query text in Column C about Perfluorooctanoic Acid and append it to (chronic AND toxicity). Figure 14 shows the constructed query. We can then click on *Submit* and the query gets sent to PubMed and we can then see the results on the Main page. The

number of articles retrieved from PubMed is 40. That count is placed in the corresponding Landscape cell that we just clicked on.

<i>Queries:</i>		neoplasms or cancer	chronic AND toxicity
Chemical / entity query		Cancer	Chronic
Tetrahydrocurcumin OR 36062-04-1		42	1
(6)-Gingerol OR 23513-14-6		116	1
Curcumin OR 458-37-7		4115	93
Doxorubicin OR 23214-92-8		51542	584
Hydroquinone OR 123-31-9		518	49
Coumarin OR 91-64-5		1066	37
Perfluorooctanoic acid OR PFOA OR 335-67-1		106	40

Figure 13. Double-click on article count cells

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Modify the PubMed query and click on Submit.

Submit

(Perfluorooctanoic acid[nm] OR PFOA OR 335-67-1 OR 3825-26-1) AND ((chronic AND toxicity))

When this form goes away, your query is done.

Figure 14. Constructed query

Now let's add to the Landscape sheet. Figure 15 shows how we added a new chemical to the list:

atrazine. To find out the article counts for atrazine, select empty cells on the same row as atrazine, then click on *Update Article Counts* button. Excel will build each query from the atrazine part and the subject

matter part and send each query to PubMed to find out how many citations satisfy the query. The article counts are placed in the corresponding cells. To run the query and retrieve the results, just double-click on any of the article count cells.

1	Landscape View																	
2			Update Article Counts	Hide queries	View / edit queries	Heat Map by column	Heat Map by row											
3													(dna/drug effects OR DNA Damage OR chromosome aberrations OR genotoxicity OR micronucleus OR DNA Repair OR mutagenicity)	(neoplasms OR cancer)	(chronic AND toxicity)	(reproduction AND (toxicity OR adverse effects))	(development OR embryonic OR morphogenesis OR congenital abnormalities OR birth defects)	neurotoxic OR neurological OR neurotoxicity OR behavior OR intelligence OR cognition OR Nervous System OR sense organs OR autism or parkinsons or huntington or brain OR neurons OR
4	Preferred Name	Chemical / entity query	Cancer	Chronic	Genetox	Reproduction	Development	NeuroTox										
5	Tetrahydrocurcumin	Tetrahydrocurcumin OR 36062-04-1	40	1	9	0	22	20										
6	(6)-Gingerol	(6)-Gingerol OR 23513-14-6 OR gingerol	142	1	119	3	68	73										
7	Curcumin	Curcumin OR 458-37-7	3929	88	604	27	1651	1709										
8	Doxorubicin	Doxorubicin OR 23214-92-8	50581	572	16446	274	5710	5012										
9	Hydroquinone	Hydroquinone OR 123-31-9	506	47	1788	21	437	429										
10	Coumarin	Coumarin OR 91-64-5	1017	37	247	105	961	896										
11	PFOA	Perfluorooctanoic acid[nm] OR PFOA	98	37	56	154	347	198										
12	Atrazine	atrazine																

Figure 15. Adding rows to the Landscape sheet

Coumarin OR 91-64-5	1017	37	247	105	961	896
Perfluorooctanoic acid[nm] OR PFOA OR 335-67-1 OR 3825-26-1	98	37	56	154	347	198
atrazine	114	81	175	160	786	401

Figure 16. After clicking on Update Article Counts

New subject matter queries can be entered as well. The query part goes into Row 3 and a heading (of your choice) goes into Row 4. See the example below where the PubMed query part: skin OR dermatitis is entered with the heading skin. Next highlight the cells underneath and click on the *Update Article Counts* button. The counts of articles satisfying the queries are placed in the cells. What's happening behind the scenes? For each cell, a query is being built by the Abstract Sifter and sent to PubMed to retrieve a record count. That record count is then inserted into the corresponding cell. (Figure 17.)

Keep in mind that our examples revolve around chemicals, but that does not mean anyone is limited to chemicals. The entries in Column C and in Row 3 can be whatever you the end-user want them to be: genes, proteins, diseases, authors ...



Figure 17. Steps for retrieving counts

Making things look good

The Landscape sheet has three buttons that make formatting easy (Figure 18). You can choose to hide the query row or show it. The heat map buttons will quickly apply heat map coloring to the cells with article counts either by column or by row. Try them out!

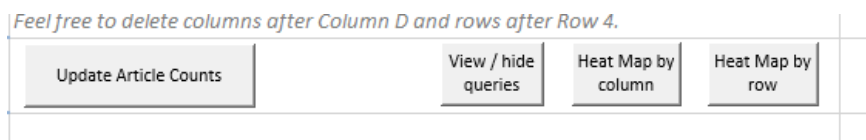


Figure 18. Buttons on the Landscape page include formatting actions

SampleQueries Sheet

The SampleQueries sheet contains a number of sample subject matter queries that the end user can use as a starting point for building a Landscape view of a set of entities. Let's see how. First, we will clean off the old subject matter queries by deleting columns E-J on the Landscape sheet. Next, on the SampleQueries sheet we will select rows with queries of interest then we click on the button *Send Queries to Landscape* (Figure 19). A form will ask for confirmation, to which we reply *OK*.

A B C		
1	Sample Queries	Note: these are starting points ... please expand and customize
2		
3	Category	Heading Query (double-click to see how the query looks to PubMed)
4	Ecological	HAB "harmful algal bloom" OR eutrophication OR (marine toxins AND algae)
5	Epidemiology	Epi epidemiology
6	Exposure	Dust exposure environmental exposure AND dust
7	Exposure	Food exposure environmental exposure AND food
8	Exposure	Water exposure Environmental Exposure AND (water OR groundwater OR drinking water)
9	Mechanism	Oxidative stress "oxidative stress" OR "free radicals" OR "reactive oxygen species" OR peroxides
10	Methods	Analytical chemistry "Chemistry Techniques, Analytical" OR analytical chemistry
11	Methods	Statistical Statistics as Topic[mh] OR statistics OR statistical
12	Methods	In vitro In Vitro Techniques[mh] OR cell culture or "in vitro"
13	Mixtures	Mixtures (Drug synergism[mh] OR cocarcinogenesis OR pesticide synergists[mh] OR mixture[tiab] OR mixtures[tiab] OR
14	Pharmacology/medicine	Clinical trials ((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trial[Publication Type])
15	Pharmacology/medicine	Clinical trials in children ((children OR child OR infants) AND human) AND ((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical
16	Toxicity	Genetox (dna/drug effects OR DNA Damage OR chromosome aberrations OR genotoxicity OR micronucleus OR DNA Rep
17	Toxicity	Cancer neoplasms or cancer
18	Toxicity	Skin sensitization ("allergic" AND "contact" AND dermatitis) OR Dermatitis, Allergic Contact[mh]
19	Toxicity	ReproTox (reproduction AND (toxicity OR abnormal OR adverse effects))
20	Use	Pharmaceutical ("therapeutic use" OR "therapeutic use"[subheading]) OR pharmacologic actions[mh]
21	Use	Pesticide pesticide OR insecticide OR rodenticide OR fungicide
22	Use	Cosmetics cosmetics OR beauty
23	Use	Explosive Agents Explosive Agents OR explosive OR explosives
24	Use	Food food OR diet OR beverage OR nutrition
25	Use	Surface-acting Antifoaming OR Anti-foaming OR detergent OR detergents OR soap OR detergent
26	Use	Dye/coloring dye OR "coloring agent" OR pigment OR pigments
27	Use	Fertilizer fertilizer OR fertilize
28	Use	Solvents solvents OR solvent
29		

Figure 19. Selecting rows with queries of interest

Our Landscape sheet then looks like Figure 20.

	B	C	E	F	G
1	Landscape View	Feel free to delete columns after Column D and rows after Row 4.			
2		Update Article Counts	View / hide queries	Heat Map by column	Heat Map by row
3			"algal bloom" OR eutrophication OR algae)	environmental exposure AND dust	Title/Abstract] AND trial[Title /Abstract]) OR clinical trial[Publication
4	Preferred Name	Chemical / entity query	Algae	Dust exposure	Clinical trials
5	Tetrahydrocurcumin	Tetrahydrocurcumin OR 36062-04-1			
6	(6)-Gingerol	(6)-Gingerol OR 23513-14-6			
7	Curcumin	Curcumin OR 458-37-7			
8	Doxorubicin	Doxorubicin OR 23214-92-8			
9	Hydroquinone	Hydroquinone OR 123-31-9			
10	Coumarin	Coumarin OR 91-64-5			
11	PFOA	Perfluorooctanoic acid OR PFOA OR 335-67-1			
12		Atrazine			

Figure 20. New queries on Landscape sheet

Next, we select the article count area and then click on *Update Article Counts*.

Algae	Dust exposure	Clinical trials

Figure 21. Selecting the cells for article counts

Once the article counts are populated, we click on Heat Map by Row and then on Hide queries. Our resulting Landscape view looks like Figure 22. To run the query and retrieve the results, just double-click on any of the article count cells.

	B	C	E	F	G
1	Landscape View	<i>Feel free to delete columns after Column D and rows after Row 4.</i>			
2		Update Article Counts	View / hide queries	Heat Map by column	Heat Map by row
3					
4	Preferred Name	Chemical / entity query	Algae	Dust exposure	Clinical trials
5	Tetrahydrocurcumin	Tetrahydrocurcumin OR 36062-04-1	0	0	3
6	(6)-Gingerol	(6)-Gingerol OR 23513-14-6	0	0	5
7	Curcumin	Curcumin OR 458-37-7	4	0	258
8	Doxorubicin	Doxorubicin OR 23214-92-8	6	1	9206
9	Hydroquinone	Hydroquinone OR 123-31-9	12	1	130
10	Coumarin	Coumarin OR 91-64-5	5	1	162
11	PFOA	Perfluorooctanoic acid OR PFOA OR 335-67-1	7	52	5
12		Atrazine	90	14	3

Figure 22. New Landscape view

Exporting to other applications from the Notes sheet

The Abstract Sifter allows the user to export articles from the Notes sheet to outside applications. On the Notes sheet there are two buttons labeled *Get References* and *For HAWC*. By clicking on the *Get References* button, the form in Figure 24 appears. The box on the left contains the PMIDs for each of the rows in the Notes sheet. Clicking on Send to PubMed will send the PMIDs to PubMed for retrieval. In PubMed, the citation records will be displayed. At the top of the screen, the user can click on *Send to* (Figure 25). This starts a dialog leading the user through the steps of downloading the citations to a reference management software. (Figure 26). The user can download all the PubMed IDs on the Notes page, or a selected set of rows through the All or Selected radio buttons shown in Figure 24.

<div> <div>Get references</div> <div>For HAWC</div> </div>
--

Figure 23. Buttons on Notes sheet that allow export

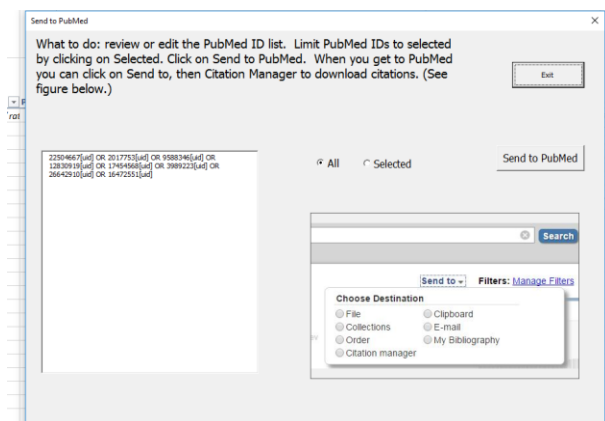


Figure 24. Form that appears after clicking on Get references button

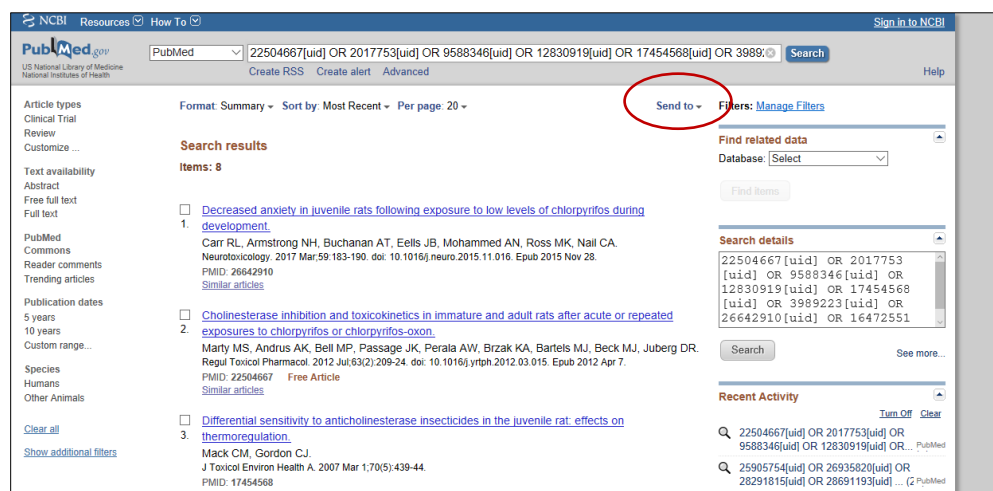


Figure 25. In PubMed, click on Send to

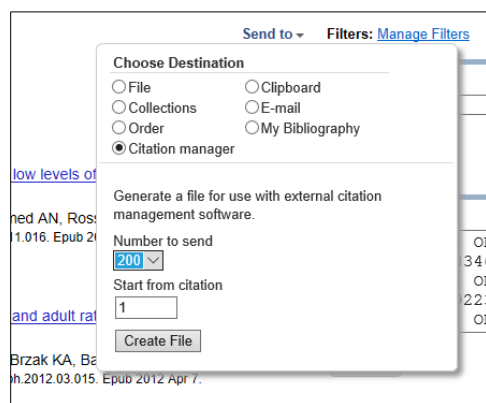


Figure 26. Dialog box for exporting to citation manager

When the user clicks on the Create File button, a file is created and downloaded in nbib format and can be imported into most common reference manager software.

Similarly, the PMIDs can be formatted for input into HAWC (Health Assessment Workspace Collaborative) (Figure 27). HAWC tutorials are available at <https://hawcproject.org/about/> . The import process is demonstrated there, so it will not be covered here.

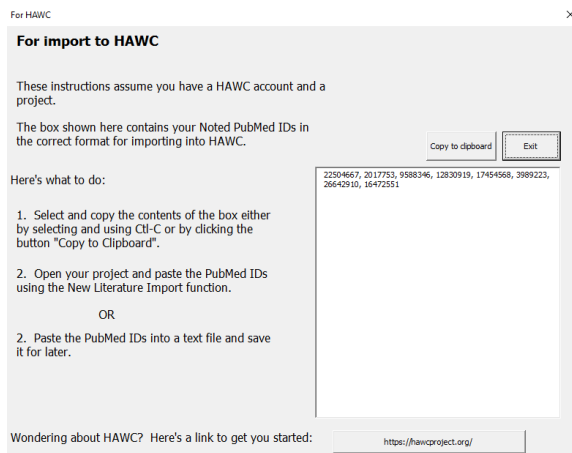


Figure 27. Form to send PMIDs to HAWC

Helpful Tips and Guidelines

Tip 1 – checking quality of results

The Landscape sheet is a great way to explore a set of chemicals, but some chemical names are long, complex, and a challenge to PubMed. If you get unexpected results from a chemical query, it's a good idea to check it in PubMed. You can take any query generated by the Abstract Sifter and copy and paste it into PubMed using Ctl-C to copy and Ctl-V to paste. For example, the query in the box shown in Figure 28 is selected and copied (with Ctl-C). Then in PubMed the query is pasted into the query line at the top as shown in Figure 29. After we click on search we see that PubMed brings back 51 records. On the right side of the page is a box entitled *Search Details*. Click on the *See More ...* link to expand this box. (Figure 30) Figure 31 shows the information provided by PubMed about how it expands the query. If you need to learn more about PubMed queries, click on *Help* on the PubMed home page.

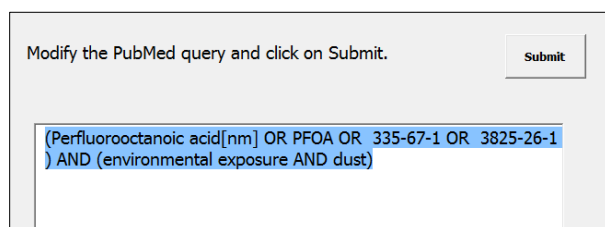


Figure 28. Select and Ctl-C to copy

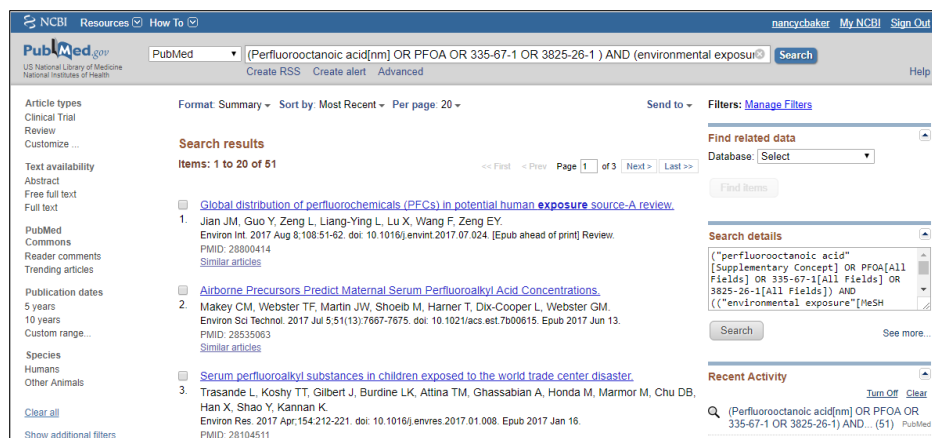


Figure 29. Ctl-V to paste in PubMed then search

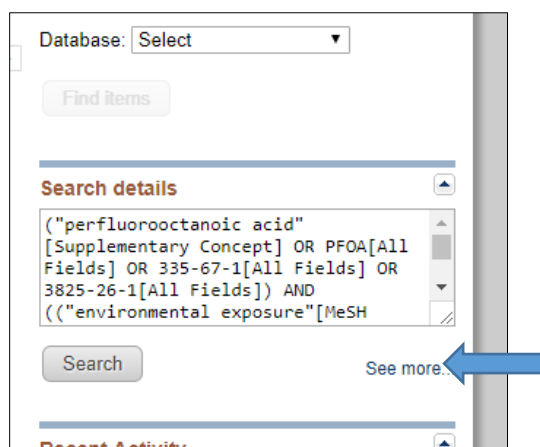


Figure 30. See what PubMed does to expand your search

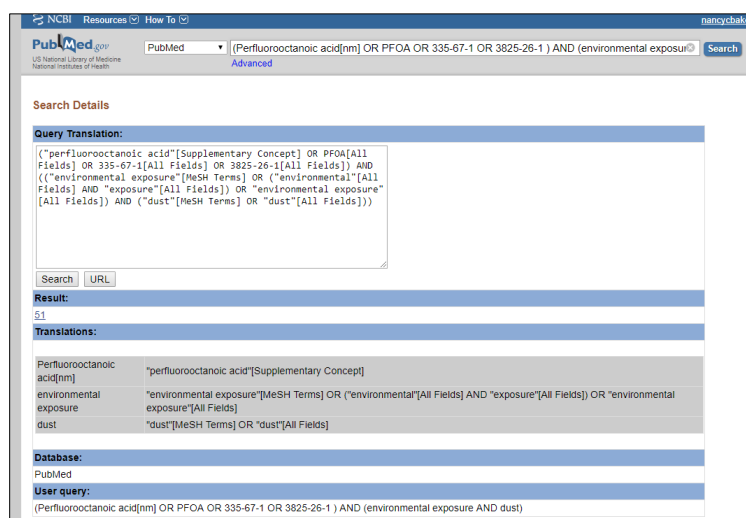


Figure 31. PubMed query breakdown and expansion

Tip 2 – Sifting the chemical literature

It can be very helpful in chemical research to include the chemical name in the sifting process. This is because a chemical can be mentioned in an abstract even in cases where the article is not really about the chemical and will be retrieved in the PubMed query (depending on how the query is worded). Counting the occurrences of the chemical name in the abstract through the sifting process can help the user discriminate between articles mentioning a chemical or those that are actually about the chemical.

Tip 3 – cleanup and customization

The Abstract Sifter can be cleaned up by deleting rows and columns from previous work, but the Abstract Sifter programming requires certain columns and rows to be in certain places. To learn how to clean up your sifter without disrupting the behind-the-scenes coding, consult the table below.

Sheet name	Sheet Function
Main	Do not add columns. Rows will be added and deleted by the Sifter.
Abstract	Do not add or delete rows or columns. The Sifter software updates this sheet.
Notes	Delete any unwanted rows after Row 2. Do not add or delete columns.
Log	Delete any unwanted rows after Row 2. Do not add or delete columns.
SampleQueries	Delete unwanted rows after Row 3. Modify and add rows as desired, following the pattern of current rows. (That is, keep the heading in column B and the query text in column C.) <i>Hint: use this sheet to keep queries important to your organization.</i>
Landscape	Delete or modify rows after Row 4 and columns after Column D.

Keep in mind that the Abstract Sifter is an Excel file. You can rename it, mail it, and of course, if you want to keep your Log, Notes, and Landscape entries, you should save it. The SampleQueries sheet

provides an opportunity for you and your organization to start collecting and organizing queries that you have found useful.

Tip 4 – Connections to the EPA Chemistry Dashboard

The Environmental Protection Agency's Chemistry Dashboard is a great place to find chemical information to enhance your chemical search queries with synonyms and CAS numbers. Future releases of the Dashboard will offer opportunities to download a list of chemicals formatted for easy insertion into the Landscape sheet. You'll find the Chemistry Dashboard here:
<https://comptox.epa.gov/dashboard>.

The EPA Chemical Dashboard also contains its own (slightly different) version of the Abstract Sifter. It works on the same basic premise as the Excel version, but has some interesting differences. To see it, start with a chemical search. Let's look at the chemical fipronil by entering the name in the search box and clicking on the search icon (magnifying glass) (Figure 32).

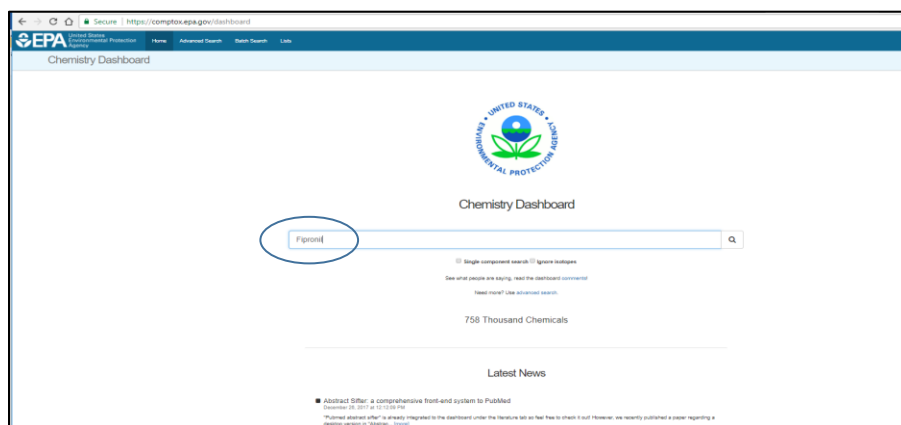


Figure 32. Searching for fipronil on the EPA's Chemistry Dashboard entry form

The main page for fipronil is displayed with the structure diagram and a selection of tabs below that lead to other information about the chemical. Click on the Literature tab as shown in Figure 33.

Figure 33. Select the Literature tab then on PubMed Abstract Sifter (see below).

Figure 34. How to select prepared queries.

Select PubMed Abstract Sifter on the left set of buttons. The Dashboard helps you to build queries for this chemical. The chemical identifier part of the query is prepopulated on the right with name and CAS number. The subject matter part of the query is determined by selecting a topic area in the pull-down box in the center of the form. The user has several pre-composed queries to choose from. When one of them is chosen, the query is modified by appending the subject matter text. Figure 35 shows that when Metabolism/PK/PD is chosen, the text (metabolism OR metabolite OR tissue distribution OR pharmacokinetics OR pharmacodynamics) is appended to the chemical identifiers. The query can be modified manually as well. When ready, the user clicks on Retrieve Articles.

1) Select PubMed starting point query then 2) click on Retrieve.

Metabolism/PK/PD Retrieve Articles 322 of 322 articles loaded...

Optionally, edit the query before retrieving.
 ("120068-37-3" OR "Fipronil" OR "Fipronil") AND (metabolism OR metabolite OR tissue distribution OR pharmacokinetics OR pharmacodynamics)

To find articles quickly, enter terms to sift abstracts.

Tissue: kinetic: Download / Send to... Download Sifter for Excel

Here's the query that gets built:

You can modify this query if you want.

Sifter terms are entered here.

Occurrence counts are here. Click on a row to see its abstract here.

Issue	kinetic	Total	PMID	Year	Title	Authors	Journal	Rev
5	0	5	24016525	2013	Disposition of fipronil in rats.	Cravedi, Delous; Zalko, Viguie, Debrauwer	Chemosphere	
0	4	4	26960908	2016	DBS-platform for biomonitoring and toxicokinetics of toxicants: proof of concept...	Raju, Taneja, Rashid, Sonkar, Wahajuddin, Singh	Scientific reports	
0	4	4	24703069	2014	Pharmacokinetics and metabolism of epinomecin in cats when administered I...	Kvaternick, Kellermann, Knaus, Rehbein, Rosentel	Veterinary parasitology	
2	1	3	27289396	2016	Fipronil and two of its transformation products in water and European eel from I...	Michel, Freese, Brinkmann, Pohlmann, Holert, Kam...	The Science of the total environment	
3	0	3			bioconcentration in Arme...	Van Meter, Glinksi, Henderson, Purucker	Environmental toxicology and chemistry	
3	0	3	25307460	2014	ation enzymes in juve...	Wu, Gao, Guo, Zhang, Zhang, Ma	Pesticide biochemistry and physiology	
3	0	3	22502899	2012	onil enantiomers in Tubi...	Liu, Wang, Lu, Zhou, Qiao, Zhou	Journal of hazardous materials	
3	0	3	22078114	2011	on the non-target orga...	Classen, Loro, Cattaneo, Moraes, López, de Avila, Z...	Ecotoxicology and environmental safety	
3	0	3	21227481	2011	anus: reduced feeding	Khulagodaga, Isanhart, Bultner, Hooper, Astheimer	Chemosphere	
0	2	2	26867652	2017	Biomimetalisation of fipronil and its m...	Gajendran, Abraham	3 Biotech	
0	2	2	27722395	2016	Metabolization and degradation kine...	Wolffand, LeFevre, Luthy	Environmental science: Processes & impacts	

Fipronil and two of its transformation products in water and European eel from the river Elbe.

Fipronil is an insecticide which, based on its mode of action, is intended to be predominantly toxic towards insects. Fipronil bioaccumulates and some of its transformation products were reported to be similar or even more stable in the environment and to show an enhanced toxicity against non-target organisms compared to the parent compound. The current study investigated the occurrence of Fipronil and two of its transformation products, Fipronil-desulfinyl and Fipronil-sulfone, in water as well as muscle and liver samples of eels from the river Elbe (Germany). In water samples total concentrations of FIP, FIP-d and FIP-s ranged between 0.5-1.5 ng/L (-1) with FIP being the main component in all water samples followed by FIP-s and FIP-d. In contrast, FIP-s was the main component in muscle and liver samples with concentrations of 4.05±3.73 ng/g (-1) ww and 19.91±9.96 ng/g (-1) ww, respectively. Using a physiologically based toxicokinetic (PBTK) model for moderately hydrophobic organic chemicals, the different distributions of FIP, FIP-d and FIP-s in water and related samples could be attributed to metabolic processes of eels. The measured concentrations in water of all analytes and their fractional distribution did not reflect the assumed seasonal application of FIP and it seems that the water was constantly contaminated with FIP, FIP-d and FIP-s.

Figure 35. Sifting on the EPA Chemistry Dashboard's PubMed Abstract Sifter.

After the user clicks on Retrieve Articles, the article information is retrieved from PubMed and inserted into the results table. The articles can be sifted by entering terms into the boxes shown. In the example in Figure 35, the user has entered tissue into one box and kinetic into the other. The occurrences of these terms are counted for each PubMed citation and displayed. The table can be sorted on these values. Clicking on a row tells the Dashboard Sifter to display the title and abstract below the table with the sifter terms highlighted.

Check back periodically with the EPA's Chemistry Dashboard to learn about enhancements to PubMed Abstract Sifter.

Contact:

Contact Nancy Baker at baker.nancy@epa.gov with issues, ideas, and feedback.