Toxics Use Reduction Institute

Policy Analysis: Recommendation on 14 CERCLA chemicals with initial 'no action' recommendations

Statutory amendments to the Toxics Use Reduction Act (TURA) in 2006 required the Science Advisory Board (SAB) and TURI to review the existing chemicals on the TURA Toxic or Hazardous Substance List originating from the CERCLA chemical list and make a recommendation to the Council as to which chemicals should be retained. The Council has until August 1, 2009, to make decisions taking these recommendations into account. The goal of this process is to help facilities focus their efforts more closely on substances that present greater hazards to human health and the environment in Massachusetts.

The CERCLA chemicals in this document are chemicals which:

- Are currently reported by TURA filers, and
- The SAB initially recommended for 'no action'

These substances were initially recommended for 'no action' by the SAB in the bulk review of CERCLA chemcials by the SAB. The Administrative Council asked that the SAB review these chemicals in more depth. This document presents information on all 14 of these substances.

This policy analysis presents the scientific information reviewed by the Science Advisory Board in developing its recommendations. In addition, it summarizes information on the most recent year in which the substance was reported, the number of filers that reported use of the substance in the most recent reporting year, and regulations that apply to these substances at the state, federal, and international levels.

Based on the information presented here, TURI supports the SAB's recommendations to take no action on 11 of the substances and retain 3 of the substances.

1. Summary SAB Recommendations:

Retain:
Aluminum Sulfate
Butyl Acetate
Iso-Butyl Acetate

No Action:
Ammonium Bicarbonate
Ferric Chloride
Ferrous Chloride
Ferric Sulfate
Ferrous Sulfate
Fumaric Acid
Maleic Acid
Adipic Acid
Ammonium chloride
Amyl Acetate
Ammonium Sulfamate

2. Basis for SAB recommendations

Overall Considerations

The discussion below provides an overview of the information considered by the SAB. Points discussed by the SAB for each substance are summarized briefly in Appendix A.

Specific information for each substance is shown in Appendix C. In addition to these data, in many instances individual SAB members brought additional scientific information to the meeting.

In general, if there was any significant concern about a substance on the list, the SAB recommended retaining it. Thus, the substances recommended for no action are those for which the SAB saw no particular basis for retention.

In reviewing the substances, the SAB considered the following data:

- International Agency for Research on Cancer (IARC) rating.
    - The SAB recommended retaining any substance that has an IARC rating (Group 1, 2, or 3)[1]. Thus, of the substances recommended for no action, none has an IARC rating.
- Data from the EPA PBT profiler (persistence in water, soil, sediment, and air; bioconcentration factor; and chronic toxicity in fish).[2]
    - A number of the substances recommended for no action cannot be profiled on the EPA PBT profiler. Of those able to be profiled and recommended for no action, a number have high persistence in air. The SAB considered persistence in air to be less of a concern than persistence in other media. One substance has high persistent in sediment; however, the SAB considered this to be counterbalanced by data indicating low toxicity.
- Neurotoxicity (based on Scorecard's list of neurotoxicants, and other sources in some cases).[3]
    - Of the substances recommended for no action, none are identified as neurotoxicants.
- Developmental/reproductive toxicity (based on California's Proposition 65 list, and other sources in some cases).[4]
    - Of the substances recommended for no action, none is listed as a developmental or reproductive toxicant on California's Proposition 65 list. For one substance (aluminum sulfate), a search of government databases indicated that there is some basis for concern about reproductive or developmental toxicity.

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[1] IARC Group 1: carcinogenic to humans, Group 2: probably or possibly carcinogenic to humans, Group 3: not classifiable - evidence of carcinogenicity is inadequate in humans and inadequate or limited in experimental animals

[2] EPA PBT Profiler, available at http://www.epa.gov/oppt/sf/tools/pbtprofiler.htm.

[3] Scorecard's list of suspected neurotoxicants, and the sources used to compile the list, is available at http://www.scorecard.org/health-effects/ (select the link for neurotoxicity).

[4] The California Proposition 65 List is available at http://www.oehha.org/prop65/prop65_list/Newlist.html. Additional information is drawn from the NIOSH Registry of Toxic Effects of Chemical Substances (RTECS) and the New Jersey Department of Health and Senior Services Hazardous Substances Fact Sheet for di-n-octyl phthalate (http://nj.gov/health/eoh/rtkweb/documents/fs/0787.pdf).

- Mutagenicity (based on the European Union's Consolidated List of Carcinogens, Mutagens, and Reproductive Toxicants [CMR], and other sources in some cases).[5]

    - Of the substances recommended for no action, none appears on the EU CMR list. For one substance (aluminum sulfate), a search of government databases indicated that some studies have found some evidence of mutagenicity.

- Lethal dose or concentration information (LD50 and LC50). In general, the LD50 and LC50 for the substances recommended for no action are relatively high, indicating relatively low toxicity.

- Exposure limits required or recommended by Federal agencies
    - Reference dose and reference concentration (RfD and RfC, from EPA Integrated Risk Information System).[6] The reference dose and reference concentration values for the substances recommended for no action indicate relatively low toxicity. For some substances, these values are not available.
    - NIOSH Recommended Exposure Limit (REL); Threshold Limit Value – Time Weighted Average (TLV-TWA); and Threshold Limit Value – Short Term Exposure Limit (TLV-STEL).[7] For several of the substances, these values indicate moderate toxicity.

- Flash point. For those substances on the list that have a flash point, the values of most are intermediate to high, indicating that flash point is not a major concern for those substances.

- The SAB did not consider specific data points related to sensitization or the potential to cause or exacerbate asthma. However, in response to a recommendation from the Advisory Committee, TURI checked the list of substances recommended for no action against a list of asthmagens compiled by UMass Lowell researchers based on information from the Institute of Medicine, the Association of Occupational and Environmental Clinics, and other sources. TURI also checked a list of substances identified as sensitizers in the EU (EU Risk Phrase 42).[8] None of the substances is listed as either a sensitizer or an asthmagen.

Approach for second review of chemicals

For the SAB's more in depth review of these 14 CERCLA chemicals, the SAB looked to fill data gaps, most commonly in the mutagenicity field. Further data was collected from the **R**egistry of **T**oxic **E**ffects of

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[5] The EU Consolidated CMR List is available at http://www.chemicalspolicy.org/downloads/cmrlist.pdf. Additional information is drawn from the US National Library of Medicine Toxicology Data Network (TOXNET).

[6] EPA Integrated Risk Information System, available at http://www.epa.gov/iris/.

[7] REL, TLV-TWA, and TLV-STEL are drawn from the National Institutes of Occupational Safety and Health (NIOSH) Pocket Guide to Chemical Hazards, available at http://www.cdc.gov/niosh/npg/.

[8] EU risk phrase information is available at http://ecb.jrc.it/classification-labelling/search-classlab/ (choose "search Annex 1" and "Risk phrase 42"); viewed March 2008. Information on asthma is drawn from the following sources: (a) Association of Occupational and Environmental Clinics, "Explanatory Protocol: Criteria for Designating Substances as Occupational Asthmagens on the AOEC List of Exposure Codes." Revised April 2005. Accessed 11-2-07 at: http://www.aoec.org/tools.htm.. (b) Janssen S, Solomon G, Schettler T., "Chemical Contaminants and Human Disease: A Summary of Evidence," 2004. Accessed 11-2-07 at: http://www.protectingourhealth.org/corethemes/links/2004-0203spreadsheet.htm. (c) Institute of Medicine (IOM), Committee on the Assessment of Asthma and Indoor Air, Division of Health Promotion and Disease Prevention, 2000, *Clearing the Air: Asthma and Indoor Air Exposures*. Washington, D.C., National Academy Press, http://books.nap.edu/books/0309064961/html.; (d) Malo J-L, Chan-Yeung M. Appendix: Agents Causing Occupational Asthma with Key References. In: Bernstein LI, Chan-Yeung M, Malo J-L, Bernstein DI (eds). *Asthma in the Workplace.* 3rd Ed. New York: Taylor & Francis, 2006.

Chemical **S**ubstances (RTECS), **H**azardous **S**ubstances **D**ata **B**ank (HSDB), **C**hemical **C**arcinogenesis **R**esearch **I**nformation **S**ystem (CCRIS), and **I**nternational **U**niform **C**hemica**L** **I**nformation **D**atabase (IUCLID).

Also, since many of the chemicals were identified as GRAS (Generally Recognized as Safe), U.S. Food and Drug Administration GRAS data was researched (See Table 2 in Appendix D). As a part of the investigation process, the SAB considered the criteria for designation of substances as GRAS.[9]

"Generally recognized as safe (GRAS) is an American Food and Drug Administration (FDA) designation that a chemical or substance added to food is considered safe by experts, and so is exempted from the usual Federal Food, Drug, and Cosmetic Act (FFDCA) food additive tolerance requirements.

GRAS exemptions are granted for substances that are generally recognized, among experts qualified by scientific training and experience to evaluate their safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or through experience based on common use in food) to be safe under the conditions of their intended use."[10]

Chemical Specific Considerations

Aluminum Sulfate

Mutagenicity and reproductive effects were the primary data points that were further pursued for aluminum sulfate. Positive mutagenicity data and reproductive effects were noted, specifically chromatid breaks, cell aberrations, dose-based abnormalities. There were also concerns regarding caustic potential in the workplace. Due to this additional data, the Board voted unanimously to retain this substance.

Butyl Acetate and iso Butyl Acetate

In addition to the initial data for butyl and isobutyl acetate the following data were reviewed:

	Butyl acetate	**Iso-butyl acetate**
LD_{50}	10,768 mg/kg	13,400 mg/kg
Vapor Pressure	11.5-18.9 mmHg	17.8 mmHg
Flashpoint	73ºF	64ºF
Persistence	Air = high	Air = high
IDLH	1700 ppm	1300 ppm
Reactivity	+	n/a
Mutagen	59 negative tests	1 negative test
Neurotoxicant	Short term +	no evidence
PEL	150 ppm	150 ppm

No mutagenic or developmental effects were seen (only weight decreases for subjects exposed). It was also noted that the oral LD50's were fairly high for both, and that butyl acetate was listed as a GRAS substance. Recovery from acute neurological effects was rapid and began with removal from chamber; the minimum effect concentration was high (8000 ppm)**.** There was less information available on iso-butyl acetate. Information states that it is not a genotoxicant, not persistent in the environment and not likely to bioaccumulate. The Board reviewed structural properties by and discussed expected toxicity based on structure-activity relationships.

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[9] http://www.cfsan.fda.gov/~lrd/cfr17030.html
[10] http://en.wikipedia.org/wiki/Generally_recognized_as_safe

The IDLHs are based on lower explosive limits.

Vote on motion to retain and consider for Lower Hazard substance 3 in favor, 2 abstaining
The information was not compelling to retain or delist the substances. The issues supporting retention were: Neutoxicity (animal studies – acute) and the uncertainty regarding how this translates to a long term worker health situation. Short term effects are reversible, the long terms effects are yet unknown. Both are less well understood for iso-butyl. Flash point – flammability is of moderate concern. Low birth weight could be a risk factor for diseases later in life. For Isobutyl there is less information available. Available information was similar to butyl, and based on structure-activity relationships, they do not anticipate other significant concerns. There is an acknowledgement of the difference in the two materials.
At this point the SAB is considering these substances to be possible lower hazard substances.

Ammonium Bicarbonate
Further information regarding mutagenicity was considered for ammonium bicarbonate. The mutagenicity studies were all negative. This substance has low toxicity and is GRAS (used as a leavening agent in baked goods). There was a unanimous vote to take no action.

Ferric and Ferrous Compounds: Ferric Chloride, Ferrous Chloride, Ferric Sulfate, Ferrous Sulfate
Further information regarding mutagenicity was considered for the ferric and ferrous compounds. There were many negative studies and few positive mutagenicity studies; the positive studies were uncompelling(there were confounding factors such as Arochlor/magnetic field/studied individuals predisposed to iron sensitivity). Low LD50s, indicating toxicity via intraperitoneal, intravenous and oral routes. Low occupational exposure limits due to irritant effects.. They are all considered GRAS. There was a unanimous vote to take no action.

DEP still has concerns regarding the acute and chronic toxicity of these compounds, as well as the lack of consensus toxicity data for many endpoints. Their primary concerns are the low LD50 values and low occupational exposure limits due to irritant effects.

Maleic Acid
Maleic Acid discussion: Discussion about maleic acid centered around mutagenicity. All Ames tests were negative. Attempts were made to follow up reference to sarcomas in a reviewed study (Yanagisawa). The referenced study (Nagao) is in Japanese. Further investigation into Nagao found that only anhydrous maleic acid was studied. DEP inquired if there were any negative mutagenicity tests other than Ames systems, i.e. in mammalian studies. The LD50 is 708 mg/kg (oral rat), persistence is medium in sediment, low elsewhere. Maleic acid is an indirect food additive. Vote was unanimous to take no action on maleic acid.

Fumaric Acid
Fumaric Acid is a direct and indirect GRAS. LD50 indicated low toxicity at 10,700 mg/kg (oral rat). It has moderate persistence in sediment, low persistence in other medium. Regarding mutagenicity, it was negative in Ames and negative for mouse lymphomas. Only positive at very high doses (a magnitude higher [Ishidate]). Vote was unanimous to take no action..

Adipic Acid
Further information regarding mutagenicity was reviewed for adipic acid. No positive mutagenicity studies were found and 53 negative mutagenicity studies were found. Adipic acid is GRAS. The LD50 is high and the persistence in air is not considered a concern. There was a unanimous vote to take no action.

Ammonium chloride

Further information regarding mutagenicity was reviewed for Ammonium Chloride. There were 1 positive and 2 negative mutagenicity studies. The negatives were Ames tests, the positive was in chromosome tests at high levels. There was a high oral LD50 (1300 mg/kg), some low LD50s in non-oral routes. It does have a high persistence in air (180 days). Vote was unanimous to take no action..

Amyl Acetate
Further information regarding mutagenicity was reviewed for Amyl Acetate. All mutagenicity studies are negative. Ethyl acetate was retained in past delisting- Ethyl acetate is the most potent, butyl acetate is in the middle, amyl acetate is the least potent. All have flammability issues. The IDLH is of concern; Amyl Acetate is the lowest at 1000 ppm. There were two negative neurotoxicity studies on amyl acetate. There was a unanimous vote to take no action Amyl Acetate.

Ammonium Sulfamate
According to HSDB, this substance has low toxicity, limited human health data, and animal data indicating no irritation or systemic toxicity with repeated applications to shaved skin. Ecotoxicology data indicates that it is practically non toxic to birds and aquatic organisms (fish). It is listed as toxic to perch. It is low to moderately persistent in soil, decomposed by microbes; absorbs moisture readily; highly soluble in water. It is known as a contact herbicide which is only used to targeted parts of plants. This substance is noted as part of FIFRA, but is not currently registered as a pesticide. It liberates ammonia at elevated temperatures and poisonous gases may be produced in fire. It is approved as an adhesive in food packaging. The main issue for this substance is as a respiratory irritant, as a dust (rationale for low PEL). The substance is mild from a skin irritation standpoint. Tumor inhibition potential was acknowledged. There was previously a gap in the mutagenicity field. Ames assay listed as negative per Toxnet. Information also indicates that it does not cause permanent changes in genetic material and is not carcinogenic at 25 mg/kg/day. Vote was unanimous to take no action.

3. Use Information

As shown in Appendix B, these substances have been reported by TURA filers within the last three years for which data are available (2003 to 2005).. The number of filers for a given substance in the most recent reporting year ranges from one to eleven.

4. Regulatory Context

Appendix B shows selected regulatory information for each of the substances.

- None of the substances is identified as an EPA Clean Water Act Priority Pollutant. All of the substances are identified on the EPA Clean Water Act 311 List of Hazardous Substances.
- None of the substances are found on the EPA Superfund Amendments and Reauthorization Act (SARA) 302A Extremely Hazardous Substances List.
- None of the substances are listed as hazardous constituents under the Resource Conservation and Recovery Act (RCRA).
- None of the substances have maximum contaminant levels (MCLs) under the Safe Drinking Water Act. None are regulated as criteria air pollutants under the Clean Air Act.
- All of the substances are on both the New Jersey Right-to-Know list and the Pennsylvania Hazardous Substances list.
- Five of the substances meet the categorization criteria for the Government of Canada's Domestic Substances List categorization, indicating that there is a need for further attention to these substances based on human health and/or environmental criteria. These are: ammonium bicarbonate; aluminum sulfate; isobutyl acetate; ammonium chloride; and ammonium sulfamate.

5. Implications for the TURA Program

If the Council chooses to take no action on any of these substances, they will be removed from Toxic and Hazardous Substance List as of January 1, 2009. This means that TURA-covered facilities will no longer be required to report, pay a fee, and do toxics use reduction planning as a result of using these substances. The goal of this change is to help facilities focus their efforts more closely on substances that present more significant hazards to human health and the environment in Massachusetts. If the Council chooses to retain any of these substances, there will be no change in reporting or planning requirements.

According to the 2005 TURA data, there were filers for all 14 of the substances. There were a total of 58 Form S's for these 14 substances. For the three substances that the SAB now recommends retaining, the updated 2006 data show 18 filers: 6 for Aluminum Sulfate, 1 for iso Butyl Acetate, and 11 for Butyl Acetate. For the 11 substances that the SAB still recommends taking no action on, the 2006 data show 26 filers: 4 for Adipic Acid, 2 each for Amyl Acetate and Ferrous Chloride, 11 for Ferric Chloride, 3 for Ferric Sulfate, 1 each for Fumaric Acid, Ammonium Bicarbonate, Ammonium Chloride, and Ammonium Sulfamate, none for Maleic Acid or Ferrous Sulfate. Most facilities are expected to continue to report and plan for other substances, thus no facilities are expected to drop out of the program completely.

The total reduction in fees for these 26 Form S's is $28,600 ($1,100 per Form S).

Appendix A: CERCLA substances initially recommended for no action				
CAS#	**Chemical Name**	**Synonym**	**Date(s) Considered by SAB**	**Justification** Note: Unless otherwise noted, votes were unanimous.
1066-33-7	Ammonium bicarbonate		7/16/2007	No important concerns identified.
7705-08-0	Ferric chloride	Iron chloride hexahydrate	3/20/07; 4/23/2007; 7/16/07	Board discussed worker exposure issues as principal concern; deemed not significant.
10028-22-5	Ferric sulfate			Board discussed worker exposure issues as principal concern; deemed not significant.
7758-94-3	Ferrous Chloride			Board discussed worker exposure issues as principal concern; deemed not significant.
7782-63-0	Ferrous sulfate	Iron Sulfate Heptahydrate		Board discussed worker exposure issues as principal concern; deemed not significant.
10043-01-3	Aluminum sulfate	Alum	12/19/2007	Compared to ferrous and ferric sulfate. Mild irritant.
110-16-7	Maleic acid		6/25/07; 10/17/2007	No important concerns identified.
110-17-8	Fumaric acid		10/17/2007	Food additive.
110-19-0	iso-Butyl acetate		10/17/2007	The flammability and flash point were discussed for iso-butyl acetate. Flash point is 64°F and it has a low vapor pressure.
12125-02-9	Ammonium chloride		10/17/2007	Ammonium chloride is found in shampoo, adhesives, candies, and anti-perspirants. Ammonium chloride is an upper respiratory tract irritant. Persistence in air is 180. TLV is nuisance dust standard.
123-86-4	Butyl acetate		10/17/2007	The flammability and flash point were discussed for butyl acetate. The flash point is 72°F. The vapor pressure is low.
124-04-9	Adipic acid		6/25/07; 10/17/2007	Chronic fish toxicity and RfD are high. ScoreCard ranked this chemical in the lowest percentile. TLV 5mg – same as nuisance dust. It is used in plasticizers and is also a food ingredient in jelly.
628-63-7	Amyl acetate		12/19/2007	Amyl acetate is used for fit testing respirators. It has a high explosion limit (100 ppm), is an eye irritant, and is persistent in air. 5 votes to take no action, 2 abstaining.
7773-06-0	Ammonium sulfamate		12/19/2007	Ammonium sulfamate is a nuisance dust issue. It does not present other concerns.

Appendix B: Regulatory Data													
Cas #	Chemical Name	Synonym	Last Reported	Number of Filers	EPA SARA 110 Priority List of Hazardous Substances	EPA SARA 302A Extremely Hazardous Substances List	EPA Clean Water Act 126 Priority Pollutants	EPA Clean Water Act 311 List of Hazardous Substances	NJ Right to Know List	PA Hazardous Substances List	Meets Canadian substances categorization criteria	Hazardous Constituents (Resource Conservation and Recovery Act)	Hazardous Air Pollutants (Clean Air Act)
Substances recommended for Retention by the SAB													
10043-01-3	Aluminum sulfate	Alum	2005	8	-	-	-	Y	Y	Y	Y	N	-
123-86-4	Butyl acetate		2005	11	Y	-	-	Y	Y	Y	N	N	-
110-19-0	iso-Butyl acetate		2005	4	-	-	-	Y	Y	Y	Y	N	-
Substances recommended for 'No Action' by the SAB													
1066-33-7	Ammonium bicarbonate		2005	2	-	-	-	Y	Y	Y	Y	N	-
7705-08-0	Ferric chloride	Iron chloride hexahydrate	2005	10	-	-	-	Y	Y	Y	N	N	-
7758-94-3	Ferrous Chloride		2005	1	-	-	-	Y	Y	Y	N	N	-
10028-22-5	Ferric sulfate		2005	2	-	-	-	Y	Y	Y	N	N	-
7720-78-7	Ferrous sulfate		2004	1	-	-	-	Y	Y	Y	N	N	-
110-16-7	Maleic acid		2005	1	-	-	-	Y	Y	Y	N	N	-
110-17-8	Fumaric acid		2005	1	-	-	-	Y	Y	Y	N	N	-
124-04-9	Adipic acid		2005	5	-	-	-	Y	Y	Y	N	N	-
12125-02-9	Ammonium chloride		2005	3	-	-	-	Y	Y	Y	Y	N	-
628-63-7	Amyl acetate		2005	2	-	-	-	Y	Y	Y	N	N	-
7773-06-0	Ammonium sulfamate		2005	8	-	-	-	Y	Y	Y	Y	N	-
Key: Y = found on list; N = does not meet criteria; - = not found on list or in database													

Appendix B: Regulatory Data												
Cas #	Chemical Name	Synonym	Last Reported	Number of Filers	EPA SARA 110 Priority List of Hazardous Substances	EPA SARA 302A Extremely Hazardous Substances List	EPA Clean Water Act 126 Priority Pollutants	EPA Clean Water Act 311 List of Hazardous Substances	NJ Right to Know List	PA Hazardous Substances List	Meets Canadian substances categorization criteria	Hazardous Constituents (Resource Conservation and Recovery Act)
Substances recommended for Retention by the SAB												
10043-01-3	Aluminum sulfate	Alum	2005	8	-	-	-	Y	Y	Y	Y	N
123-86-4	Butyl acetate		2005	11	Y	-	-	Y	Y	Y	N	N
110-19-0	iso-Butyl acetate		2005	4	-	-	-	Y	Y	Y	Y	N
Substances recommended for 'No Action' by the SAB												
1066-33-7	Ammonium bicarbonate		2005	2	-	-	-	Y	Y	Y	Y	N
7705-08-0	Ferric chloride	Iron chloride hexahydrate	2005	10	-	-	-	Y	Y	Y	N	N
7758-94-3	Ferrous Chloride		2005	1	-	-	-	Y	Y	Y	N	N
10028-22-5	Ferric sulfate		2005	2	-	-	-	Y	Y	Y	N	N
7782-63-0	Ferrous sulfate	Iron Sulfate Heptahydrate	2005	1	-	-	-	Y	N	Y	-	N
110-16-7	Maleic acid		2005	1	-	-	-	Y	Y	Y	N	N
110-17-8	Fumaric acid		2005	1	-	-	-	Y	Y	Y	N	N
124-04-9	Adipic acid		2005	5	-	-	-	Y	Y	Y	N	N
12125-02-9	Ammonium chloride		2005	3	-	-	-	Y	Y	Y	Y	N
628-63-7	Amyl acetate		2005	2	-	-	-	Y	Y	Y	N	N
7773-06-0	Ammonium sulfamate		2005	8	-	-	-	Y	Y	Y	Y	N

Key: Y = found on list; N = does not meet criteria; - = not found on list or in database

Appendix C: Data considered by the SAB for substances recommended for no action																									
CAS#	Chemical Name	Synonyms	IARC	Water	Soil	Sediment	Air	BCF	Chronic Fish ChV (mg/l)	Neurotoxicity	Developmental / Reproductive Toxicity	Mutagenicity	LD50 (mg/kg)	LC50 (mg/m*3)	LC50 (mg/m3/4hr)	RfD(mg/kg/day)	RfC (mg/m3)	Minimum Risk Levels (ATSDR MRL list)				NIOSH-REL	TLV(TWA) mg/m3	TLV-STEL mg/m3	FP (°F)
TURI Report No. 18, 1999			http://monographs.iarc.fr/index.php	PBT Profiler: http://www.pbtprofiler.net/						Scorecard's List of Neurotoxicants: http://www.scorecard.org/health-effects/chemicals-2.tcl?short_hazard_name=neuro&all_p=t	California Prop 65 list: http://www.oehha.ca.gov/prop65/prop65_list/files/P65single092906.pdf; expub.com	EU Consolidated CMR list: http://www.chemicalspolicy.org/downloads/cmrlist.pdf	RTEC from NIOSH pkt guide or MSDS (SEE NOTES but many from Mallinckrodt/JT baker, Phys chem dept @ Oxford Univ. many updated in 2005/2006) http://www.cdc.gov/niosh/npg/ http://www.mallbaker.com/default.asp			Integrated Risk Information System: http://www.epa.gov/iris/		http://www.atsdr.cdc.gov/mrllist_12_05.pdf http://www.atsdr.cdc.gov/mrls/pdfs/mrllist_11_07.pdf				NIOSH Pocket Guide. NIOSH limits unless otherwise specified (CA means a chemical is thought to be a carcinogen by NIOSH) C= ceiling and ST = short term exposure limits http://www.cdc.gov/niosh/npg/			NIOSH or MSDS's
			HLE = Human Limited Evidence	Low < 60 days (green), Medium 60-180 days (orange), High > 180 days (red)			<= 2 days (green), > 2 days (red)	< 1000 (green), 1000 to 5000 orange, > 5000 red	> 10 (green), 0.1 to 10 (orange), < 0.1 (red)				mg/kg	mg/m3	mg/m3/4hr	mg/kg/day	mg/m3	Inhalation (ppm)		Oral (mg/kg/day)			mg/m3	mg/m3	F
1066-33-7	Ammonium bicarbonate		N	15	30	140	31	3.2	200,000	N	N	N	not avail	not avail		not avail	not avail					Not listed for NIOSH, ACGIH or OSHA			not applicable
7705-08-0	Ferric chloride	Iron chloride hexahydrate	N	Cannot be profiled using PBT profiler						N	N	N				not avail	not avail						1.0 (TWA) soluble iron salt as Fe		not applicable
10028-22-5	Ferric sulfate		N	Cannot be profiled using PBT profiler						N	N	N											ACGIH TLV 1.0 (TWA) soluble iron salt as Fe		not applicable
7758-94-3	Ferrous Chloride		N	Cannot be profiled using PBT profiler						N	N	N											ACGIH TLV 1.0 (TWA) soluble iron salt as Fe		not applicable
7782-63-0	Ferrous sulfate	Iron Sulfate Heptahydrate	N	Cannot be profiled using PBT profiler						N	N	N	Oral mouse 1520										ACGIH TLV 1.0 (TWA) soluble iron salt as Fe		not applicable
110-16-7	Maleic acid		N	8.7	17	78	1.8	3.2	5500	N	N	N	orl rat 708 mg/kg												
110-17-8	Fumaric acid		N	8.7	17	78	1.8	3.2	5500	N	N	N	orl rat 10700 mg/kg												
12125-02-9	Ammonium chloride		N	15	30	140	180	3.2	1800000	N	N	N													
124-04-9	Adipic acid		N	8.7	17	78	2.9	3.2	4800	N	N	N	Rat oral >11000 mg/kg												
628-63-7	Amyl acetate		N	8.7	17	78	2.1	12	4	N	N	N	oral rat >1600mg/kg									REL: TWA 100ppm (525 mg/m3)	PEL: TWA 100 ppm TLV: 50 ppm	TLV: ST 100 ppm	77F; 69F c.c.
7773-06-0	Ammonium sulfamate		N	Cannot be profiled using PBT profiler						N	N	N	oral rat 2000mg/kg			2E-1 mg/kg/day									

Appendix C: Data considered by the SAB for substances recommended for retention																										
CAS#	Chemical Name	Synonyms	IARC	Water	Soil	Sediment	Air	BCF	Chronic Fish ChV (mg/l)	Neurotoxicity	Developmental / Reproductive Toxicity	Mutagenicity	LD50 (mg/kg)	LC50 (mg/m*3)	LC50 (mg/m3/4hr)	RfD(mg/kg/day)	RfC (mg/m3)	Minimum Risk Levels (ATSDR MRL list)				NIOSH-REL	TLV(TWA) mg/m3	TLV-STEL mg/m3	FP (°F)
TURI Report No. 18, 1999			http://monographs.iarc.fr/index.php	PBT Profiler: http://www.pbtprofiler.net/						Scorecard's List of Neurotoxicants: http://www.scorecard.org/health-effects/chemicals-2.tcl?short_hazard_name=neuro&all_p=1	California Prop 65 list: http://www.oehha.ca.gov/prop65/prop65_list/files/P65single052906.pdf; expub.com	EU Consolidated CMR list: http://www.chemicalspolicy.org/downloads/cmrlist.pdf	RTEC from NIOSH pkt guide or MSDS (SEE NOTES but many from Mallinckrodt/JT baker, Phys chem dept @ Oxford Univ. many updated in 2005/2006) http://www.cdc.gov/niosh/npg/ http://www.mallbaker.com/default.asp			Integrated Risk Information System: http://www.epa.gov/iris/		http://www.atsdr.cdc.gov/mrllist_12_05.pdf http://www.atsdr.cdc.gov/mrls/pdfs/mrllist_11_07.pdf			NIOSH Pocket Guide. NIOSH limits unless otherwise specified (CA means a chemical is thought to be a carcinogen by NIOSH) C= ceiling and ST = short term exposure limits http://www.cdc.gov/niosh/npg/			NIOSH or MSDS's
			HLE = Human Limited Evidence	Low < 60 days (green), Medium 60-180 days (orange), High > 180 days (red)			<= 2 days (green), > 2 days (red)	< 1000 (green), 1000 to 5000 orange, > 5000 red	> 10 (green), 0.1 to 10 (orange), < 0.1 (red)				mg/kg	mg/m3	mg/m3/4hr	mg/kg/day	mg/m3	Inhalation (ppm)		Oral (mg/kg/day)			mg/m3	mg/m3	F
10043-01-3	Aluminum sulfate	Alum	N	Not found						N	Y (a)	Y (b)	274 mg/kg: Orl, mse, 6207mg/kg	n/a	Gold fish; LC50=100mg/L 12-96hr						Oral, 1 mg Al/kg/day		TLV (as Al soluble salt): 2 mg/m^3		NA
123-86-4	Butyl acetate		N	8.7	17	78	3.3	4.7	9	N	N	N	orl rat 14000 mg/kg		ihl rat 2000 ppm/4H										
110-19-0	iso-Butyl acetate		N	15	30	140	2.9	4.7	10	N	N	N	Rabbit oral 4800mg/kg												

(a) Data found in Registry of Toxic Effects of Chemical Substances (RTECS); (b) Data found http://toxnet.nlm.nih.gov/cgi-bin/sis/search

Appendix D. Data Sources

RTECS is sponsored by the National Institute for Occupational Safety and Health (NIOSH). "RTECS is a compendium of data extracted from the open scientific literature. The data are recorded in the format developed by the RTECS staff and arranged in alphabetical order by prime chemical name. Six types of toxicity data are included in the file: (1) primary irritation; (2) mutagenic effects; (3) reproductive effects; (4) tumorigenic effects; (5) acute toxicity; and (6) other multiple dose toxicity. Specific numeric toxicity values such as LD50, LC50, TDLo, and TCLo are noted as well as species studied and route of administration used. For each citation, the bibliographic source is listed thereby enabling the user to access the actual studies cited. No attempt has been made to evaluate the studies cited in RTECS. The user has the responsibility of making such assessments." [11]

HSDB includes "comprehensive, peer-reviewed toxicology data for about 5,000 chemicals". The Division of Specialized Information Services (SIS, http://sis.nlm.nih.gov/), National Library of Medicine (NLM), creates information resources and services in toxicology, environmental health, chemistry, and HIV/AIDS. SIS's Toxicology and Environmental Health Information Program (TEHIP, http://tox.nlm.nih.gov) produces TOXNET® (http://toxnet.nlm.nih.gov), a collection of toxicology and environmental health databases. TOXNET includes the Hazardous Substances Data Bank (HSDB®), a database of potentially hazardous chemicals).[12]

CCRIS includes carcinogenicity, mutagenicity, tumor promotion, and tumor inhibition data provided by the National Cancer Institute (NCI).[13]

IUCLID is a software application to capture, store, maintain and exchange data on intrinsic and hazard properties of chemical substances. Distributed free of charge, the software is especially useful to chemical industry companies and to government authorities. It is the key tool for chemical industry to fulfill data submission obligations under REACH, a European Union law covering the production and use of chemical substances. The software is maintained by the European Chemicals Agency, ECHA.[1] The latest version, version 5.1, was made available on 16 January 2009. [14]

Datasets and referenced studies were obtained where necessary (see Table 1 below).

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[11] http://www.cdc.gov/niosh/rtecs/
[12] http://www.nlm.nih.gov/pubs/factsheets/sis.html
[13] http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?DescCCRIS.htm
[14] http://en.wikipedia.org/wiki/IUCLID

Table 1: Additional References Considered for Pending CERCLA Chemical Decisions	
Chemical	**Additional References Considered**
Aluminum Sulfate	1) "Antitesticular Effect of Metallic and Rare Earth Salts", Kamboj and Kar, *Journal of Reproduction and Fertility.* 2) "Alterations to the Pattern of Ultrasonic Calling after Prenatal Exposure to Aluminum Sulfate", Rankin, J, Manning A; *Behavioral and Neural Biology.* 3) "Effects of aluminum salts on bone marrow chromosomes in rates in vivo", Roy, et al.; *Cytobios* 4) "Effects of aluminum sulphate on human leukocyte chromosomes in vitro", Roy, et al.; *Mutation Research*
Butyl Acetate	"Developmental toxic effects of ethylbenzene or toluene alone and in combination with butyl acetate in rats after inhalation exposure", Saillenfait, et al.; *Journal of Applied Toxicology*
Ferric Chloride	1) "DNA Damage in Human Transitional Cell Carcinoma Cells After Exposure to the Proximate Metabolite of the Bladder Carcinogen 4-Aminobiphenyl", Burger, et al; *Environmental and Molecular Mutagenesis* 2) "Performance of 133 compounds in the lambda prophage induction endpoint of the Microscreen assay and a comparison with S. typhimurium Mutagenicity and rodent carcinogenicity assays", Rossman, et al; *Mutation Research*
Ferrous Chloride	1) "Performance of 133 compounds in the lambda prophage induction endpoint of the Microscreen assay and a comparison with S. typhimurium Mutagenicity and rodent carcinogenicity assays", Rossman, et al; *Mutation Research* 2) "Enhancement of Viral Transformation for Evaluation of the Carcinogenic or Mutagenic Potential of Inorganic Metal Salts", Casto, et al; *Cancer Research* 3) "Protective effect of melatonin against in vitro iron ions and 7 mT 50 Hz magnetic field-induced DNA damage in rat lymphocytes", Jajte, et. al; *Mutation Research*
Ferrous Sulfate	*1)* "Possible repair action of Vitamin C on DNA damage induced by methyl methanesulfonate, cyclophosphamide, $FeSO_4$ and Cu SO_4 in mouse blood cells in vivo", Franke, et al.; *Mutation Research* 2) "A Compilation of Two Decades of Mutagenicity Test Results with the Ames *Salmonella typhimurium* and L5178Y Mouse Lymphoma Cell Mutation Assays", Seifried, et al.; *Chemical Research in Toxicology* 3) "The Gene", Demerec, et al.; *Annual report of the director of the Department of genetics, Carnegie Institution of Washington*
Maleic Acid	1) "Experiments on the Chemotherapy of Cancer 4. Further Experiments with Aldehydes and Their Derivatives", Boyland; *Chester Beatty Research Institute* *2)* "Screening for carcinogens by the DNA synthesis inhibition test using human fibroblasts", Yanagisawa, K., et al.; *Mutation Research* 3) "Environmental Mutagens and Carcinogens", Nagao, et al; *Ann. Rev. Genet.* 4) "Does carcinogenic potency correlate with mutagenic potency in the Ames assay?", Ames, B.N., et al; *Nature*
Fumaric Acid	1) "A Compilation of Two Decades of Mutagenicity Test Results with the Ames *Salmonella typhimurium* and L5178Y Mouse Lymphoma Cell Mutation Assays", Seifried, et al.; *Chemical Research in Toxicology* 2) "Fumaric-Acid Enhances DNA-Synthesis of Rat Hepatocytes By Counteracting The Toxicities of Mitomycin-C and Aflatoxin B1", Kuroda, K., et al.; *Japanese Journal of Cancer Research* 3) "A Study of anticarcinogenic effects of fumaric acid on models of carcinogenesis in the esophagus, nervous system and kidney", Bespalov VG, et al; *Voprosy onkologii.*
Ammonium Chloride	"Primary Mutagenicity Screening of Food Additives Currently Used in Japan", Ishidate, Jr., et al.; *Food and Chemical Toxicology*

Table 2: GRAS Substance Designations		
Chemical	GRAS (Y/N?)	Information pertaining to addition
Aluminum Sulfate (10043-01-3)	Y	DOC TYPE: ASP; DOC #: 1671 Reg. #: 172.892, 182.1125
Ammonium Bicarbonate (1066-33-7)	Y	DOC TYPE: ASP; DOC #: 1680 Reg. #: 163.110, 163.111, 163.112, 184.1135, 73.85
Ammonium Chloride (12125-02-9)	Y	DOC TYPE: ASP; DOC #: 1682 Reg. #: 178.1010, 184.1138
Ammonium Sulfamate (7773-06-0)	N	Listed as an indirect food additive for use only as a component of adhesives.
Ferric Chloride (7705-08-0)	Y	DOC TYPE: ASP; DOC #: 2095 Reg. #: 175.105, 176.170, 184.1297
Ferrous Chloride (7758-94-3)	N	HSDB: Iron reduced used as a dietary supplement in food for human consumption is generally recognized as safe when used in accordance with good manufacturing practice.
Ferric Sulfate (10028-22-5)	Y	DOC TYPE: ASP; DOC #: 2102 Reg. #: 582.80, 184.1307
Ferrous Sulfate (7782-63-0)	Y	DOC TYPE: ASP; DOC #: 2110 Reg. #: 184.1315
Adipic Acid (124-04-9)	Y	DOC TYPE: ASP; DOC #: 1610 Reg. #: 175.300, 175.320, 176.170, 176.180, 177.1200, 177.1390, 177.1500, 177.1630, 177.1680, 177.2420, 177.2600, 184.1009
Fumaric Acid (110-17-8)	Y	DOC TYPE: ASP; DOC #: 0546 Reg. #: 150.141, 150.161, 172.350, 172.808, 172.810, 172.822, 175.105, 175.300, 175.320, 176.170, 177.1200, 177.2420
Maleic Acid (110-16-7)	N	Listed as an indirect food additive for use only as a component of adhesives.
Amyl Acetate (628-63-7)	N	Listed as an indirect food additive for use only as a component of adhesives.
Butyl Acetate (123-86-4)	Y	DOC TYPE: ASP; DOC #: 0151 Reg. #: 172.515, 175.105, 175.320, 177.1200
Iso-Butyl Acetate (110-19-0)	Y	DOC TYPE: ASP; DOC #: 0747 Reg. #: 172.515
KEY:		
DOC TYPE	An indicator of the status of the toxicology information available for the substance in PAFA (administrative and chemical information is available on all substances):	
ASP	Fully up-to-date toxicology information has been sought	
DOC NUM	PAFA database number of the *Food Additive Safety Profile* volume containing the printed source information concerning the substance.	
REG NUM	Regulation numbers in Title 21 of the U.S. Code of Federal Regulations where the chemical appears.	
Information found at: http://vm.cfsan.fda.gov/~dms/eafus.html		