

# **Prioritization: October 2011 Update**

**Oct. 12-13, 2011**

**Carcinogen Identification Committee Meeting**

**Martha S. Sandy, Ph.D., Chief  
Cancer Toxicology and Epidemiology Section  
Reproductive and Cancer Hazard Assessment Branch**



# Prioritization Process

- **Purpose** – to identify chemicals for evaluation by the CIC
- **Goal** – to focus the efforts of the CIC on chemicals that may pose significant hazards to Californians

*Prioritization is a **preliminary appraisal** of the evidence of hazard*



# Prioritization Process

Tracking Database



Candidate Chemicals



**Screens: Focused Literature Review**

Chemicals Proposed for Committee Consideration



*Consultation with the Committee on Chemicals for Review*



OEHHA Selection of Chemicals for  
Preparation of Hazard Identification Materials



# Screening of Candidate Chemicals

1. Re-apply **Human Data Screen**
2. Apply **Animal Data Screen**
3. Conduct ***Preliminary Toxicological Evaluation*** of chemicals identified through these screens
4. Identify **Chemicals Proposed for CIC Consideration**



# Animal Data Screen

- **Two or more positive\*** animal cancer bioassays;  
or
- **One positive** animal cancer bioassay, **with**
  - Malignant (or combined malignant and benign) tumors ***occurring to an unusual degree*** with regard to incidence, site or type of tumor or age at onset; **or**
  - Findings of ***tumors at multiple sites***; **or**
  - Evidence from a ***second animal study*** of ***benign tumors known to progress to malignancy***

\*An increased incidence of malignant or combined malignant and benign tumors



# Prioritization Process

Tracking Database



Candidate Chemicals



**Screens: Focused Literature Review**

Chemicals Proposed for Committee Consideration



*Consultation with the Committee on Chemicals for Review*



OEHHA Selection of Chemicals for  
Preparation of Hazard Identification Materials



# Screening of 380+ Candidate Chemicals

➤ **2009** ~50% complete: 38 chemicals to CIC

➤ **2010** ~75% complete: 27 chemicals to CIC

➤ **2011** 100% complete: 39 chemicals to CIC

## ➤ Ongoing

➤ Screening of new additions to the Tracking Database

➤ Proposals of chemicals for CIC consideration

➤ Consultation with CIC



# **Some Chemicals Have Been *Grouped Together* for Consultation**

- **Chloroalkyl Ethers**
- **Dibenzanthracenes & Dibenz[a,c]anthracene**
- **Dinitroaniline Pesticides & Prodiamine & Trifluralin**
- **N-methyl-N-Nitroso-1-alkylamines & the -Octanamine, -Decanamine, -Dodecanamine, -Tetradecanamine**
- **Topoisomerase II Inhibitors**
- **Triazole Antifungal Agents**





# 2009 & 2010 Chemical Prioritization\*

## High Priority

- Amphetamine & its salts
- Atrazine
- Clomiphene & its salts
- Diisononyl phthalate
- 2,6-Dimethyl-Nitrosomorpholine
- Haloperidol
- Methylphenidate & its salts
- N-Nitrosohexamethylenimine
- Omeprazole & its salts
- Pantoprazole & its salts
- PFOA & its salts & transformation & degradation precursors
- Rabeprozole & its salts

## Medium Priority

- Aceptate
- Alpha-methyl styrene
- 11-Aminoundecanoic acid
- Aspartame
- Budesonide
- C.I. Acid Orange 3
- Decabromodiphenyl ether
- Dicofof
- Diethanolamine
- Furfural
- Gentian Violet
- Hydroquinone
- 4-Hydroxymethyl, 4-Methyl, & 4-Hydroxy benzenediazonium & their salts
- Malathion
- Methoxychlor
- Methyl ethyl ketoxime
- N-Methyl-N-formylhydrazine
- 3-Nitrofluoranthene
- N-Nitrosoanabasine
- PFOS & its salts & transformation & degradation precursors
- Permethrin
- Quinoxaline-1,4-dioxide compounds & Desoxycarbadox
- Tetrachlorvinphos
- Thiamethoxam

## Low Priority

- 2-Amino-5-nitrothiazole
- Amitraz
- Anthanthrene
- Benoxacor
- 2-Biphenylamine & its salts
- 4-Chloro-*m*-phenylenediamine
- 2-Chloro-1,1,1-trifluoroethane
- Ciprofibrate
- D&C Yellow #11
- Decalin
- 2,6-Dichloro-*p*-pheylenediamine
- N,N-Diethylthiourea
- 1,3-Dinitropyrene
- Ethylnodiol diacetate
- Isoniazid
- 7-Methylbenz[*a*]anthracene
- Molybdenum trioxide
- Nitrofurantoin
- 5-Nitro-*o*-toluidine
- Phosmet
- Rock wool
- Triamterene
- Triclosan
- Triethanolamine
- Vinylidene chloride



# 2011: Chemicals for Prioritization (1)

Chemical Name	Exposure				Human Data				Animal Data					Other Relevant Data				
	Widespread	High in frequent consumers	Limited / occupational	High in infrequent consumers	Analytical	Descriptive	Analytical: mixed / poorly defined	exposure Case series / reports	Two or more studies	One study w/ unusual incidence, site/type, age at onset	One study and second study with benign tumors only	One study	Tumor initiation / promotion or co-carcinogenicity studies	Genotoxicity	Carcinogenic metabolites	Structural similarity with tumorigens or P65 carcinogens	Hormonal activity / disruption	Other mechanistic studies
Abacavir and Its Salts		x						x					x		x			
Acetaminophen	x				x			x				x	x					x
Bisphenol A	x							x				x	x				x	x
Butyl Benzyl Phthalate	x							x				x	x				x	x
Butylated Hydroxytoluene	x							x				x	x		x			
C.I. Disperse Yellow 3	x							x					x		x			
Chloroalkyl Ethers	x				x		x	x				x	x		x			
Chloropicrin	x									x			x					
Clodinafop-Propargyl	x							x					x		x			x
Coumarin	x							x					x	x				
Dapsone		x			x		x	x				x	x		x			
Dibenzanthracenes and Dibenz[a,c]anthracene	x							x				x	x	x	x			
3,3'-Dichlorobenzidine-based Compounds Metabolized to 3,3'-Dichlorobenzidine			x			x		x					x	x	x			x
2,4-Dichlorophenoxyacetic acid and Its Salts and Esters	x				x			x					x				x	x



# 2011: Chemicals for Prioritization (2)

Chemical Name	Exposure				Human Data				Animal Data				Other Relevant Data					
	Widespread	High in frequent consumers	Limited / occupational	High in infrequent consumers	Analytical	Descriptive	Analytical: mixed / poorly defined exposure	Case series / reports	Two or more studies	One study w/ unusual incidence, site/type, age at onset	One study and second study with benign tumors only	One study	Tumor initiation / promotion or co-carcinogenicity studies	Genotoxicity	Carcinogenic metabolites	Structural similarity with tumorigens or P65 carcinogens	Hormonal activity / disruption	Other mechanistic studies
Dicloran	x									x			x		x			
Dinitroaniline Pesticides and Prodiamine and Trifluralin	x				x			x					x		x	x		
Entecavir		x						x					x		x			
Flonicamid	x							x					x		x			x
Fluazinam	x							x					x					
Hexythiazox	x									x			x					
Hydralazine and Its Salts		x			x		x	x					x					x
Isophosphamide		x						x					x		x			
Metofluthrin				x				x					x		x			x
Mixtures Containing Pentabromochlorocyclohexane	x									x			x					
N-Methyl-N-Nitroso-1-Alkylamines	x							x					x		x			
N-Nitroso-N-Methylaniline	x							x					x		x			
N-Methylpyrrolidone	x							x					x					
6-Nitrobenzimidazole			x					x					x		x			
Pentachloronitrobenzene	x							x					x					



# 2011: Chemicals for Prioritization (3)

Chemical Name	Exposure				Human Data				Animal Data				Other Relevant Data					
	Widespread	High in frequent consumers	Limited / occupational	High in infrequent consumers	Analytical	Descriptive	Analytical: mixed / poorly defined exposure	Case series / reports	Two or more studies	One study w/ unusual incidence, site/type, age at onset	One study and second study with benign tumors only	One study	Tumor initiation / promotion or co-carcinogenicity studies	Genotoxicity	Carcinogenic metabolites	Structural similarity with tumorigens or P65 carcinogens	Hormonal activity / disruption	Other mechanistic studies
Pimecrolimus and Tacrolimus		x			x			x	x					x				x
Pivalolactone			x						x					x		x		
Pyraflufen Ethyl	x								x					x				
Raloxifen and Its Salts		x			x				x					x		x		
Stavudine		x							x					x		x		
Thiophanate Methyl	x								x					x		x	x	
Topoisomerase II Inhibitors				x	x			x	x					x		x		x
Triazole Antifungal Agents	x								x					x		x		x
2,4,6-Trimethylaniline and Its Salts	x								x					x		x		
Tris(2-Ethylhexyl)Phosphate	x								x					x		x		





# Chloroalkyl Ethers

**Advise whether the *chemical group* should be considered for listing at a future meeting.**



# Dibenzanthracenes & Dibenz[a,c]anthracene

**Advise whether the *chemical group*, or *dibenz[a,c]anthracene* alone, or *both* should be considered for listing at a future meeting.**



# Dinitroaniline Pesticides & Prodiamine & Trifluralin

**Advise whether the *chemical group*, or *prodiamine* alone, or *trifluralin* alone, or *some combination* of these compounds should be considered for listing at a future meeting.**





# **N-methyl-N-Nitroso-1-alkylamines & the -Octanamine, -Decanamine, -Dodecanamine, -Tetradecanamine**

**Advise whether the *chemical group*, or *MNOA* alone, or *MNDEA* alone, or *MNDodeA* alone, or *MNTA* alone, or *some combination* of these compounds should be considered for listing at a future meeting.**



# Topoisomerase II Inhibitors

**Advise whether the *chemical group* should be considered for listing at a future meeting.**



# Triazole Antifungal Agents

**Advise whether the *chemical group* or *any individual triazoles* should be considered for listing at a future meeting.**

