

PROPOSAL FOR PRIORITIZING CANDIDATE AGENTS FOR CONSIDERATION UNDER PROPOSITION 65 BY THE OEHHA SCIENCE ADVISORY BOARD

**Reproductive and Cancer Hazard Assessment Section
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency
April 7, 1995**

1 BACKGROUND

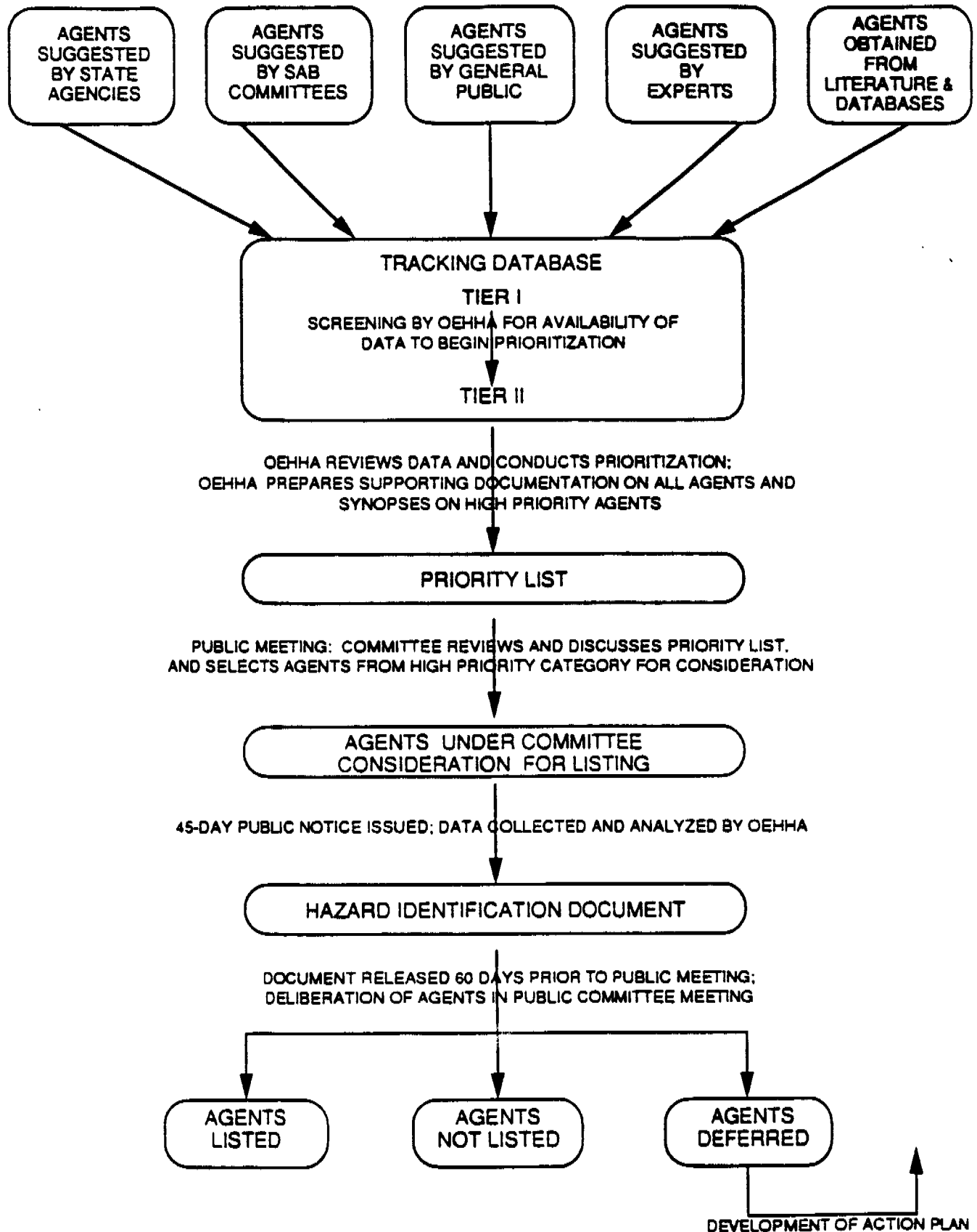
The Safe Drinking Water and Toxic Enforcement Act (Proposition 65, California Health and Safety Code 25249.5 *et seq.*) requires the Governor to publish lists of agents known to cause cancer and reproductive toxicity. One of the mechanisms by which an agent is placed on this list is a finding by the "state's qualified experts" that an agent has been clearly shown through scientifically valid testing according to generally accepted principles to cause cancer or reproductive toxicity. As lead agency for the implementation of Proposition 65, the Office of Environmental Health Hazard Assessment (OEHHA) has formed two committees of the Science Advisory Board (SAB) to serve as the state's qualified experts. These committees are the Developmental and Reproductive Toxicant (DART) Identification Committee and the Carcinogen Identification Committee.

The purpose of this draft document is to propose a mechanism for compiling and prioritizing candidate agents for consideration by the SAB Identification Committees. The proposed mechanism provides a systematic process for compiling and tracking possible candidate agents and for prioritizing these agents for consideration by the Identification Committees. Key elements include (1) a database to track agents suggested for consideration, (2) development by OEHHA of a priority list of agents, grouped into high, medium, or low priority on the basis of their potential for human exposure and developmental/reproductive or carcinogenic hazard, and (3) expert review in the final prioritization of agents. Opportunity is provided for input and review by state agencies and departments, the scientific community, and other interested parties both in the suggestion of candidate agents and the development of the priority lists.

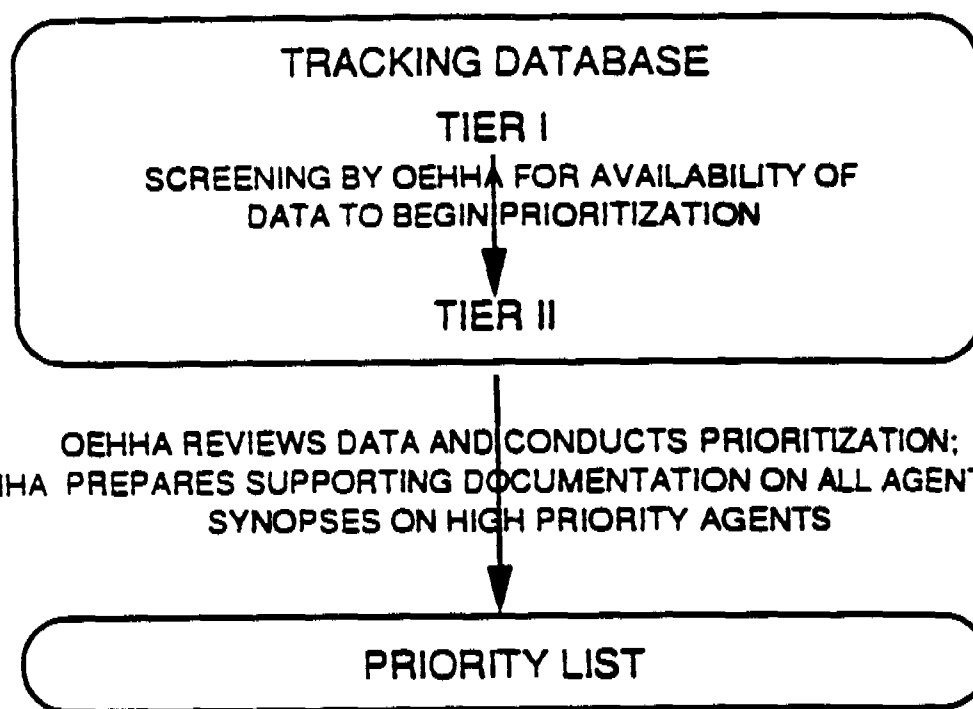
As emphasized by California's Court of Appeal (1989), Proposition 65 directs the state "to engage in a diligent, thorough, and continuing search for additional chemicals which evolving scientific knowledge demonstrates are subject to the Act." Accordingly, the meeting agendas of the Identification Committees will largely be taken up by consideration of potential candidates for listing generated by this process. Other items that may compete for space on the agendas include, for example, proposed delistings of particular agents or general scientific issues to be considered in listing.

SL 108139

FIGURE 1: FLOWCHART FOR CONSIDERATION OF AGENTS UNDER PROPOSITION 65



SL 108140



SL 108141

Name of Agent	CAS#
acetazolamide	59665
acrylamide	79061
acrylonitrile	107131
aldrin	309002
aminoacetonitrile	540614
aminonicotinamide, 6-	329895
aminopropionitrile, B-	151188
ammonium perfluorooctanoate	3825261
aniline	62533
apholate	52460
arsenic (inorganic)	7440382
arsenous oxide	1327533
asparaginase, L	9015683
AY-9944	366938
azacytidine, 5-	320672
azaundine	54251
balagrin	71330433
benzene	71432
benzo[a]pyrene	50328
beryllium	7440417
betamethasone	378449
boric acid	10043353
boron	7440428
bromo-2'-deoxyuridine, 5-	59143
bromodichloromethane	75274
butadiene, 1,3-	106990
butyl ester, 2,4,5-T	93798
butyl ester, 2,4-D	94804
cadmium	7440439
cadmium sulfate	10124364
caffeine	58082
cannabis	8063147
captan	133062
carbamazepine	36507309
carbon dioxide	124389
carbon tetrachloride	56235
carbutamide	339435
chloramphenicol	56757
chlordan	57749
chlorfenvinfos	470906
chloroform	67663
chlorohydrin	96242
chloroprene	126998
chromium trioxide	1333820
chromium VI	18540299
copper sulfate	7758987
corticosterone	50226
cyclizine	82928
DDE	72559

SL 108142

**PROPOSITION 65 PRIORITY LIST - CANDIDATE AGENTS UNDER CONSIDERATION FOR
DEVELOPMENTAL AND REPRODUCTIVE TOXICITY EVALUTATION⁽¹⁾**

Nam of Ag nt	CAS#	Level of Toxicological Concern ⁽²⁾	Level of Exposure Concern	Priority Status - DART
Acrylamide	79061	High	Medium	High
Aldrin	309002	High	Low	Medium
1,3-Butadien	106990	Medium	Medium	Medium
Carbamazepine	36507309	High	Low	Medium
Carbon tetrachloride	56235	Medium	Medium	Medium
Chlordane	57749	High	Low	Medium
DDT ⁽³⁾	50293	High	Medium	High
Ethylen dibromide	106934	High	Low	Medium
Formaldehyde	50000	Low	High	Medium
Heptachlor	76448	High	Low	Medium
Methylene chloride	75092	Low	High	Medium
Progesterone	57830	High	Low	Medium ⁽⁴⁾
2,4,5-T, butyl ester	93798	Low	Low	Low
Trichloroethylene	79016	Medium	High	High
Vinyl chlorid	75014	Medium	Medium	Medium

(1) Priority chemicals from Donald, JM, Monserrat, LG, Hooper, K, Book, SA and Chernoff, GF (1992). Prioritizing candidate reproductive/developmental toxicants for evaluation. *Reprod Toxicol* 6:99-108.

(2) The evaluation of the level of toxicological concern is based on secondary sources (databases and reviews). It is likely that data exist which have not been considered in the evaluation. In a more detailed review, additional data may be found that will alter the assigned "level of toxicologic concern". Consequently, a "low" or "medium" level of toxicologic concern should not be interpreted to mean that the chemical has little or no potential to cause reproductive or developmental effects.

(3) Would also include consideration of major metabolites and breakdown products such as DDE (CAS # 72559) and DDD (CAS # 72548).

(4) Progesterone is intentionally used as a contraceptive. Unintentional exposures are believed to be low.

LO exposure concern;
HI/MED toxicity concern

aldrin
chlordane
ethylene dibromide
heptachlor
2,4,5-butyl ester

progesterone
carbamazepine

HI exposure concern;
LO toxicity concern

formaldehyde
methylene chloride

MED exposure concern;
MED toxicity concern

1,3-butadiene
carbon tetrachloride
vinyl chloride

HI PRIORITY AGENTS

acrylamide
DDT
trichloroethylene

Name of Agent	CAS#
acetazolamide	58665
acrylamide	79081
acrylonitrile	107131
aldrin	309002
aminoacetonitrile	540614
aminonicotinamide, 6-	329895
aminopropionitrile, B-	151188
ammonium perfluorooctanoate	3825261
aniline	62533
apholate	52460
arsenic (inorganic)	7440382
arsenous oxide	1327533
asparaginase, L	9015683
AY-9944	386938
azacytidine, 5-	320672
azaundine	54251
balagmn	71330433
benzene	71432
benzo[a]pyrene	50328
beryllium	7440417
betamethasone	378449
boric acid	10043353
boron	7440428
bromo-2'-deoxyuridine, 5-	59143
bromodichloromethane	75274
butadiene, 1,3-	108990
butyl ester, 2,4,5-T	93798
butyl ester, 2,4-D	94804
cadmium	7440439
cadmium sulfate	10124364
caffeine	58082
cannabis	8063147
captan	133062
carbamazepine	38507309
carbon dioxide	124389
carbon tetrachloride	56235
carbutamide	339435
chloramphenicol	56757
chlordan	57749
chlorfenvinfos	470906
chloroform	67663
chlorohydrin	96242
chloroprene	126998
chromium trioxide	1333820
chromium VI	18540299
copper sulfate	7758987
corticosterone	50226
cyclizine	82928
DDE	72559

DDT	50293
diaminostilbene	621965
dichloroethylene, 1,1-	75354
dichloropropane, 1,2-	78875
dieldrin	60571
diethylene glycol diethyl ether	112367
diethylene glycol dimethyl ether	111966
diethylene glycol methyl ether	111773
diethylhexyl phthalate	117817
diltiazem	42399417
dimethyl acetamide	127195
dimethyl-1,2-benz(a)anthracene, 7,12-	57976
dimpylate	333415
dinitrotoluene, 2,6-	25321146
dromostanolone propionate	521120
EM 12	26581817
endrin	72208
enflurane	13838169
environmental tobacco smoke	
epichlorohydrin	106898
estradiol, 17-beta	50282
ethisterone	434037
ethosuximide	77678
ethoxyethyl acetate, 2-	111159
ethylene dibromide	106934
ethylene glycol diethyl ether	629141
ethylene glycol dimethyl ether	110714
ethylnitrosourea	759739
ethinyliestradiol	57636
etizolam	40054691
fluoroacetate	144490
folpet	133073
formaldehyde	50000
formamide	75127
furylfuramide	3688537
griseofulvin	126078
hadacidin	689134
halothane	151677
heptachlor	78448
heroin	561273
hexamethylene diisocyanate	822060
hexane, N-	110543
hydroxy-oxo-L-norvaline	4439843
hydroxyprogesterone	68962
hydroxytryptophan, 5-	56899
hydroxyurea	127071
idoxundine	54422
indomethacin	53861
insulin (natural)	9004108
karathane	39300453

manganese	7439965
mestranol	72333
methadone	76993
methandrostenolone	72639
methoxyethyl acetate, 2-	110496
methoxyflurane	76380
methyl 2(p-allophanoylbenzyl)hydrazine, 1-	60344
methyl butyl ketone	591786
methyl chloride	74873
methyl PGA, X-	
methyl salicylate	119368
methylacetamide, N-	79163
methylazoxymethanol	590965
methylene bis(4-cyclohexylisocyanate)	5124301
methylene chloride	75092
methylformamide	123397
methylpyrrolidone, N-	872504
monocrotophos	6923224
monosodium glutamate	142472
myclobutanol	88671890
N-methylnitrosourea (n-nitroso-n-methylurea)	684935
n-nitroso bis(2-oxopropyl)amine	60599384
nickel carbonyl	13463393
nitrochlorobenzene, p-	100005
nitrofen	1836755
nitroquinolone-1-oxide, 4-	56575
nitrous oxide	10024972
ochratoxin A	303479
oxydemeton-methyl	301122
oxytocin	50566
phencyclidine (PCP)	77101
phenol	108952
phenoxybenzamine	59961
phenylalanine (DL)	3617445
prednisolone	50248
primidone	125337
progesterone	57830
propargite	2312358
propylene glycol methyl ether, beta-isomer (PGME-beta, 2-methoxy-1-propanol)	1589497
pyrimethamine	58140
razoxane	24584096
red palm oil	8002753
Ro 10-9359	54350480
strontium (unspecified salt)	543942
styrene	100425
tetrachloroacetone	31422614
tetrahydrocannabinol (THC)	1972083
thiouracil	141902
thiram	137268
thyroxine	51'89

DRAFT

P65 DART TRACKING DATABASE - TIER I AGENTS

4/7/95

tolbutamide	64777
toluene 2,4-diisocyanate	584849
toxaphene	8001352
triamcinolone	124947
trichloroethylene	79016
trichlorofon	52686
tricyanoaminopropene	
triethylene glycol dimethyl ether	112492
trypan blue	72571
vinyl chloride	75014
vitamin D	1406162
xylene	1330207

**PROPOSITION 65 PRIORITY LIST - CANDIDATE AGENTS UNDER CONSIDERATION FOR
DEVELOPMENTAL AND REPRODUCTIVE TOXICITY EVALUTATION⁽¹⁾**

Name of Ag nt	CAS#	Level of Toxicological Concern ⁽²⁾	Level of Exposure Concern	Priority Status - DART
Acrylamide	79061	High	Medium	High
Aldrin	309002	High	Low	Medium
1,3-Butadiene	106990	Medium	Medium	Medium
Carbamazepine	36507309	High	Low	Medium
Carbon tetrachloride	56235	Medium	Medium	Medium
Chlordane	57749	High	Low	Medium
DDT ⁽³⁾	50293	High	Medium	High
Ethylene dibromide	106934	High	Low	Medium
Formaldehyde	50000	Low	High	Medium
Heptachlor	76448	High	Low	Medium
Methylen chloride	75092	Low	High	Medium
Progesterone	57830	High	Low	Medium ⁽⁴⁾
2,4,5-T, butyl ester	93798	Low	Low	Low
Trichloroethylene	79016	Medium	High	High
Vinyl chloride	75014	Medium	Medium	Medium

(1) Priority chemicals from Donald, JM, Monserrat, LG, Hooper, K, Book, SA and Chemoff, GF (1992). Prioritizing candidate reproductive/developmental toxicants for evaluation. *Reprod Toxicol* 6:99-108.

(2) The evaluation of the level of toxicological concern is based on secondary sources (databases and reviews). It is likely that data exist which have not been considered in the evaluation. In a more detailed review, additional data may be found that will alter the assigned "level of toxicologic concern". Consequently, a "low" or "medium" level of toxicologic concern should not be interpreted to mean that the chemical has little or no potential to cause reproductive or developmental effects.

(3) Would also include consideration of major metabolites and breakdown products such as DDE (CAS # 72559) and DDD (CAS # 72548).

(4) Progesterone is intentionally used as a contraceptive. Unintentional exposures are believed to be low.

SL 108149