"We have to first confirm these health effects, and then see if they fit into a pattern," Goldman remarked. "After that, we can develop an appropriate response," she said.

In the consent agreement, DowElanco said it would:

— assist EPA by using its best efforts to review files of its parent companies for any information concerning health and environmental effects incidents for pesticide products registered under FIFRA, which the company obtained as a consequence of its 1989 formation;

— waive its right to request a judicial or administrative hearing on the matter, and

— pay the penalty within 30 days, or pay the total civil penalty originally proposed in the complaint, $1.635 million. (☎5PTCN 2712, 15 pages, $8)

●

2-VINYL-1,3-DIOXOLANE EXPOSURE LINKED TO RABBIT DEATHS IN SECTION 8(e) REPORT

Rabbits exposed to 1,3-dioxolane, 2-ethenyl, also known as 2-vinyl-1,3-dioxolane, died after displaying a variety of neurotoxic symptoms, according to TSCA Section 8(e) submission #8EHQ-0495-13021, said Degussa Corp.

The test substance was used undiluted and applied at 6.61 mg/kg, 66.1 mg/kg and 208.6 mg/kg on male and female rabbits, according to the study. The results were intoxication characterized by hypokinesia, decrease in muscle tone, loss of righting reflexes and salivation, which appeared about two hours after treatment and lasted until death.

According to the study, deaths occurred between five and 24 hours after treatment, with the LD50 dose for males and females calculated at 25.1 mg/kg.

In TSCA 8(e) submission #8EHQ-95-13426, Cytec Industries reported the results of a guinea pig maximization study conducted with acrylamide, 50% aqueous, by Stockhausen Laboratory for Toxicology in Germany. The results indicated a sensitization rate of 85%, indicative of a positive sensitization reaction, the submission said. (☎5PTCN 2716, 2 pages, $5)

●

VINYL CHLORIDE CANCER RISK LINKED TO EARLY-LIFE EXPOSURE

A new quantitative cancer assessment on lifetime exposures to vinyl chloride in animals suggests that the risk of cancer depends on the age at exposure, with higher risks attributed to exposure at younger ages, said Environmental Protection Agency's V. James Cogliano at a recent toxicology meeting.

Speaking at the April 25 Conference on Risk Assessment Issues for Sensitive Human Populations at Wright-Patterson Air Force Base in Ohio, Cogliano said newborn animal exposure studies demonstrate that a brief exposure can induce unseen tumors and higher incidence of apparent tumors following long-term exposure later in life.

Cogliano, chief, Carcinogen Assessment Statistics and Epidemiology Branch, EPA's Office of Research and Development, said new quantitative approaches reflecting early-life sensitivity have been developed to supplement conventional approaches to estimating the increased cancer risk from inhaling vinyl chloride.

Vinyl Chloride Studies May Have Superfund Implications

These studies may have implications for Superfund risk assessments as EPA must decipher the risk of inhaling vinyl chloride from nearby dumps, he said, as well as estimating early risks for other chemicals.

Cogliano told attendees of the Ohio meeting that studies on early-life effects of vinyl chloride exposure, especially in a species other than rats, would help resolve how the sensitive period corresponds with humans. But he encouraged more studies in young animals to identify other carcinogens that affect sensitive stages of development.

When asked whether other chemicals had been tested, Cogliano replied that vinyl chloride was the first tested and that he would not expect to see a dramatic result with every chemical. "We think it could happen with other chemicals, but we have no data yet," he added.

University of Mississippi's Harihara Mehendale also focused on young animals — specifically, why early postnatal development rats were resistant to a deadly combination of chlordecone (CD) + CCl4 at individually nontoxic doses. Mehendale found that young rats responded faster to tissue injury than adults, and were less susceptible to acute exposure since they were more efficient in stimulating tissue repair.

Mehendale focused on liver injury occurring in postnatally developing and adult male rats and found that prompt and exacting stimulation of tissue repair permitted efficient recovery from injury for the younger rats. Mehendale said that perhaps kidneys and lungs should be examined as well.

Past research has focused on qualitatively defining causal relationships, but the U.S. Army-sponsored conference focused on the need to better define sources and calculate the magnitude of quantitative estimates of risk to sensitive populations.

While the meeting showed a convergence on different methods in variability issues, "early efforts are just that in showing the feasibility of different analyses," said Dale Hattis, a research associate professor at Clark University's Center for Technology, Environment and Development. According to Hattis, there is pressure to better characterize uncertainties to determine whether population subgroups are being adequately protected and whether policymakers are getting the biggest bang for their buck. "There is a need in the current environment to count the bodies," he added.

According to Hattis, it is unlikely that the same factor of 10 rule is appropriate for all different kinds of noncancer risks and different kind of agents, despite the need for relatively straightforward and standardized treatment of variability in toxic risks.

Sociodemographic Factors Affect Susceptibility to Chemicals

Ken Sexton of the University of Minnesota's School of Public Health noted how sociodemographic variables, such as class and race, can affect exposure-related and susceptibility-related attributes which, in turn, can lead to the well-documented disparities in health status among populations.

"There has been a surprising lack of research" in occupational and environmental studies on this issue, said Sexton, who helped launch EPA's National Human Exposure Assessment Survey, an interagency initiative to conduct exposure surveillance of Americans.

Sexton defined individuals and groups at potentially greater risk when they are exposed above a health-related benchmark, more susceptible to the effects of exposure, or both.

Too much regulation also can render groups more susceptible to risk, Sexton said. Increasing regulation can affect socioeconomic status, in turn adversely affecting health, he said.

The congressional debate on risk assessment is raising important questions, such as the impact of cumulative risk, comparative risk and total risk, and bringing together epidemiology and toxicology into "one sphere," he said.

Multiple Chemical Sensitivity Syndrome Explored

How multiple chemical sensitivity is defined will determine how many people are affected, said Claudia Miller, who for the past two years has been involved with Houston Veterans Affairs' Regional Referral Center for Gulf War veterans.

Miller outlined an emerging theory on chemical sensitivity. The idea that it "may be a mechanism for disease posits that a broad spectrum of chronic illnesses, ranging from asthma and migraine to depression and chronic fatigue, may be the consequences of environmental chemical exposures," she said.

First, an initial exposure event interacts with a susceptible individual, causing loss of tolerance to everyday, low-level chemicals, Miller said, adding that substances then trigger symptoms that perpetuate the illness. Seventy-one percent of Gulf War veterans surveyed said they have chemical intolerances, Miller said.

David Oberstreet, research associate professor, University of North Carolina at Chapel Hill, presented findings on his research on Flinders Sensitive Line rats, which are selectively bred to be more sensitive to organophosphate diisopropylfluorophosphate. These rats showed similar symptoms to MCS humans, including depression and reduced activity and appetite, he said.

Please [illegible] to EA Staff — [illegible]
and Jane McNamore - [illegible]

. This test was accepted for review on 3/1?/95
From: John Phillips
5/23/95

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

Name of Agent	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	36507300	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
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 chloride	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 l

BFG41874

BFG 01386

4/7/95

Post-it™ brand fax transmittal memo 7671 | # of pages ▸ 21
To C. Norman... | From B HAYES
Co. PB&B | Co. DOW
Dept. | Phone # (517) 636-3664
Fax # | Fax #

Dr Shah
FYI
JE Bamlet

ATSDR Chemicals Added to MTL

EPA is adding 12 chemicals to the Master Testing List in response to a request for testing by the Agency for Toxic Substances and Disease Registry (ATSDR). The chemicals are: benzene, beryllium, chloroethane, chromium, cyanide, di (2-ethylhexyl) phthalate, mercury, methylene chloride, tetrachloroethylene, toluene, trichloroethylene, and vinyl chloride.

ATSDR is required to identify the hazardous substances most commonly found at Superfund sites, prepare toxicological profiles, and identify priority data needs for those substances. ATSDR is also required to initiate a research program to meet the priority data needs it identifies.

In October 1992, ATSDR requested EPA to use its authorities under TSCA and FIFRA to fill some of the data needs it identified on 37 chemicals. In its response to ATSDR, EPA agreed to develop a test rule under section 4 of TSCA to obtain data on 12 of the chemicals, but noted that a TSCA test rule would not be an appropriate mechanism for obtaining data on the other 25 chemicals. Before initiating rulemaking, EPA is inviting manufacturers of the 12 chemicals listed in the following table to submit testing plans and enter into consent agreements for testing. EPA intends to issue a test rule in late 1994 for any of the 12 substances which are not covered by a consent order or a voluntary testing agreement.

Chemical	Testing to be Proposed
Mercury	Immunotoxicity oral Chronic oral Reproductive oral Acute oral
Vinyl chloride	Reproductive inhalation Developmental inhalation
Benzene	Subchronic oral Neurotoxicity oral
Tichloroethylene	Subchronic oral Neurotoxicity oral
Chromium	Acute oral Reproductive oral Immunotoxicity oral
Tetrachloroethylene	Reproductive inhalation Neurotoxicity inhalation Immunotoxicity inhalation Developmental inhalation
Cyanide	Acute inhalation Subchronic inhalation Developmental inhalation Fate in soil
Beryllium	Acute inhalation Subchronic inhalation with reproductive and pulmonary pathology Developmental inhalation Immuotoxicity inhalation Bioavailability Fate in air
Toluene	Comparative Pharmacokinetics Immunotoxicity oral
Methylene chloride	Subchronic oral Immunotoxicity oral Developmental oral Neurotoxicity oral
Chloroethane	Comparative Pharmacokinetics Immunotoxicity oral

BFG41875

BFG 01387

SCIENTIFIC SEMINAR ON VINYL CHLORIDE

Thursday, October 6, 1994

U.S. EPA — WASHINGTON DC

Name	Affiliation	Address
Jim Cogliano	U.S. EPA — ORD	401 M Street SW Wash DC 20460
Jonathan Rambow	Dow Chemical	1803 Building, Midland, MI 48674
Patrick Wofford	Georgia Gulf	PO Box 2109 Plaquemine LA
Larry Valcovic	USEPA ORD	
LINDA TUXEN	U.S. EPA/ORD	
Alan Yorkeles	US EPA/OERR	5203G
John Balbus Kornfeld	USEPA/ Johns Hopkins U.	
Jean D. Kynaak	Occ Chem, Niagara Falls.	360 Rainbow Blvd S.
Karen Hogan	US EPA - OPPT	7403
Elizabeth Margosches	USEPA - OPPT	7403
MARK GRUENWALD	BORDEN INC	1105 SCHROCK RD. COLUMBUS OH 43229
Charli Hiremath	U.S. EPA HHAG/OHEA/OD	
BILL PEPELKO	US EPA HHAG	
Chao W. Chen	EPA/HHAG/OD	8602
ED BEELER	THE GEON CO.	6100 OAK TREE BLVD CLEV. OH 44131
MIKE GARGAS	CHEMRISK McLAREN/HART	29225 CHAGRIN BLVD, CLEVE. OH 44122
DAVID BAYNES	USEPA - ORD	MAIL CODE 8602
Arthur Chiu	EPA/OHEA/ORD	mail code 8602
Hugh McKinnon	EPA/ORD	MC 8602
Jim Holder	EPA/ORD/OHEA/HHAG	8602 2605721
Hasmukh Shah	CMA	2501 M St., N.W., phone Wash. D.C. 202/887 1192
Dave Penney	Vista Chemical Co	12024 Vista Park Dr. Austin, TX
James Swenberg	Univ. of North Carolina	CB# 7400 Chapel Hill NC 27599-7400
Richard Reitz	ChemRisk McLaren/Hart	Cleveland OH
Harvey Clewell	ICF/Kaiser	Ruston LA
David Reese	EPA - ORD	
Sheila Rosenthal	EPA - ORD	
JAMES A. BARTER	PPG INDUSTRIES	ONE PPG PLACE PITTSBURGH PA 15272

BFG 01388

BFG41876