MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for polyethylene glycol (CAS #25322-68-3)

FROM: Anne Kim, Air Quality Division, Toxics Unit

SUBJECT: Screening Level Derivation

DATE: ~~July~~ 2, 2007
June 29

The initial threshold screening level (ITSL) for polyethylene glycol 3350 (PEG 3350) is 8 µg/m³ based on an annual averaging time. ITSLs will not be established for PEG 200, PEG 400, or PEG 100,000 at this time due to their particulate nature, and relatively low levels of apparent toxicity. Instead, the National Ambient Air Quality Standard for particulate matter (NAAQS PM) should be utilized for establishing acceptable emission rates and ambient air impacts.

The following references or databases were searched to identify data to determine the screening level: U.S. Environmental Protection Agency (EPA) Integrated Risk Information System, Registry for Toxic Effects of Chemical Substances, American Conference of Governmental and Industrial Hygienists Threshold Limit Values, National Institute for Occupational Safety and Health Pocket Guide to Hazardous Chemicals, Environmental Protection Bureau Library, International Agency for Research on Cancer Monographs, Chemical Abstract Service (CAS) - Online (1967 – 2006), National Library of Medicine, Health Effects Assessment Summary Tables, and National Toxicology Program Status Report. The EPA has not established a reference concentration or reference dose for polyethylene glycol.

Background

Polyethylene glycols (PEGs) are polymers of ethylene oxide. The molecular weight of PEGs can range between 200 and 8,000,000. PEGs with molecular weights below about 600 are clear liquids and PEGs with molecular weights approximately 1000 to 10,000 are white, waxy solids (Carbowax). PEGs with molecular weights higher than 10,000 are highly polymerized molecules, known as Polyox Water Soluble Resins. PEGs are used in a variety of applications: as lubricants, plasticizers, binders, water-soluble ointment bases and suppository bases, carriers for medicaments, ingredients for skin creams and hair dressings, and solvents for dyes used in lipsticks. (Crook et al., 1981; Leung et al., 2000)

Animal Toxicity

Acute:

An acute toxicity experiment was conducted (Bartsch et al., 1976) using SPF-NMRI mice and SPF-Sprague-Dawley rats. Each dose group consisted of five males and five females. 10 mL/kg PEG 400 was administered intravenously and intraperitoneally, and 20 mL/kg or 30 mL/kg PEG 400 was administered perorally. The LD50 results for the mouse and rat are in Table 1 below.

Table 1. LD50 results in mL/kg

	IV	IP	PO
mouse LD50	7.6	12.9	26
rat LD50	6.5	13.1	30

A study conducted in 1961 (Boyland et al., 1961) tested the carcinogenic effect of PEG 1000 (Carbowax 1000) in 20 mice exposed vaginally twice weekly for one year. After 18 months, all surviving mice were sacrificed. At 12 months, 11 mice were still alive; at 18 months, 7 mice were still alive, and five mice were found to be with carcinomata. Because there was a high incidence of tumors in the mice treated with PEG, the investigators questioned the procedure by which the chemical was administered pointing out that there was a possibility that the occurrence of tumors was due to low osmotic pressure. Another experiment followed, where 30 mice were vaginally exposed to PEG or to PEG mixed with sodium chloride. The results of this experiment are tabulated below in Table 2.

Table 2. Survival numbers and carcinomata incidence

	12 months	18 months	carcinomata
PEG alone	24	20	2
PEG with 0.8% NaCl	22	14	5
PEG with 30% NaCl	18	14	8

The investigators concluded that the second experiment showed that "the carcinogenic action of PEG is unlikely to be due to the effect of the low osmotic pressure... [and that] [a]lthough the PEG used in the experiment may have induced tumors, the material would probably not present a hazard to man" (Boyland et al., 1961).

A study was conducted using Sprague-Dawley rats for oral toxicity testing and Fischer 344 rats and B6C3F1 mice for inhalation toxicity testing (Crook et al., 1981). Three male and 3 female rats were given 15.8 mL/kg to 32.0 mL/kg of PEG 200 by oral intubation after having fasted from the night before. Six hours after dosing, food and water were again provided. These rats were observed for 14 days for signs of toxicity and mortality. Groups of 12 rats and 12 mice were exposed by inhalation to a concentration of 2516 mg/m^3 aerosolized PEG 200 for six hours. Ninety percent of the aerosolized particles was less than 2 microns in diameter. These animals were observed for toxic signs and mortality during a 14-day post-exposure period.

Oral study results: All rats in the 32.0 mL/kg group showed ataxia before death. The LD50 values for male and female rats were 28.77 g/kg and 27.56 g/kg, respectively. These animals exhibited ataxia and convulsions which progressed to prostration and death. Blood chemistry, hematology, respiratory physiology, and pathology were examined in the animals exposed by inhalation. Blood chemistry results showed no significant alterations in both rats and mice. Hematological examination showed that one of the exposed male rats showed a significantly increased hematocrit value compared to control values. A significant difference was found in the differential lymphocyte percentages in all exposed female rats. The authors, however, pointed out that all values were within historical control limits.

Inhalation study results: Respiratory physiology testing resulted in lower fR values in the exposed females compared to control, but these lower values were within historical values. Pathological examination showed no significant lesions that could be directly attributed to PEG 200 exposure. Mild lesions were found in a few organs (eg., lung, kidney, liver, and adrenal cortex) in both treated and control animals. Because there were no deaths after six hours of inhalation exposure to 2516 mg/m^3 of PEG 200, the LC50 was established at a value greater than 2516 mg/m^3.

Oral:
A subchronic, chronic, and pharmacokinetic study was conducted using Fischer 344 rats to evaluate the toxicity of a PEG of higher molecular weight (Leung et al., 2000). The PEG tested had a molecular weight of about 100,000 daltons. The subchronic study exposed 20 rats/sex/group to PEG in the diet at concentrations of 0%, 0.1%, 0.5%, 1.5%, or 3% for 13 weeks. The control and high-dose group had an extra 10 rats/sex for a 6-week recovery period. The chronic study exposed 100 rats/sex/group to PEG in the diet at concentrations of 0%, 0.1%, 0.5%, or 2% for 104 weeks. Two interim sacrifices were performed on 10 rats/sex/group at 12 months and 18 months. For both the subchronic and chronic studies, observations for mortality were made twice daily, detailed clinical observations were made once weekly, and observations for overt clinical signs were made once daily. Before the first exposure and before sacrifice, ophthalmic examinations were made. Body weight and food consumption were recorded once weekly for thirteen weeks and every other week thereafter. Only for the chronic study was water consumption also measured in 10 rats/sex/group once a week for two weeks. Blood samples were taken at 4 and 13 weeks in the subchronic study and at 3, 6, 12, 18, and 24 months in the chronic study. The animals in the 6-week recovery group (from the subchronic study) had blood samples taken during the 19th week. Urine samples were taken one week before each week that blood samples were taken. At necropsy, the brain, heart, liver, spleen, kidneys, adrenals, and gonads were weighed. Microscopic examinations of tissues from the control and high-dose groups were performed during the 13th week of the subchronic study. For the chronic study, microscopic examinations of tissues from the control and 2% group were performed at all interim and the final sacrifices. A smaller subset of tissues was examined microscopically in all other dose groups for both the subchronic and chronic studies. The livers of 5 male and 5 female rats from the control group and 3% group that were exposed for 90 days (the subchronic study) were morphometrically analyzed upon sacrifice. After 16 hours of fasting, the rats in the pharmacokinetic study were given 1% 14-C labeled PEG by gavage. A group of 4 male and 4 female rats were used to collect blood samples, and another set of 4 male and 4 female rats were used to collect urine, feces, and expired air.

Subchronic study results: No deaths occurred and no clinical observations were found attributable to PEG exposure. Although mean food consumption was increased in both male and female rats, it did not increase with increasing dose. Male rats of the 0.5% and 1.5% groups showed slight, but statistically significant, increases in the mean body weight gains in the first and second weeks of exposure. Female rats consistently showed increased mean absolute body weights and mean body weight gains, but this effect was not dose-dependent. The mean absolute liver weight was statistically significantly increased in female rats by 5%, 7%, and 8% in the 0.1%, 1.5%, and 3% groups, respectively. The liver weights relative to the final body weights and brain weights were also found to be statistically significantly increased in the 1.5% and 3% groups. The female rats from the 6-week recovery group showed persistently increased mean absolute liver and kidney weights and increased liver weight relative to the brain weight. The only statistically significant finding from morphometric analyses of the liver was an increased mean nuclear to cytoplasmic ratio in the female rats in the 3% group.

Chronic study results: No change in survival rate, mean survival time, clinical observations, mean absolute body weight and body weight gain, or mean consumption was found. An increase and decrease in absolute brain weight were noted for the 0.5% females and the 2% females, respectively; these changes were not attributed to PEG exposure because it was not dose-dependent. An increase in mean kidney weights relative to the final body weight was seen in the 2% female rats but was discounted after finding no associated biochemical or histological changes. The histopathological results were reported as sporadic "with no apparent dose-response relationship".

Pharmacokinetic study results: Seventy-two hours after the radiolabeled dose was administered via gavage, almost all was excreted in the feces, and less than 1% was detected in the urine and the expired air combined.

Increases in the mean absolute body weights and mean body weight gains in the 1.5% and 3% group females were explained by the observed increased food consumption, which was proposed to be due to increased palpability from the addition of PEG or compensation for decreased nutritional value with the addition of PEG. The authors did not attribute PEG exposure as the cause of the increases seen in liver weight but, rather, to the, again, increased food consumption. The microscopic changes noted in the liver were also not attributed to PEG exposure because "they were random in nature." Kidney weight increases were seen in the 1.5% and 3% females, but they were not considered to be related to PEG exposure since there were no accompanying clinical, anatomical, or pathological changes and also because this increase was not seen in the results of the chronic study. Thus, the NOEL was established at about 1000 mg/kg/day (2% dose level of the chronic study), and the conclusion that PEG "is not absorbed from the gastrointestinal tract" was based on the results of the pharmacokinetic study.

A study conducted in 1995 (Hermansky et al., 1995) tested the effects of PEG 400 exposure by gavage in Fischer 344 rats. Ten male rats and 10 female rats were exposed to concentrations of 0, 1.0, 2.5, or 5.0 mL/kg body weight/day (1.1, 2.8, and 5.6 g/kg, respectively) five days per week for thirteen weeks. The control group was given 5.0 mL water/kg body weight/day. An additional 10 rats per sex were placed in the control and high-dose groups for a 6-week recovery period. A preliminary study had been conducted to select the study dose levels. Exposure to 10 mL of PEG 400/kg for 12 days caused loose feces in all animals, but exposure to 5 mL of PEG 400/kg caused loose feces in only half of the animals. Therefore, the high dose for this subchronic study was set at 5.0 mL/kg/day. Observations for clinical signs of toxicity were made once a day, and twice a day for mortality. Once a week, body weight measurements and more detailed clinical observations were made. Food and water consumption were recorded weekly. Blood samples were taken after the last day of exposure and at the end of the recovery period (weeks 13 and 19, respectively). Twenty-four-hour urine samples were taken one week before blood samples were collected (weeks 12 and 18, respectively). Animals were fasted before termination by exanguination. Complete autopsy was performed and several organs were weighed. Five females (3 low-dose and 2 high-dose) died before study termination. Due to findings of esophageal or respiratory injury, these deaths were not attributed to PEG 400 exposure but, rather, to dose administration trauma. One low-dose male was also found dead during the study period for unknown reasons, but because there were no other deaths in other groups, this was not considered due to PEG 400 exposure.

Loose feces occurred in most all animals in the high-dose group during the first week of exposure and returned towards the end of the dosing period, being apparent in 20% of the 2.5 mL/kg males, 70% of the 5.0 mL/kg males, and 61% of the 5.0 mL/kg females. Male and female mean absolute body weights were slightly decreased during exposure and recovery.

Although not statistically significant, the 2.5 and 5.0 mL/kg males showed decreased food consumption throughout the entire study. Water consumption was increased in all dose groups showing a dose-dependent trend. During recovery, the water consumption measurements normalized to control values. No adverse effects were noted from hematological or clinical chemistry analyses. Urinalysis results showed a dose-dependent increase in NAG activity, osmolality, and specific gravity for the exposed male rats. The female rats in the high dose showed statistically significant increased specific gravity. The urine pH was decreased in all exposed animals except the low-dose females. Protein and bilirubin concentrations in the urine were increased in all exposed male rats. The 2.5 and 5.0 mL/kg females also showed increased urinary protein concentrations. The high-dose male rats showed increased levels of red and white blood cells in the urine. The relative kidney weights of the males were increased by 2%, 4%, and 4% in the 1.0, 2.5, and 5.0 mL/kg groups, respectively. The female rats showed a slight increase in relative kidney weights in the 2.5 and 5.0 mL/kg dose levels and persisted in this increase after the 6-week recovery period. The kidney weight changes in the male rats, however, reverted to control values after recovery. No animal was found to have any gross or microscopic lesions in the kidney or bladder. Though microscopic examination of the kidney did not reveal any lesions, because of the increased urinary NAG activity and increased urinary protein and bilirubin concentrations found in the male rats at 2.5 mL/kg and both sexes at 5.0 mL/kg, the investigators concluded that slight, reversible renal toxicity may have been caused by exposure to PEG 400.

Inhalation:
An inhalation study was conducted to determine the effects of subchronic exposure to PEG 200 (Crook et al., 1981). A total of 216 Fischer 344 rats and 90 B6C3F1 mice were exposed to 100 or 1000 mg/m^3 PEG 200 six hours per day, five days per week for thirteen weeks. The animals were observed daily for toxic signs and mortality. Body weights were recorded every other week, at which point more detailed clinical observations were made. Each dose group, including control, contained 30 mice: 10 were exposed for six weeks, 10 were exposed for thirteen weeks, and 10 were given a 30-day recovery period after thirteen weeks of exposure (a total of 90 mice). Each dose group, including control, contained 72 rats: 24 were exposed for six weeks, 24 were exposed for thirteen weeks, and 24 were given a 30-day recovery period after thirteen weeks of exposure (a total of 216 rats). Hematological and pathological examinations were conducted after each respective exposure period and post-exposure period. Pulmonary function tests were also conducted at the end of each exposure and post-exposure period. Tissues and organs were evaluated grossly and microscopically, and organs were weighed.

Combined Study results: Animals exposed to the high dose showed oily fur after each exposure. No death occurred in the rats exposed to PEG 200, and of the mice that died, none were considered to be treatment-related deaths; only one male mouse died prematurely from a cage-loading injury in the low-dose group. Body weight changes were not significant, with both rats and mice leaning toward the greater during the 30 days of recovery. Pathological examination revealed no treatment-related lesions in either rat or mouse.

Rat study results: Three control, 2 low-dose, and 3 high-dose males and 1 low-dose female rat showed proliferative interstitial pneumonia after six weeks of exposure. Inflammation of the turbinates was also seen in a control female and 2 low-dose male rats. After thirteen weeks of exposure, foamy macrophages were found in the lung of a high-dose male. In two separate control females, suppurative inflammation of the turbinates and a renal cortical cyst were observed. Rats given the 30-day recovery period after thirteen weeks of exposure also showed evidence of suppurative inflammation of the turbinates (low-dose female) and foamy

macrophages in three females (1 control, 1 low-dose, and 1 high-dose). One high-dose female had inflammation of the renal pelvis.

Mouse study results: A decrease in respiratory rate and an increase in pulmonary resistance were observed only in the female mice exposed to 1000 mg/m^3 for 6 weeks. Because this change in pulmonary function was not seen in the females of 13 weeks of exposure or 30 days of post-exposure and not seen in the males of any group, this change was considered transient. Three low-dose mice (1 male and 2 female) had interstitial pneumonia after six weeks of exposure. A control female mouse showed degeneration of the adrenal cortex. Degeneration of the renal tubule was found in all male mice, including controls. One high-dose female showed degenerative changes in the liver. Cystic endometrial hyperplasia was seen in five control and five exposed female mice (which dose levels were not indicated). After 13 weeks of exposure, foamy macrophages in the lung were observed in a low-dose male. Three controls (2 male and 1 female) and one high-dose male had interstitial pneumonia. As in the 6-week male mice, all male mice in the 13 week-study showed degeneration of the renal tubule. Cystic endometrial hyperplasia was seen in five control, four low-dose, and one high-dose female mice. One low-dose female mouse showed signs of endometriosis. The mice that were allowed 30 days to recover also showed evidence of foamy macrophage infiltration in the lung (one high-dose male), interstitial pneumonia (one control, 2 low-dose, and 1 high-dose males), and renal tubular degeneration in all males. A single low-dose female showed degeneration of the adrenal cortex. Endometrial cysts were found in five control, four low-dose, and three high-dose females. One high-dose male had hydronephrosis.

The study investigators concluded that none of the lesions found were related to PEG 200 exposure because there was no dose-response relationship evident, and many lesions occurred in control animals as well.

A two-week study was conducted exposing F344 rats to PEG 3350 aerosols at concentrations of 0, 109, 567, or 1008 mg/m^3 six hours per day, five days per week (Klonne et al., 1989). Each dose group consisted of 10 male and 10 female rats with the control and high-dose group having an additional 10 rats per sex for a 2-week recovery period. Clinical observations were made for signs of toxicity before, during, and after exposure. Body weights were measured before exposure and on days 1, 2, 5, 6, 7, and 9 of exposure, and the additional rats were weighed once a week during the 2-week recovery period. Prior to sacrifice, all rats were weighed one last time. Organ weights were measured and ophthalmologic, pathologic, and microscopic examinations were performed. Blood and urine samples were collected the day after the last exposure was given. The mass median aerodynamic diameters (MMADs) for each concentration level were 6.1, 5.0, and 3.8 for the 109, 567, and 1008 mg/m^3 groups, respectively. No deaths were found, and no treatment-related effects were found from the ophthalmic examination or from the blood and urine tests.

Statistically significant decreases in body weight gain were seen in the male rats of the 567 and 1008 mg/m^3 groups; there was no dose-response relationship since the amount of decrease was similar for both dose groups. Additionally, the recovery rats showed no difference in body weight gain from that of control. Male rats exposed to 1008 mg/m^3 showed increased neutrophil count by 50%, but this change was not observed in any other group, including the recovery group animals. The only organ that showed any weight differences was the lung. The absolute and relative lung weights were statistically significantly increased for the 1008 mg/m^3 group rats. Absolute and relative lung weights of the 567 mg/m^3 group rats were also increased, being statistically significant only in the male rats. The animals from the two-week recovery group also showed increased absolute and relative lung weights. The percent difference from control

lung weights was small in the recovery group animals compared to the 1008 mg/m^3-exposed animals. Histologic examination revealed a concentration-dependent finding of alveolar histiocytosis (alveoli containing macrophages) and foamy vacuolated cytoplasms. The presence of macrophages was detected in the animals allowed two weeks to recover. The authors depicted this finding in the lung as a natural response to any particle entering the lung; therefore, concluding that the incidence of alveolar histiocytosis is not specifically due to PEG 3350 exposure.

Human Toxicity

In the industrial setting, the only route of exposure that is practically applicable is the dermal route; PEGs are "essentially inert" when exposed to orally, and the inhalation route is normally of no concern since the vapor pressure is extremely low. PEGs are considered to be chemicals that are not significantly irritating to the eyes, skin, or mucous membranes. In fact, PEGs have been used in solutions in direct contact with human eyes for decontamination purposes. For the general human population, humans are expected to be exposed frequently via the oral and dermal routes because of the heavy use of PEGs in the cosmetic and pharmaceutical industries. A workplace environmental exposure level (WEEL) for a PEG aerosol is set at 10 mg/m^3, an 8-hour TWA. (HSDB, 2007)

Discussion

The interesting thing about this chemical is that the CAS number is identified with all PEGs no matter the molecular weight or degree of polymerization. With toxicity study results based on a variety of PEGs – yet having the same CAS number – it is perplexing to try to identify which toxicity study results ought to be used to represent the whole class of PEGs under this single CAS number. For initial screening purposes, the toxicity study results producing the most protective initial threshold screening level (ITSL) will be selected to be the critical study with the critical effect on which the ITSL will be based.

The two inhalation studies, one testing PEG 200 (a 13-week – Crook et al., 1981) and the other testing PEG 3350 (a 2-week – Klonne et al., 1989), reported effects in the respiratory system. The changes found in these studies, however, were suggested by the investigators to be adaptive, or a natural response, or not related to PEG exposure. In any case, lung effects were observed and persisted even after two weeks of recovery (Klonne et al., 1989). Using these studies' results, the ITSLs for PEG 200 and PEG 3500 were calculated to be 100 ug/m^3 based on a 24-hour averaging time and 8 ug/m^3 based on an annual averaging time, respectively.

The two oral studies, one testing PEG 100,000 (a 104-week – Leung et al., 2000) and the other testing PEG 400 (a 13-week – Hermansky et al., 1995), produced relatively high ITSLs – ranging from 3500 to 35000 ug/m^3 based on a 24-hour averaging time. This supports the notion that oral exposure to PEG is not particularly toxic.

***Appendix A** presents the ITSL derivation calculations for PEGs 200, 400, and 100,000.*

In addition to background particulate matter levels, the ITSLs for PEG 200, PEG 400, and PEG 100,000 are greater than the National Ambient Air Quality Standard for particulate matter (NAAQS PM) (Table 3).

Table 3. National Ambient Air Quality Standard for Particulate Matter

	PM10	PM2.5
annual	50 ug/m^3	15 ug/m^3
24-hour	150 ug/m^3	65 ug/m^3

It is considered inappropriate to set an ITSL for a chemical emitted as particulate matter that is greater than the NAAQS, especially considering the lack of chronic inhalation toxicity data for PEG 400 and PEG 100,000. Therefore, as long as the predicted ambient impact (PAI) of polyethylene glycol combined with the background particulate matter concentration is less than the NAAQS PM for both PM10 and PM2.5, then adverse health effects would not be expected to occur, and compliance with health-based screening level requirements of the air toxic rules is satisfied, except as noted below.

In the case, however, the PEG in question has a molecular weight of about 3000 to 4000, the PEG 3350-specific ITSL should be used to determine compliance.

PEG 3350: The NOAEL of 109 mg/m^3 derived from Klonne et al.'s study, based on the critical effect of lung weight increases and associated histologic alveolar histiocytosis and foamy vacuolated cytoplasms, will be used to calculate the ITSL.

Derivation of Screening Level

$$ITSL = \frac{NOAEL}{35 \times 100} \times \frac{\text{hours exposed per day}}{24 \text{ hours per day}}$$

>where NOAEL = no-observed-adverse-effect level

Note NOAEL & hours exposed per day:
NOAEL = 109 mg/m^3 from Klonne et al. (1989)
Hours exposed per day = 6 hours from Klonne et al. (1989)

$$ITSL = \frac{109 \text{ mg/m}^3}{35 \times 100} \times \frac{6 \text{ hours per day}}{24 \text{ hours per day}}$$

ITSL = 0.0077857 mg/m^3

ITSL = 7.7857 ug/m^3 = **8 ug/m^3**

Therefore, the ITSL for polyethylene glycol 3350 (25322-68-3) is 8 ug/m^3 based on an annual averaging time.

References

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APPENDIX A

PEG 200:

Calculation of $NOAEL_{[ADJ]}$:

$NOAEL_{[ADJ]}$ (mg/m^3) = E (mg/m^3) x D (hrs/24 hrs) x W (days/7 days)

$NOAEL_{[ADJ]}$ = the effect level obtained with an alternate approach, adjusted for duration of experimental regimen

E = experimental concentration level

D = number of hours exposed/24 hours

W = number of days of exposure/7 days

$NOAEL_{[ADJ]}$ = 1000 mg/m^3 x (6 hrs/24 hrs) x (5 days/7 days)

$NOAEL_{[ADJ]}$ = 180 mg/m^3

Calculation of $NOAEL_{[HEC]}$:

$NOAEL_{[HEC]}$ (mg/m^3) = $NOAEL_{[ADJ]}$ (mg/m^3) x $RDDR_r$

$NOAEL_{[HEC]}$ = the effect level obtained with an alternate approach, dosimetrically adjusted to an HEC

$NOAEL_{[ADJ]}$ = defined above

$RDDR_r$ = the regional deposited dose ratio; a dosimetric adjustment factor for respiratory tract region, r (in this case total respiratory – TOT)

Calculation of $RDDR_{TOT}$: via RDDR program (EPA, YEAR)

*MMAD = 0.71 *geo std dev = 1.97			Extrathoracic		Tracheobronchial		Pulmonary		Thoracic		Total RT		Extrarespiratory	
Species	BW (g)	VE (mL)	SA (cm^2)	dep	SA (cm^2)	dep	SA (cm^2)	dep	SA (cm^2)	dep	SA (cm^2)	dep	BW (g)	dep
Rat	110	91.7	15.00	0.056	22.500	0.091	0.340	0.065	0.342	0.155	0.344	0.212	110	0.212
Human	70000	13800.0	200.0	0.114	3200.0	0.028	54.000	0.272	54.320	0.125	54.340	0.415	70000	0.415
RATIO	0.002	0.007	0.075	0.493	0.007	3.247	0.006	0.237	0.006	1.242	0.006	0.511	0.002	0.511
RDDR			0.044		3.067		0.250		0.546		**0.536**		2.159	

*These values obtained from a study evaluating PEG 3500 (Klonne et al., 1989).

$NOAEL_{[HEC]}$ (mg/m^3) = 180 mg/m^3 x 0.536

$NOAEL_{[HEC]}$ (mg/m^3) = 96.48 mg/m^3

Calculation of RfC:

$$RfC = \frac{NOAEL_{[HEC]}}{UF}$$

RfC = reference concentration
$NOAEL_{[HEC]}$ = defined above
UF = uncertainty factor

> UFs that apply: 1) variation in sensitivity among members of the human population = 10
2) extrapolation from animal data to humans = 10
3) extrapolation from sub-chronic to chronic = 10

$$RfC = \frac{96.48\ mg/m^3}{10 \times 10 \times 10}$$

RfC = 0.09648mg/m^3 = **100 ug/m^3** - based on a 24-hour averaging time

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PEG 400:

$$ITSL = \frac{1}{500} \times \frac{1}{40} \times \frac{1}{100} \times \frac{LD50\ (mg/kg) \times W_A}{0.167 \times I_A}$$

>where W_A = Body weight of experimental animal in kilograms (kg)
I_A = Daily inhalation rate of experimental animal in m^3/day

Note LD50:
LD50 = 28.63 g/kg from Bartsch et al. (1976)
LD50 = 28.63 g/kg x (1000 mg/g) = 28630 mg/kg

W_A = mean value of the weights 15 g and 25 g (Bartsch et al., 1976)

$$W_A = \frac{15 + 25}{2}$$

W_A = 20 g (1 kg/1000 g) = 0.02 kg

$I_A = 1.99W_A^{1.0496}$
$I_A = 0.8(0.02)^{1.0496}$
I_A = 0.0328 m^3/day

$$ITSL = \frac{1}{500} \times \frac{1}{40} \times \frac{1}{100} \times \frac{28630 \times 0.02}{0.167 \times 0.0328}$$

ITSL = 0.052267 mg/m^3

ITSL = 52.27 ug/m^3 = **50 ug/m^3** - based on an annual averaging time

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PEG 100,000:
Note: NOAEL = 1000 mg/kg
Derivations of Screening Level
ITSL = RfD x (70 kg)/(20 m^3)
>where RfD = reference dose

Calculation of RfD:

$$RfD = \frac{NOAEL}{UF}$$

>where RfD = defined above
UF = uncertainty factor
UFs that apply: 1) variation in sensitivity among members of the human population = 10
2) extrapolation from animal data to humans = 10

$$RfD = \frac{1000\ mg/kg}{10 \times 10}$$

RfD = 10 mg/kg

ITSL = 10 mg/kg x (70 kg)/(20 m^3)

ITSL = 35 mg/m^3

ITSL = **35000 ug/m^3** - based on a 24-hour averaging time