File No: NA/817

August 2000

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

Triethylene Glycol Dibenzoate

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Director
Chemicals Notification and Assessment

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Triethylene Glycol Dibenzoate

1. APPLICANT

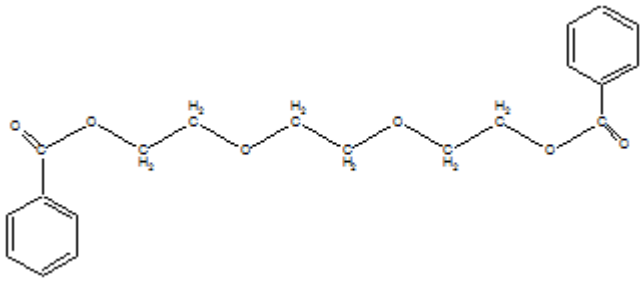
Velsicol Australia Limited of 10 William Street TURRAMURRA NSW 2074 has submitted a standard notification statement in support of their application for an assessment certificate for 'Triethylene Glycol Dibenzoate'.

2. IDENTITY OF THE CHEMICAL

The notifier did not apply for any information relating to 'Triethylene Glycol Dibenzoate' to be exempt from publication in the Full Public Report and Summary Report.

Chemical Name:	Triethylene glycol dibenzoate.
Chemical Abstracts Service (CAS) Registry No.:	120-56-9
Other Names:	Benzoflex S-358; Ethanol, 2,2'-[1,2-ethanediylbis(oxy)]bis-, dibenzoate; Ethylenbis(oxyethylene)dibenzoate.
Marketing Name:	Benzoflex 2088 (product containing 25% Benzoflex S-358).
Molecular Formula:	$C_{20}H_{22}O_6$

Structural Formula:



Molecular Weight: 358.39

Method of Detection and Determination: UV, IR, NMR and GC

Spectral Data: Spectra of UV, IR and NMR were provided. The characteristic absorbances serve to identify and characterise the new chemical.

- **Comments on Chemical Identity**

The new chemical is the di-ester of triethylene glycol with benzoic acid, although the commercial product contains around 1.3% of the mono-ester and a small percentage of dipropylene glycol esters.

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C & 101.3 kPa: White to off-white solid with a mild ester odour.

Melting Point: 43.5-49.0°C (see comments below).

Boiling Point: Not determined; decomposes above 230°C without boiling.

Specific Gravity: 1.256

Vapour Pressure: 2.5×10^{-8} kPa at 25°C (see comments below).

Henry's law Constant: 2.83×10^{-4} Pa.m^3/mol (see comments below).

Water Solubility: 30.4 mg/L (see comments below).

Partition Co-efficient (n-octanol/water): Log P_{OW}=3.2 (see comments below).

Hydrolysis as a Function of pH: $T_{1/2}$ at pH 9 = 4.9 days (calculated);
$T_{1/2}$ at pH 8 = 49 days (calculated);
$T_{1/2}$ at pH 7 = 1.3 years (calculated);
(see comments below).

Adsorption/Desorption: Log K_{OC}=3.2 (see comments below).

Dissociation Constant:	Not determined (see comments below).
Flash Point:	151°C
Flammability Limits:	Non-pyrophoric.
Autoignition Temperature:	None below 400°C.
Explosive Properties:	Not explosive.
Reactivity/Stability:	Non-oxidising.

Comments on Physico-Chemical Properties

The physico-chemical properties of the compound were determined using OECD test protocols.

The melting point range was determined using the capillary tube method. The 5.5 ºC range of melting temperatures is in accordance with the presence of congeners of the notified chemical in the test material. The boiling point could not be determined since the test substance decomposed without boiling at temperatures above 230 ºC.

The vapour pressure (VP) was determined using a balance system where the VP was determined at a number of temperatures between ambient and 250 ºC using a mass difference technique. The data were then fitted to a linear relation relating LogVP to reciprocal temperature (degrees K), and this relationship used to calculate the VP at 25 ºC. The relationship derived from the data was:

$$\text{Log VP (Pa)} = -3729.81/T(^{o}K) + 7.895$$

A lowVP for a compound of this nature with high molecular weight is expected, but it should be noted that since the material contains an appreciable amount of lower molecular weight impurities (eg. triethylene glycol monobenzoate) which are likely to be more volatile, the measured VP may be appreciably higher than that of the pure notified chemical.

The water solubility was determined in triplicate using the shake flask method. Approximately 2 g of the test material was weighed into five separate flasks, then shaken with 100 mL of pH 7.0 buffer ($H_2PO_4^-/OH^-$) at 30 ºC for 1, 2, 3, 4 and 5 days. Following this period of agitation the flask was allowed to stand for at least 24 hours at 20 ºC, and the resulting solutions were filtered and analysed for the dissolved material. Each aqueous solution was extracted three times with ethyl acetate, the combined extracts evaporated to dryness, the resulting residue taken up in acetone, and the acetone solutions then analysed (in duplicate) for the test compound using gas chromatography. The resultant concentrations of triethylene glycol dibenzoate in the aqueous phase were determined as 19.0, 22.2, 29.7, 31.8 and 29.7 mg/L for the agitation periods of 1, 2, 3, 4 and 5 days respectively. The mean for the last three days is 30.4±1.1 mg/L, and this was taken as the solubility of triethylene glycol dibenzoate in water. It should be noted that the gas chromatogram also detected impurities in the aqueous extract, and the test report noted that the triethylene glycol monobenzoate is appreciably more water soluble than the dibenzoate.

The Henry's Law Constant at 20 ºC was calculated from the measured VP and water solubility at this temperature (see above) using the formula:

H = Vapour pressure x MW/Water solubility.

Hydrolytic degradation and fat solubility of the compound were not determined experimentally. However, in respect of hydrolytic degradation, although the ester functionalities may be susceptible to hydrolytic cleavage under extremes of pH, hydrolysis is unlikely in the environmental pH range between 4 and 9.

The n-octanol/water partition coefficient was determined in triplicate using the HPLC method, where the retention time of the test compound on C_{18} columns was compared with those for seven reference compounds of known Pow. The reference compounds ranged from ethyl benzoate (Log Pow = 2.6) to triphenylamine (Log Pow = 5.7). The retention times of the major component of the new material indicated a Log Pow of 3.2 for all three samples tested. The report also included an estimate of Log Pow of 2.77 based on Quantitative Structure Activity Relationships (QSAR).

Log Pow values of this magnitude indicate that the compound has a moderately high affinity for the oil phase, a property expected for compounds with high aliphatic and aromatic hydrocarbon content.

The value for Log Koc, a measure of the compound's ability to bind to the organic component of soils and sediments, was also determined using comparison of retention times on a C_{18} HPLC column. Six standard compounds were employed ranging from phenol with Log Koc = 1.43, to 4, 4'-DDT with Log Koc = 5.38. The retention time of the new compound was intermediate between the values of these two end sequence reference compounds, and provided the value for Log Koc of 3.2. This high value for Log Koc indicates that the chemical will bind strongly to the organic component of soils and sediments, although some mobility in these media may be possible.

The new compound contains no acidic or basic groups, so dissociation constant data are not relevant.

The ASTER data base of the US EPA is a source of physico-chemical information derived from QSARs, and it is of interest to compare this derived data with the measured parameters discussed above. For the present compound (USEPA, 2000) the relevant derived data are tabulated below.

Data From ASTER Data Base of US EPA.

VP:	1.2×10^{-7} Pa at 25 ºC.
Water Solubility:	30.8 mg/L at 20 ºC
Henry's Law Constant:	1.38×10^{-6} Pa/mol m^3
Hydrolysis:	Half life = 400 days.
Partition Co-efficient:	Log Pow = 3.95
Adsorption/Desorption:	Log Koc =3.48

The calculated water solubility is in excellent agreement with the measured value, and the estimated values for Log Pow and Log Koc are also in reasonable accord with experimental data. However, the QSAR estimates of VP (and consequently the Henrys Law Constant) are two orders of magnitude lower than the experimental values. This discrepancy is due to the presence of lower molecular weight impurities in the commercial product, and consequently the ASTER data is to be preferred when using VP for estimating the environmental fate of the chemical.

4. PURITY OF THE CHEMICAL

Degree of Purity: 96.9%

Hazardous Impurities: None

Non-hazardous Impurities (> 1% by weight):

Chemical name:	Triethylene glycol monobenzoate
Weight percentage:	1.26
CAS No.:	25022-51-7
Chemical name:	Dipropylene glycol dibenzoate
Synonyms:	Propanol, oxybis-, dibenzoate
Weight percentage:	1.5
CAS No.:	27138-31-4

Additives/Adjuvants: None

5. USE, VOLUME AND FORMULATION

The notified chemical, Benzoflex S-358, is a plasticiser in adhesive formulations. It will be imported as a component (25%) in a product named Benzoflex 2088. Benzoflex 2088 can be used in a variety of adhesive applications, such as consumer white glue, carpenter glue, packaging adhesives, wood glue, book binding or forms.

Benzoflex 2088 will be shipped in (US) 55 gallon drums or 205 L Intermediate Bulk Containers (IBC). The import volume for the notified chemical, Benzoflex S-358, is 25 to 250 tonnes per annum, or 100 to 1 000 tonnes of Benzoflex 2088 annually in the first 5 years.

Benzoflex 2088 containing the notified chemical will be formulated into various adhesive products in Australia. The notified chemical will comprise between 10 and 20% (w/w) of the final adhesive products. The adhesives can be sold directly to consumers or adhesive industries. The package size will vary depending on the product, from 200 g containers (containing up to 40 g of triethylene glycol dibenzoate) for consumers to several tonnes for industrial use.

6. OCCUPATIONAL EXPOSURE

The notifier provided occupational exposure data on 2 manufacturing sites, which use approximately 30% of the total import volume. The data of category and number of workers and duration of handling are summarised in the table. The processes will be fairly uniform across sites.

Manufacturing Site	*Category of Workers*	*Number of Workers*	*Duration*
Site A	Operators	20	6 hours/day, 230 days/year
	Maintenance workers	1	1 hour/week
	Quality Control workers	4	3 hours/day, 230 days/year
	Warehouse workers	4	6 hours/day, 230 days/year
Site B	Plant staff	15	4 hours/day, 200 days/year

Transport and storage

The product, Benzoflex 2088 containing 25% the notified chemical, will be shipped in 55 gallon drums or 33 000 pound IBCs. Warehouse workers will handle the product on arrival into the plants. They will also take the finished products containing approximately 9 to 17% notified chemical from the plant floor either to the finished good warehouse or directly to wholesale stores. Occupational exposure to the notified chemical is not expected during transport, storage and distribution, except in the event of a spill.

Manufacture

When manufacturing a small batch, operators will weigh the required quantity into a container manually for addition to the mixing tank. Full drums are used for large batches, the material is pumped directly into the vertical mixing tank. Empty drums will be disposed of without rinsing or washing. The mixing process starts when all the raw materials are added. Benzoflex 2088 remains a liquid throughout the cold blend process. After the blending process, the operators will carry out the packaging task to the point of shipment or storage. The finished products contain approximately 9 to 17% notified chemical. The package size will vary depending on the product, from 200 g containers for consumers to large containers for industrial use. Due to the low vapour pressure of the notified chemical, very limited inhalation exposure is expected. The main route of exposure during blending, filling and packaging will be dermal contamination. Eye contamination from splashes may occur during decanting. When transferring large batches, the operators can only be exposed to the notified chemical when the connecting and disconnecting hoses.

There will be quality control staff who take spot samples during the manufacturing process. They analyse these samples on the plant floor or in the laboratories. Dermal exposure may occur, however, the exposure of quality control staff is expected to be low due to the small sample sizes.

There will be several maintenance workers on call to repair manufacturing equipment. They are typically trained and experienced former plant operators. The level and frequency of

exposure depends on the nature of the job. It is estimated that they may contact the notified chemical for 1 hour per week per person.

All mixing tanks have specialised extraction equipment systems above the mixing area. Ventilation systems are also in place. All operators, quality control staff and maintenance workers wear overalls, safety glasses, hard hats, gloves and hard tipped industrial footwear.

End use

Adhesive products containing approximately 9 to 17% notified chemical may be applied manually to the substrates to be joined, using spray roll coater, knife over roll or by numerous other application techniques. The main route of exposure will be dermal contact. Limited inhalation and eye exposure is expected since most adhesives are viscous liquids. Limited information was provided on application methods and work practices. Based on the low concentration of the notified chemical in the adhesive products, the occupational exposure during end use is expected to be low.

When the adhesives have been dried and fixed, the adhesive products, hence the notified chemical, will be incorporated into the joints of the articles.

7. PUBLIC EXPOSURE

Benzoflex 2088 containing up to 25% of the notified chemical will be used as a plasticiser in adhesive products for use in the packaging industry and for domestic uses. Exposure of the general public as a result of manufacture, transport and disposal of the product containing the notified chemical is assessed as being negligible. Adhesive products containing notified chemical are to be used by the general public and the packaging industry. The general public may make dermal and possibly ocular contact with adhesive products during the application of these products in domestic situations.

8. ENVIRONMENTAL EXPOSURE

Release

Wastes generated at facilities manufacturing adhesive formulations are retained on site and are used in the preparation of subsequent batches of adhesive. All spills are absorbed with appropriate materials and disposed of into landfill. The notifier did not quantify the amount of waste chemical likely to be lost in this manner, the quantity of material left in emptied drums, or the fate of the drums. However, if it is assumed as a worst case that 1% of the chemical is lost through spills and leaks during manufacturing, this equates to a release of up to 2.5 tonnes of the chemical to the soil compartment (i.e. landfill). Similarly, if 1% of the chemical remains in the drums after emptying and is placed into landfill, a further 2.5 tonnes could be released. It is more likely that the drums would be sent to a drum refurbishment/recycling facility where residual chemical would be removed with solvents and/or steam. The waste liquids containing the residual chemical would then be treated prior to release to the sewer, and most of the unused chemical would be recovered into a sludge or filter cake. The sludge or filter cake would then be either incinerated or placed into landfill. In any case, it is estimated that a maximum of 5 tonnes of the new chemical could be placed into landfill each year as a result of waste and residuals from adhesive manufacture.

Application of the adhesives to the parts to be joined could be either manual, or (in industrial situations) by using automated mechanical equipment including rollers and hot knife blades.

The notifier did not indicate the amount of waste adhesive generated by end users, but this is likely to be small in industrial situations and 1% is a reasonable default figure. However, waste percentages may be very large in the case of domestic users of small quantities of adhesive, and it would not be unusual to find 50% of a container of glue unused before being disposed of with domestic garbage.

The adhesives would be used in fabrication and repair of a very wide selection of articles, which at the end of their useful lives would be either incinerated or be placed into landfill. Because of the diverse nature of these articles it is not possible to quantify the likely fate of old products containing the adhesives and plasticiser, and as a worst case scenario it is assumed that all will eventually be disposed into landfill. Consequently, on the basis of these considerations, if all the new chemical is eventually placed into landfill, a maximum of 250 tonnes per annum would be released to the soil compartment. However, since articles containing the adhesive will be spread out across Australia, release will be diffuse.

Fate

Aerobic Biodegradation

A test for ready biodegradability was conducted (Jenkins, 1998a) according to the Modified Sturm Test (OECD Test Guideline 301B) which measures the rate of CO_2 evolution from the test material when incubated with sewage bacteria in culture medium. Results of this test indicated that the chemical is readily biodegradable. Benzoflex S-358 and sodium benzoate were added to the test vessel – both at nominal concentrations of 10 mg organic carbon per litre – and the CO_2 evolution monitored over a 28 day test period. The test material was degraded 16% after 2 days, 62% after 7 days and 92% after 28 days, and since over 60% degradation had occurred within 10 days of the 10% point being reached, the test material is considered to be readily biodegradable. Further, comparison of the CO_2 evolution rate from this test with that from the test with sodium benzoate alone indicated that the Benzoflex S-358 is not inhibitory to bacterial activity. Also, the sodium benzoate alone was degraded by 67% after 7 days and 83% after 29 days, indicating that the bacterial culture used in the test was viable.

Anaerobic Biodegradation

A report on biodegradation of the compound under anaerobic conditions was supplied (Barnes, 1998). This test measured the rate of production of biogas (i.e. carbon dioxide and methane) using International Standards Organisation (ISO) Method ISO 11734. In this method, samples of the test compound were digested in a suspension of anaerobic sludge (obtained from the anaerobic digester of a metropolitan sewage plant) in an aqueous mineral salt medium at 35 ºC for period of 56 days. The volume of gas produced in the headspace above the liquor was monitored over the test period, and comparison of this volume at any particular time with the theoretical volume of biogas production for complete degradation provided the degree of degradation at that time.

Since the compound has low solubility in water, the test material was dissolved in acetone (36 g/L) and 0.5 mL of this solution added to the digester. The acetone was evaporated off using a nitrogen stream, the sludge suspension added to a volume of 120 mL and the digester

vessel sealed. The nominal concentration of the test material in the digester was consequently 150 mg/L, which equated to a nominal 100 mg/L of organic carbon. The degree of degradation as determined from the biogas production, increased steadily from approximately 12% after 6 days to 61% after 56 days. This result indicated that the test compound is ultimately biodegradable under anaerobic conditions. A reference test using polyethylene glycol (MW = 400 g/mol), also at a nominal concentration of 100 mg/L organic carbon, gave 67% degradation of this compound after 14 days, and approximately 85% after 56 days, indicating that the inoculum was viable and that the test was valid.

General

Some new chemical will be released during manufacturing processes, and is likely to be placed into landfill. The notifier indicates that this is the preferred method for disposal. The eventual fate of the majority of the imported chemical will be strongly linked to that of discarded consumer articles, namely placement into landfill or incineration. As a worst case, if all is assumed to be placed into landfill, up to 250 tonnes per annum could be released to the soil compartment. Although the new chemical will be incorporated into the polymer mass of the adhesive, this will degrade over time with the release of the Benzoflex S-358. The high value for Log Koc (3.2) indicates that initially the chemical will become associated with the organic component of the soil, but since it is readily biodegradable it is not expected to be persistent in this medium, and will be degraded to carbon dioxide, methane (anaerobic conditions) and water. If articles containing the chemical are incinerated, it will be destroyed with formation of water and oxides of carbon.

The compound is moderately water soluble (30.4 mg/L). The moderate value for Log Koc indicates the possibility for some mobility in soil. However, it is unlikely that much chemical would reach the water compartment as it is readily biodegradable. This, together with the low Log Pow (3.2) and water solubility (30.4 mg/L) indicate little potential for bioaccumulation (Connell, 1990). The notifier calculated the Bioconcentration Factor (BCF) of 58.1 which was derived from a QSAR relating BCF to Log Pow. The equation used was –

$$\text{Log BCF} = 0.77 \times \text{Log Pow} - 0.70,$$

and the value of Log Pow used was the measured value of 3.2.

The ASTER data base (US EPA, 2000) also provided a QSAR estimate for the BCF in Fathead minnow (*Pimephales promelas*) of 524. Both these QSAR estimated values are low and indicate low potential for bioaccumulation.

The ASTER data (US EPA, 2000) also estimates the partitioning of the compound to the three major environmental compartments derived from Mackay Level 1 modelling. Calculations indicate that 42% of the compound would enter the water compartment, with the remainder becoming associated with soils and sediments. However, these calculations take no account of biodegradation, so may only be used as an indication of partitioning in the present case.

9. EVALUATION OF TOXICOLOGICAL DATA

The toxicological studies on the notified chemical were performed at the Huntingdon Life Sciences Ltd in UK with the compliance of OECD standard of Good Laboratory Practice in the testing of chemicals and quality assurance.

9.1 Acute Toxicity

Summary of the acute toxicity of Triethylene Glycol Dibenzoate

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	LD_{50}=5 313 mg/kg	(McRae, 1998b)
acute dermal toxicity	rat	LD_{50}>2 000 mg/kg	(McRae, 1998a)
skin irritation	rabbit	Non irritating	(Parcell, 1998b)
eye irritation	rabbit	Slight irritating	(Parcell, 1998a)
skin sensitisation	guinea pig	Non sensitising	(Coleman, 1998)

9.1.1 Oral Toxicity (McRae, 1998b)

Species/strain:	Rat/Sprague-Dawley (CD)
Number/sex of animals:	5/sex per group
Observation period:	15 days
Method of administration:	Oral (gavage) doses at 2 000, 3 200, 5 000 and 6 400 mg/kg.
Test method:	OECD TG 401
Mortality:	1 male at 3 200 mg/kg; 1 male and 3 females at 5 000 mg/kg; and 3 males at 6 400 mg/kg.
Clinical observations:	Piloerection, hunched posture, red brown stained muzzle, ungroomed appearance and walking on toes were seen in most animals at all dose levels. Increased salivation, waddling/unsteady gait, lethargy, sensitivity to handling, respiratory distress, abnormal faeces, cold extremities, body tremors, increased lacrimation, prostration, thin appearance, pallid extremities, protruding eyes and partially close eyelids were observed at one or more dosages. All symptoms reversed by day 14 except piloerection, which was still evident on day 15 in males at 5 000 mg/kg.
Morphological findings:	A generalised congestion was observed in either all or the majority of organs and tissues of the dead animals. No macroscopic abnormalities were found in surviving

	animals.
Comment:	All deaths (1 male was killed *in extremis*) occurred within 3 days of dosing.
LD_{50}*:*	5 537 mg/kg (males), 4 938 mg/kg (females), 5 313 mg/kg (combined sexes).
Result:	The notified chemical was of very low acute oral toxicity in rats.

9.1.2 Dermal Toxicity (McRae, 1998a)

Species/strain:	Rat/Sprague-Dawley(CD)
Number/sex of animals:	5/sex
Observation period:	15 days
Method of administration:	A dermal application (2 000 mg/kg in corn oil) under occlusive dressing for 24 hours.
Test method:	OECD TG 402
Mortality:	None
Clinical observations:	None
Morphological findings:	None
Comment:	3 female animals had either no bodyweight gain or low bodyweight gain.
LD_{50}*:*	> 2 000 mg/kg
Result:	The notified chemical was of low dermal toxicity in rats.

9.1.3 Inhalation Toxicity

Not provided.

9.1.4 Skin Irritation (Parcell, 1998b)

Species/strain:	Rabbit/New Zealand White

Number/sex of animals: 6 males

Observation period: 72 hours

Method of administration: A single application of the notified chemical (0.5 g) in corn oil under a semi-occlusive dressing for 4 hours.

Test method: OECD TG 404

Draize scores: Draize scores for erythema and oedema were zero for all animals at 1, 24, 48 and 72 hours after dosing.

Result: The notified chemical was not irritating to the skin of rabbits.

9.1.5 Eye Irritation (Parcell, 1998a)

Species/strain: Rabbit/New Zealand White

Number/sex of animals: 6 females

Observation period: 72 hours

Method of administration: A volume of 0.1 mL of the notified chemical was placed into the lower everted lid of one eye of each animal. The other eye served as control.

Test method: OECD TG 405

Draize scores:

	Time after instillation							
Animal	***1 hour***		***1 day***		***2 days***		***3 days***	
Conjunctiva	***r***	***c***	***r***	***c***	***r***	***c***	***r***	***c***
1	2	0	2	0	0	0	0	0
2	1	0	1	0	0	0	0	0
3	1	0	1	0	0	0	0	0
4	1	0	1	0	0	0	0	0
5	1	0	1	0	0	0	0	0
6	1	0	0	0	0	0	0	0

[1] see Attachment 1 for Draize scales
r = redness c = chemosis

Other Draize scores: Draize scores for cornea (density and area) and iris lesion in all 6 animals were zero during the study.

Comment:	Discharge from conjunctivae was not recorded.
Result:	The notified chemical was a slight irritant to the eyes of rabbits.

9.1.6 Skin Sensitisation (Coleman, 1998)

Species/strain:	Guinea pigs/albino Dunkin- Hartley
Number of animals:	20 males (test group); 20 males (test vehicle group); 10 males (positive control group); 10 males (vehicle control group).
Induction: Intradermal injection (Day 1)	3 pairs of intradermal injections (0.1 mL) were made on shaved shoulder area of each animal: Test Group • Freund's Complete Adjuvant (FCA) with water (1:1 v/v); • 100% notified chemical; • 100% notified chemical in FCA (1:1, v/v). Test Vehicle Group • Freund's Complete Adjuvant (FCA) with water (1:1 v/v); • Alembicol D; • Alembicol D in FCA (1:1, v/v). Control Group • Freund's Complete Adjuvant (FCA) with water (1:1 v/v); • Hexyl cinnamic aldehyde (HCA) in Alembicol D (10%, v/v); • 10% HCA in a mixture of Alembicol D and FCA (1:1, v/v). Control Vehicle Group As described in the Test Vehicle Group

Induction: Topical application (Day 6)	Dermal application of 10% sodium lauryl sulphate (0.5 mL) in petrolatum.
(Day 7)	Test Group Dermal application of 100% notified chemical (0.4 mL) under occlusive dressing for 48 hours. Control Group Dermal application of 10% HCA in Alembicol D under occlusive dressing for 48 hours. Test Vehicle Group and Control Vehicle Group Dermal application of Alembicol D under occlusive dressing for 48 hours.
Challenge: Topical application (Day 21)	Test Group and Test Vehicle Group One occluded application of 50% notified chemical in Alembicol D (0.2 mL) and one occluded application of 100% notified chemical (0.2 mL) were applied to the flank for 24 hours. Control Group and Control Vehicle Group These animals were treated similarly as the above groups with the exception that the notified chemical was replaced with HCA.
Test method:	OECD TG 406

Challenge outcome:

Challenge concentration	***Test Group***		***Test Vehicle Group***		***Positive Control Group****		***Control vehicle Group***	
	24 h*	***48 h****	***24 h***	***48 h***	***24 h***	***48 h***	***24 h***	***48 h***
100%	**0/20	0/20	0/20	0/20	9/9	9/9	0/10	0/10
50%	0/20	0/20	0/20	0/20	8/9	8/9	0/10	0/10

* time after patch removal.
** number of animals exhibiting positive response.
*** one animal was killed for humane reasons prior to challenge application.

Comment: Slight erythema was observed in Test Group animals after receiving intradermal injections and topical applications. Slight erythema was also seen in the Control Group animals.

Result: The notified chemical was not sensitising to the skin of guinea pigs

9.2 Repeated Dose Toxicity (Paffett, 1999)

Species/strain: Rat/Cr1:CD BR

Number/sex of animals: 10/sex per gruop

Method of administration: Dietary

Dose/Study duration: Group 1: 0 mg/kg/day (control);
Group 2: 400 mg/kg/day;
Group 3: 1 000 mg/kg/day;
Group 4: 1 600 mg/kg/day;
Group 5: 2 200 mg/kg/day.

The duration of treatment was 13 weeks. Group 1 and 5 had extra 10/sex as the recovery groups which had 4 week recovery period after treatment.

Test method: OECD TG 408

Clinical observations:

Hair loss was observed in both sexes in Group 5 during treatment and recovery period. Bodyweight gain in Group 4 and 5 were decreased in both sexes. This was more apparent in males as a slight reduction in food intake was noted in males at high level doses. At the end of recovery period, the bodyweight loss reversed fully in females and partially in males.

There were no other clinical signs considered to be treatment related.

Clinical chemistry/Haematology

Very slight increases in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were seen at week 5 in both sexes in Group 5 and females in Group 4, and at week 13 in males of Group 5 associated with periportal hepatocyte hypertrophy. At week 17, this difference was not apparent and there was no residual hepatic pathology in recovery groups.

Males of Group 4 and 5 had an increase in red blood cell count at week 5 which recovered by week 13. They also had a non-cellular specific decrease in white blood cell count at week 5 and 13.

A decrease of urinary sodium, potassium and pH levels was noted in both sexes of Group 5, and reduced pH levels, in males of Group 4 at week 13.

Histopathology:

Periportal hepatocyte hypertrophy was observed in both sexes of Group 5 at the end of treatment. This pathological change reversed after 4 week recovery period.

An increase incidence and degree of haemosiderosis in spleen was seen in Group animals, and became less significant after 4 week recovery period.

Comment:

No treatment related differences were observed between the control and test groups on water consumption, ophthalmic examination, organ weights and other tests. Lower bodyweight gain, haematological changes and changes in blood clinical chemistry were apparent at 1 600 and 2 200 mg/kg/day but not at 1 000 mg/kg/day. These effects were selected to establish the NOEL.

Result:

The NOEL established for this 13 week dietary study is 1 000 mg/kg/day.

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay (Kitching, 1998)

Strains:	*Salmonella typhimurium* TA1535, TA1537, TA98 and TA100; and *Escherichia coli* CM891 WP2 *trp urv*A
Metabolic activation:	Liver fraction (S9 mix) from rats pretreated with Aroclor 1254.
Concentration range:	Test 1 (plate incorporation assay): 0, 5, 15, 50, 150, 500, 1 500 and 5 000 μg/mL for all strains

	in the absence and presence of metabolic activation. Test 2 (pre-incubation assay): 0, 50, 150, 500, 1 500 and 5 000 μg/mL for all strains in the absence and presence of metabolic activation. Positive control (-S9): N-ethyl-N'-nitro-N-nitrosoguanidine for TA1535 (5 μg/plate), TA100 (3 μg/plate) and CM891 (2 μg/plate), 9-aminoacridine for TA1537 (80 μg/plate), and 2-nitrofluorene for TA98 (1 μg/plate). Positive control (+S9): 2-aminoanthracene for TA1535 (2 μg/plate), CM891 (10 μg/plate), and benzo[a]pyrene (5 μg/plate) for TA1537, TA98 and TA100. DMSO was used as the vehicle for all above studies.
Test method:	OECD TG 471 and 472
Comment:	No toxicity was observed in either mutation test. No substantial increases in revertant colony numbers of any of the test strains were observed following the treatment with the notified chemical at any dose level, in the presence or absence of S9 mix in either mutation test. The mean revertant colony counts for the vehicles were within the historical range. The positive controls caused marked increases of revertant colony numbers in the presence or absence of S9 mix in both mutation test.
Result:	The notified chemical was non mutagenic under the conditions of the test

9.3.2 Chromosomal Aberration Assay in Human Lymphocytes (Akhurst, 1998)

Cells:	Human lymphocyte culture
Metabolic activation system:	Liver fraction (S9 mix) from rats pretreated with Aroclor 1254.
Dosing schedule:	The notified chemical was dissolved in DMSO and tested in duplicate cultures in 2 tests with or without metabolic activation.

Metabolic Activation	Experiment/ Study Number	Test concentration	Controls
-S9	First test	Treatment/recovery time =3/18 hours 6.25, 12.5, 25, 50, 100*, 200*, 400* and 800 μg/mL	Positive: mitomycin C (0.8 μg/mL) Negative: DMSO
	Second test	Treatment time=21 hours 50, 100, 150, 200*, 300*, 400*, 500* and 600 μg/mL	Positive: mitomycin C (0.4 μg/mL) Negative: DMSO
+S9	First test	Treatment/recovery time =3/18 hours 6.25, 12.5, 25, 50, 100*, 200*, 400* and 800* μg/mL	Positive: cyclophosphamide (20 μg/mL) Negative: DMSO
	Second test	Treatment/recovery time =3/18 hours 50, 100, 200*, 400*, 500, 600, 700 and 800* μg/mL	

DMSO – dimethylsulphoxide
* cultures selected for metaphase analysis

Test method: OECD TG 473

Comment: The notified chemical showed toxic at 400 and 800 μg/mL without S9 and 800 μg/mL with S9 in the first test, and showed toxic at 600 μg/mL without S9 in the second test.

Precipitates were observed at the 235.5 μg/mL in culture medium when DMSO was used as the solvent.

The notified chemical did not show indication of inducing chromosomal aberrations in the absence or presence of metabolic activation in this *in vitro* cytogenetic test system.

Both positive control compounds caused large, statistically significant increases in the proportion of aberrant cells.

Result: The notified chemical was non clastogenic under the conditions of the test.

9.3.3 Mammalian Cell Gene Mutation Test *in vitro* in the Mouse (Adams, 1998)

Cells: Mouse lymphoma L5178Y cells

Metabolic activation system: Liver fraction (S9 mix) from rats pretreated with Aroclor 1254.

Dosing schedule: The notified chemical was dissolved in DMSO and tested in triplicate cultures in 2 tests with or without metabolic activation.

Treatment time =3 hours;
Sampling time=24 & 48 hours.

Metabolic Activation	Experiment/ Study Number	Test concentration	Controls
-S9	First test Second test	25, 50, 100, 150, 200, and 400 μg/mL 50, 100, 150, 200, 300, and 400 μg/mL	Positive control: methyl methanesulphonate (10 μg/mL in DMSO).
+S9	First test Second test	25, 50, 100, 150, 200, and 400 μg/mL 50, 100, 150, 200, 300, and 400 μg/mL	Positive control: 20-methylcholanthrene (2.5 μg/mL in DMSO).

Test method: OECD TG 476

Comment: Concentrations used in Test 1 and 2 were selected based upon the results from a preliminary test.

No substantive increases in mutant frequency were observed after treatement with the notified chemical in either test.

Both positive control compounds caused significant increases in mutant frequency in both tests.

Result: The notified chemical was not of mutagenic potential under the conditions of the test.

9.4 Other Studies

The notifier provided 3 other studies on the notified chemical. The estrogenic activity study was performed by Bioqual Inc, USA in 1997 with a quality assurance statement and in compliance with OECD GLP regulations. Both the *in vitro* digestion study and excretion study of the notified chemical were conducted by the Food and Drug Research Laboratories,

USA in 1965 and 1967, respectively. The level of reporting detail was low and these 2 studies had no statements for quality assurance or compliance with GLP guidelines.

9.4.1 Estrogenic Activity Study (Reel, 1997)

Species/strain:	Adult ovariectomized female rat/Sprague-Dawley (CD)
Number/sex of animals:	10/group
Test substance:	Benzoflex S-358 (96.9%% triethylene glycol dibenzoate)
Method of administration:	Oral (gavage)
Dose/Study duration:	The duration of treatment was 7 days. Diethylstilbestrol (DES) was employed as the positive control. Both the notified chemical and the positive control substance were administered in corn oil. Group 1: 250 mg/kg/day; Group 2: 700 mg/kg/day; Group 3: 1 400 mg/kg/day; Group 4: 2 100 mg/kg/day; Group 5: 2 800 mg/kg/day; Group 6: 5 mL/kg/day corn oil (vehicle control); Group 7: 2.5 µg/kg/day DES (positive control); Group 8: 5 µg/kg/day DES (positive control); Group 9: 10 µg/kg/day DES (positive control).

Clinical observations:

Groups 1-4: One rat in Group 3 died on day 5 due to a gavage dosing error. Piloerection and soft stool were observed in test animals. All surviving rats appeared normal at necropsy on day 7.

Group 5: Five rats in this test group showed clinical signs of toxicity after treatment including piloerection, red discharge on the muzzle, tremors, lethargy, scruffy coat, pale colour, convulsions, hyperactive and vocalization. Two of them were found dead on day 5 and 6, respectively. The 8 surviving rats had no gross abnormalities at necropsy on day 7.

Vaginal Cornification:

Vaginal cornification was not observed in the rats treated with the notified chemical (Groups 1-5) during the study.

The positive control, DES, resulted in a dose-dependent induction of vaginal cornification.

Body and Uterine Weights:

The final body weights for the animals treated with the notified chemical (Groups 1-5) were not significantly different ($p>0.05$) from that of the vehicle controls (Group 6). No increase in uterine weight or uterine/bodyweight ratio was found in rats of Groups 1-5 when compared to the vehicle control (Group 6).

DES suppressed body weight gain in a dose dependent manner over the 7 day dosing period, and induced a dose dependent increase in uterine weight and in uterine/bodyweight ratio.

Comment:

Currently, there are no OECD test guidelines for endocrine disrupting effects. Guidelines are under development.

This study was performed according to an in-house method, based on several published scientific papers. The endpoints, vaginal cornification, increase in uterine weight and increase in uterine/bodyweight ratio were determined in this study.

Result:

The notified chemical did not exhibit estrogenic activity as determined by endpoints, vaginal cornification, increase in uterine weight to body weight ratio and uterine weight under test conditions.

9.4.2 *In Vitro* Digestion Study (Kross, 1965)

The study description implies that this assay was done to ascertain the breakdown of this chemical when used as a food additive.

Digestion systems:	System 1: Simulated intestinal fluid containing pancreatin (pH adjusted) prepared according to United States Pharmacopoeia (USP) XVIth revision; System 2: Similar to System 1 except that 1 g freshly prepared rat liver homogenate replaced the pancreatin.
Sample size and duration:	A 100 mg sample was added to 50 mL of System 1 or 2 for a digestion period of 4 hours.
Degree of Hydrolysis:	The degree of hydrolysis of the notified chemical was determined by digest in 6N HCl for 4 hours.
Test method:	Similar to that described in USP.
Result:	Under test conditions, the liver homogenate produced greater (58%) hydrolytic breakdown than intestinal fluid (33%). Study authors presumed the breakdown products to be benzoic acid and triethylene glycol, and suggested that

digestion would be virtually complete under *in vivo* conditions.

9.4.3 Excretion Study in Rats and Dogs (Morgoreidge, 1967)

Species/strain:	Young adult FDRL rats and adult beagle dogs.
Number/sex of animals:	Study 1: 1/sex dogs, 1/sex rats; Study 2: 1/sex dogs, 1/sex rats; Study 3: 1 female dog.
Observation period:	Study 1: 72 hours; Study 2: 120 hours (5 days); Study 3: 0-24, 25-72 and 73-120 hours. Urine and feces samples were collected separately during the observation period. Radioactivity was measured and reported for urine and combined urine and faeces.
Method of administration:	Oral (gavage, 5 mg/kg [C^{14}] labeled notified chemical in propylene glycol solution).
Comment:	The radioactive C^{14} was in the carbonyl position of the benzoic acid moiety of the ester. The radioactive metabolites were assumed to include the known metabolites, hippuric acid and benzoyl glucuronic acid. In dogs, absorption was higher in males than females. In both species, total recovery increased over time (measured up to 120 hours), but highest excretion occurred, in both urine and faeces, in the first 24 hours. Most recovered label was found in urine (96-100% and 58-99% in rats and dogs, respectively).
Result:	The notified chemical was readily and rapidly absorbed from the gastrointestinal tract of both rats and dogs, and its benzoic acid metabolites were rapidly excreted.

9.5 Overall Assessment of Toxicological Data

The notified chemical was of very low acute oral toxicity (LD_{50}=5 313 mg/kg) and low acute dermal toxicity (LD_{50}>2 000 mg/kg) in rats. It was not an skin irritant but a slight eye irritant in rabbits. The notified chemical was not a skin sensitiser in guinea pig.

A 13 week dietary study on the notified chemical was performed in rats. The control and highest dose groups also had a recovery period of 4 weeks. Lower bodyweight gain, haematological changes and changes in blood clinical chemistry were observed in rats at

1 600 mg/kg/day and above. Based on these effects, the NOEL established for this study is 1 000 mg/kg/day.

Three *in vitro* genotoxicity studies were provided. The notified chemical was not mutagenic in bacteria, in human lymphocyte culture, or in mouse lymphoma L5178Y cells.

There were 3 other studies provided in the submission. The notified chemical did not exhibit estrogenic activity based on the endpoints of vaginal cornification, increase in uterine weight to body weight ratio and increase in uterine weight. The excretion study indicated that the notified chemical was readily and rapidly absorbed from the gastrointestinal tract of both rats and dogs, and its metabolites were rapidly excreted. This result was consistent with the *in vitro* digestion study which suggested a virtually complete digestion under *in vivo* conditions.

According to NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1999), the notified chemical is not classified as a hazardous substance.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

Due to the rapid biodegradation of the chemical, it was not possible for the notifier to obtain reliable ecotoxicity data against aquatic organisms. In preliminary test work under static conditions (medium replacement every 24 hours) with no fish, daphnia or algae present, the concentration of the test material could not be maintained within 20% of the nominal concentrations over the test periods required by the relevant protocols. This explanation is acceptable although analytical data supporting this assertion would have been of use. A QSAR estimate on the acute toxicity of the compound against the fish species *Pimephales promelas* (fathead minnow) from the ASTER data base (USEPA, 2000) was LC50 of 4 mg/L.

The notifier did supply test reports on the acute toxicity of the compound to earthworms, and on the inhibition of respiration for sewage bacteria.

Test	***Species***	***Result***
Acute Toxicity to Earthworm [OECD TG 207]	*Eisenia foetida*	LC_{50} > 1 000 mg/kg NOEL > 1 000 mg/kg
Inhibition of Bacterial Respiration [OECD TG 209]	Sewage bacteria	EC50 >100 mg/L

Earthworms

A test on the acute toxicity of the new compound to earthworms was submitted (Johnson, 1998). Groups of 40 worms were placed in soil containing nominally 0 (control), 95, 171, 309, 556 and 1,000 mg/kg of the test compound, and their condition was monitored over a 14 day period. There were no mortalities among the worms over the test period, nor were any other adverse effects observed. Accordingly, the results of this test indicate that the material is non toxic to this species. However, it is noted that the compound is rapidly biodegraded in aqueous media (see above), and it is likely that the worms were not exposed to the full nominal test levels of the compound over the 14 day period.

Sewage Bacteria

A test on the inhibition of bacterial respiration was conducted (Jenkins, 1998b). The test substance was suspended in artificial sewage at nominal loadings of 1, 10 and 100 mg/L using a 30 minute period of sonication to assist dispersion. The test flasks were inoculated with sewage sludge bacteria and aerated for 30 minutes. Following aeration, the contents of the flasks were poured into darkened 300 mL BOD bottles fitted with oxygen sensing electrodes. The rate of oxygen consumption was measured for the dispersions, and compared with that in a control vessel. None of the tests indicated any significant inhibition of bacterial respiration compared with the controls, and it was concluded that the new chemical is not toxic to sewage bacteria up to the limits of its water solubility.

In contrast to tests with the new chemical, a reference test conducted with 3,5-dichlorophenol gave an EC50 of 8.3 mg/L, indicating the viability of the bacterial culture used.

It is also to be noted that in the tests for ready biodegradation (see above), no inhibitory effects of the compound on bacterial activity was observed. This is in agreement with the present result.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The environmental hazard from the notified chemical is not expected to be high when it is used for the manufacture of adhesives as indicated in the notification. The adhesives will be used within industry and by the general domestic consumer.

Very little of the chemical is expected to be released during manufacturing of adhesive formulations, and release is estimated at a maximum of 2% of import quantity, or a maximum of 5 tonnes year. It is expected that this would be placed into landfill. Release of the compound during industrial use of adhesives is expected to be small, although comparatively larger proportions could be released when adhesives are used by the general public. The associated waste would also be placed into landfill. Old articles containing the new chemical such as furniture or books would most likely be discarded into landfill or be incinerated. Assuming none is incinerated, a maximum of 250 tonnes could be placed into landfill each year.

The compound is readily biodegradable under aerobic conditions, and is ultimately degradable under anaerobic conditions. Once placed into landfill the compound is likely to be slowly released as a consequence of the degradation of the polymer matrix of the adhesives in which it is encapsulated, and is then expected to become associated with the organic component of soils and sediments. Subsequently the compound will be degraded through biological processes to carbon dioxide, methane (in anaerobic conditions) and water.

The compound exhibited no toxicity to earthworms, with a 14 day LC_{50} > 1 000 mg/kg. Due to the rapid biodegradation of the chemical, it was not possible to generate ecotoxicity data for the compound against aquatic species although ASTER data predicted a 96 hr LC_{50} for fathead minnow of 4 mg/L. However, very little of the compound is expected to enter the water compartment so exposure to aquatic organisms is expected to be low. The new chemical is readily biodegradable and the low value for Log Pow (3.2) and water solubility

(30.4 mg/L) indicate low potential for bioaccumulation. This is supported by two low QSAR estimates of the BCF (58 and 524).

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

The notified chemical, Benzoflex S-358, was of very low acute oral toxicity and low acute dermal toxicity in rats. It was not a skin irritant but a slight eye irritant in rabbits, and not a skin sensitiser in guinea pigs. The NOEL established from a repeat dose dietary study in rats for Benzoflex S-358 is 1 000 mg/kg/day. The notified chemical was not mutagenic in bacteria, in human lymphocyte culture, or in mouse lymphoma cells. In addition, the notified chemical did not exhibit estrogenic activity in rats. An excretion study and an *in vitro* digestion study indicated that the notified chemical was readily and rapidly absorbed from the gastrointestinal tract in both rats and dogs, and its metabolites were rapidly excreted. According to NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1999), Benzoflex S-358 is not classified as a hazardous substance.

Besides Benzoflex S-358, the import product, Benzoflex 2088 contains 45% diethylene glycol dibenzoate (CAS No 120-55-8) and 23% dipropylene glycol dibenzoate (CAS No 27138-31-4). The notifier provided some toxicity data for diethylene glycol dibenzoate and dipropylene glycol dibenzoate in the material safety data sheet (MSDS). Both ingredients were of very low acute oral and inhalation toxicity, and low acute dermal toxicity. They were not skin irritants or sensitisers, but caused very slight conjunctival irritation in rabbit eyes. These two chemicals were not mutagenic in bacteria or mammalian cells, or clastogenic in Chinese hamster lung cell *in vitro*. Treated rats did not exhibit estrogenic activity and had NOELs of 1 000 mg/kg/day following repeated dosing for 13 weeks.

Occupational Health and Safety

Waterside, warehouse and transport workers will only be exposed to the notified chemical in the event of an accident or damage to packaging. The occupational health risk to these workers is negligible.

At the manufacturing sites, the blending, filling and packaging processes are expected to be within closed systems. When preparing small batches, operators will add the product containing 25% the notified chemical into blending tanks manually. For large batches, this process will be mechanical. The quality control staff and maintenance workers will handle the notified chemical in small qualities and for short periods of time. Slight eye irritation may occur on acute exposure to the notified chemical, hence, workers should wear goggles when handling the notified chemical in an open process. The notified chemical has been used overseas for a number of years, but the notifier has not observed any work related injuries or diseases in workers exposed to this chemical. Considering the low toxicity hazard of the notified chemical and the overall low occupational exposure, the health risk for workers at the manufacturing sites is low.

End users will handle the adhesive products containing approximately 9 to 17% of the notified chemical. They may apply the adhesives manually or mechanically. Based on the low percentage of the notified chemical in adhesives and low toxicity of the notified chemical, the health risk for end use workers handling the adhesive products containing the

notified chemical is low. The notified chemical becomes fixed into the articles after the adhesive dries.

Public Health

Exposure of the general public as a result of manufacture, transport and disposal of the product containing the notified chemical is assessed as negligible. Although adhesive products containing notified chemical are to be used in the packaging industry, they will also be used by the general public in domestic situations. Dermal and possible ocular contact with products containing the notified chemical are likely during use. However, the risk to public health is considered to be minimal due to the low concentration of the notified chemical in products to be used by the public, the low dermal toxicity and slight eye irritancy of the notified chemical.

13. RECOMMENDATIONS

To minimise occupational exposure to Benzoflex S-358 the following guidelines and precautions should be observed:

- Safety goggles should be selected and fitted in accordance with Australian Standard (AS) 1336 (Standards Australia, 1994) to comply with Australian/New Zealand Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand, 1992);
- Spillage of the notified chemical should be avoided. Spillages should be cleaned up promptly with absorbents which should be put into containers for disposal;
- Good personal hygiene should be practised to minimise the potential for ingestion;
- A copy of the MSDS should be easily accessible to employees.

If products containing the notified chemical are hazardous to health in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1999), workplace practices and control procedures consistent with State and territory hazardous substances regulations must be in operation.

14. MATERIAL SAFETY DATA SHEET

The MSDS for Benzoflex 2088 containing the notified chemical were provided in a format consistent with the *National Code of Practice for the Preparation of Material Safety Data Sheets* ((National Occupational Health and Safety Commission, 1994).

This MSDS was provided by the applicant as part of the notification statement. It is reproduced here as a matter of public record. The accuracy of this information remains the responsibility of the applicant.

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the Act, secondary notification of the notified chemical may be required if any of the

circumstances stipulated under subsection 64(2) of the Act arise. No other specific conditions are prescribed.

16. REFERENCES

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Attachment 1

The Draize Scale (Draize, 1959) for evaluation of skin reactions is as follows:

Erythema Formation	*Rating*	*Oedema Formation*	*Rating*
No erythema	0	No oedema	0
Very slight erythema (barely perceptible)	1	Very slight oedema (barely perceptible)	1
Well-defined erythema	2	Slight oedema (edges of area well-defined by definite raising	2
Moderate to severe erythema	3	Moderate oedema (raised approx. 1 mm)	3
Severe erythema (beet redness)	4	Severe oedema (raised more than 1 mm and extending beyond area of exposure)	4

The Draize scale (Draize *et al*., 1944) for evaluation of eye reactions is as follows:

CORNEA

Opacity	*Rating*	*Area of Cornea involved*	*Rating*
No opacity	0 none	25% or less (not zero)	1
Diffuse area, details of iris clearly visible	1 slight	25% to 50%	2
Easily visible translucent areas, details of iris slightly obscure	2 mild	50% to 75%	3
Opalescent areas, no details of iris visible, size of pupil barely discernible	3 moderate	Greater than 75%	4
Opaque, iris invisible	4 severe		

CONJUNCTIVAE

Redness	*Rating*	*Chemosis*	*Rating*	*Discharge*	*Rating*
Vessels normal	0 none	No swelling	0 none	No discharge	0 none
Vessels definitely injected above normal	1 slight	Any swelling above normal	1 slight	Any amount different from normal	1 slight
More diffuse, deeper crimson red with individual vessels not easily discernible	2 mod.	Obvious swelling with partial eversion of lids	2 mild	Discharge with moistening of lids and adjacent hairs	2 mod.
		Swelling with lids half-closed	3 mod.	Discharge with moistening of lids and hairs and considerable area around eye	3 severe
Diffuse beefy red	3 severe	Swelling with lids half-closed to completely closed	4 severe		

IRIS

Values	*Rating*
Normal	0 none
Folds above normal, congestion, swelling, circumcorneal injection, iris reacts to light	1 slight
No reaction to light, haemorrhage, gross destruction	2 severe