Version # 2.0
Author initials and location: LL (Shenzhen)
Date: 31 Dec 2013
SOP Version: 3.0
QC initials and date: BN 04 Jun 2013

# Intertek Full Toxicological Profile for

# Glycerin



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_____ _____
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Toxicological Risk Assessor

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# Glycerin



## *1.0 Substance Identity:*

1.1 Chemical Name (IUPAC name, INCI name, or CAS name):
Glycerol (CosIng, 2012)

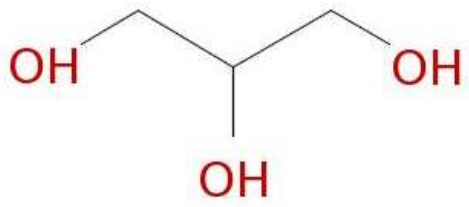
1.2 INCI Name:
Glycerin (CosIng, 2012)

1.3 CAS Number(s):
56-81-5 (CosIng, 2012)

1.4 EC Number:
200-289-5 (CosIng, 2012)

1.5 Other Synonyms and Tradenames:
Glycerine (OECD-SIDS, 2002)
Glycyl alcohol (OECD-SIDS, 2002)
Trihydroxypropane (OECD-SIDS, 2002)
1,2,3- trihydroxypropane (OECD-SIDS, 2002)
Citifluor AF 2 (OECD-SIDS, 2002)
Glycerin mist (OECD-SIDS, 2002)
Glyceritol (OECD-SIDS, 2002)
Grocolene (OECD-SIDS, 2002)
Moon (OECD-SIDS, 2002)
Osmoglyn (OECD-SIDS, 2002)
Star (OECD-SIDS, 2002)

1.6 Molecular Structure:




(OECD-SIDS, 2002)

1.7 Other (e.g., source, GM-derived):
No relevant information was available following the literature searching instructions contained within the Standard Operating Procedure for Creating New Ingredient Toxicity Profiles.

## *2.0 Regulatory Status*

2.1 Cosmetics Directive 76/768/EEC:
Not specifically listed in the Annexes of Cosmetics Directive 76/768/EEC as of December 31, 2012.

2.2 Cosmetic Regulation EC No 1223/2009:
Not specifically listed in the Annexes of Cosmetic Regulation EC No 1223/2009 as of December 31, 2012

2.3 EU CLP Classification:
Self classified by industry – Not classified by majority of notifiers (ECHA, 2012)

2.4 IARC Classification:
Not assessed by IARC as of December 31, 2012

2.5 NTP Classification:
Not listed within the 12th Report on Carcinogens

2.6 Canada Hotlist:
Listed on the March 20th, 2011 Canada Hotlist as a prohibited substance (Health Canada, 2011)
Listed as Glycerin (56-81-5):

Manufacturers of oral and leave-on products containing glycerin must ensure the raw material used is within the specifications of an accepted pharmacopoeia with respect to diethylene glycol (DEG) impurities (e.g. Glycerin Official Monograph in the most current edition of the USP).

2.7 Listed in Annexes IV, XIV, XVII of REACh (Regulation (EC) No 1907/2006):
Not listed in Annexes IV, XIV, XVII of REACh as of December 31, 2012

2.8 Substance of Very High Concern Candidate List (SVHC):
Not listed on the Substance of Very High Concern Candidate List as of December 31, 2012

2.9 California Proposition 65:
Not listed on California Proposition 65 as of December 31, 2012

2.10 EN 71-4 Experimental sets for chemistry and related activities:
Not listed in EN 71-4 as of December 31, 2012

2.11 EN 71-7 Colorants and preservatives allowed for use in finger paints:
Not listed in EN 71-7 as of December 31, 2012

2.12 EN 71-9 Organic chemical compounds in toys:
Not listed in EN 71-9 as of December 31, 2012

2.13 16 CFR § 1500.13: Listing of “strong sensitizer” substances:
Not listed as a strong sensitizer in 16 CFR 1500.13 as of December 31, 2012

2.14 21 CFR: Color additives permitted to be used in cosmetics:
Not listed in 21 CFR as of December 31, 2012

***3.0 Use / Function:***

Glycerin is used as a denaturant, humectant, perfuming and solvent agent in cosmetics. It can be used as an intermediate in industrial applications for the manufacture of products such as soaps/detergents and glycerol esters. It is found in consumer products such as pharmaceuticals, cosmetics, tobacco, food and drinks

and is present in numerous other products such as paints, resins and paper (OECD-SIDS, 2002).

### *4.0 Authoritative Review (e.g., CIR, SCCS, JECFA, NICNAS, OECD, SIDS, etc:) :*

| Authority | Reviewed | Safety Conclusion |
|---|---|---|
| CIR | No Review | Not applicable |
| SCCS | No Review | Not applicable |
| NICNAS | No Review | Not applicable |
| IUCLID | Yes | Not applicable |
| SIDS | Yes (Initial assessment) | "No further work is indicated, because of the low hazard potential of this substance" (OECD-SIDS, 2002). |
| JECFA | Yes | An ADI of "not specified" was established in 1976. Evaluation was not finalized in 2001 when it was decided that more information was necessary on the definition of "flavouring agent" (JECFA, 2012). |

**Overall Conclusion:**

The ingredient is not acutely toxic, a skin irritant, an eye irritant, a skin sensitizer, mutagenic, carcinogenic, a reproductive toxicant, nor is it bioaccumulative. No information was available on its phototoxicity. Based on this information and other scientific literature on this ingredient, safety concerns are not expected with this ingredient for use in cosmetics.

### *5.0 Physicochemical Properties*

5.1 Physical form:
Liquid at room temperature (OECD-SIDS, 2002)

5.2 Molecular weight:
92 g/mol (OECD-SIDS, 2002)

5.3 Solubility:
5.3.1 Water: Miscible in water (OECD-SIDS, 2002)

5.3.2 Other: No relevant information was available following the literature searching instructions contained within the Standard Operating Procedure for Creating New Ingredient Toxicity Profiles.

5.4 Log Kow (or Log Pow):

Log Kow = -1.76 (measured) (OECD-SIDS, 2002)

5.5 Particle Size:

Not applicable. Substance is a liquid.

## *6.0 Toxicology Information:*

6.1 Acute Toxicity

6.1.1 Oral:

6.1.1.1 Conclusion:

Based on the information summarized below, this substance can be considered as not acutely harmful

| **Species/ strain /sex/number** | **Dose range tested** | **$LD_{50}$ (units)** | **References** |
|---|---|---|---|
| Rat, 12 females (strain not reported) | 27260 mg/kg bw | 27200 mg/kg bw | (OECD-SIDS, 2002) |
| Sprague Dawley rats (sex and number not reported) | Not reported | >25300 mg/kg bw | (OECD-SIDS, 2002) |
| Fischer 344 rats, female (number not reported) | Not reported | >2400 mg/kg bw | (OECD-SIDS, 2002) |
| Rat (strain, sex and number not reported) | Not reported | >5000 to 58400 mg/kg bw | (OECD-SIDS, 2002) |
| Mouse (strain, sex and number not reported) | Not reported | 4250 mg/kg bw | (OECD-SIDS, 2002) |
| Mouse (strain, sex and number not reported) | Not reported | 23000 mg/kg bw | (OECD-SIDS, 2002) |
| Mouse (strain, sex and number not reported) | Not reported | 4250 to 38000 mg/kg bw | (OECD-SIDS, 2002) |
| Guinea pig (strain, sex and number not reported) | Not reported | 10000 mg/kg bw | (OECD-SIDS, 2002) |

6.1.1.2 Summary:

Glycerol exhibits a very low acute toxicity in mammals. The range of acute oral $LD_{50}$ values derived from studies in experimental animals (rats, mice and guinea pigs) is between >4,000 and 38000 mg/kg bw, with the majority of

values between 23000 and 38000 mg/kg bw (OECD-SIDS, 2002).

6.1.2 Dermal:

6.1.2.1 Conclusion:

Based on the information summarized below, this substance can be considered as not acutely harmful.

| **Species/ strain /sex/number** | **Dose range tested** | **$LD_{50}$ (units)** | **References** |
|---|---|---|---|
| Rabbits, 6 animals (strain and sex not reported) | 18700 mg/kg bw | >18700 mg/kg bw | (OECD-SIDS, 2002) |

6.1.2.2 Summary:

18700 mg/kg bw of synthetic or natural glycerin was applied to the skin of 6 rabbits (strain and sex not reported) for 8 hours. No deaths were observed. Further study details were not reported (OECD-SIDS, 2002).

6.1.3 Inhalation:

6.1.3.1 Conclusion:

No relevant information was available following the literature searching instructions contained within the Standard Operating Procedure for Creating New Ingredient Toxicity Profiles.

6.1.3.2 Summary:

No relevant information was available following the literature searching instructions contained within the Standard Operating Procedure for Creating New Ingredient Toxicity Profiles.

6.2 Irritation and Corrosivity

6.2.1 Skin irritation/corrosion:

6.2.1.1 Conclusion:

Non-irritating according to a skin irritation study using 0.5 mL undiluted glycerin for 24 hours in rabbits (OECD-SIDS, 2002)

6.2.1.2 Summary:

In a study following modern protocols but prior to GLP standards, 0.5 mL glycerin was applied to the skin of 8 male rabbits for 24 hours. The site was scored for irritation at 24 and 72 hours. Maximum irritation scores of 0.0 to 0.4 out of a possible 30 were reported. It was concluded that the compound was non-irritating (OECD-SIDS, 2002).

6.2.2 Eye Irritation:

6.2.2.1 Conclusion:

Non-irritating according to eye irritation studies using undiluted glycerin for up to 7 days in the eyes of rabbits (OECD-SIDS, 2002)

6.2.2.2 Summary:

In a GLP eye irritation study on rabbits according to OECD 405, the conjunctiva was slightly to moderately irritated in all rabbits one hour after treatment. However, the irritation diminished and disappeared at 48 hours after treatment. The test material was slightly irritating, but cannot be classified (OECD-SIDS, 2002).

In a study conducted to a contemporary protocol but prior to GLP standards, 0.1 mL undiluted glycerol was instilled in the eyes of 6 rabbits. No evidence of irritation was observed after 1, 24 and 72 hours and after 7 days. In another study of similar design, using 4 rabbits, irritation of unspecified severity was observed at 1 hour after instillation of glycerol but was absent after 24 h. Another test with a similar design on a glycerol/water mixture (not further specified) gave a similar result and reactions, which were reversible within 24 hours. The results from studies indicate that glycerol is not irritating to the eyes (OECD-SIDS, 2002).

6.3 Skin Sensitisation:

6.3.1 Conclusion:

Non-sensitizing according to a guinea pig sensitization test using 0.1% natural or synthetic glycerin and according to data from several human patch tests (OECD-SIDS, 2002)

6.3.2 Summary:

A group of male 24 Guinea pigs were administered 10 injections of 0.1 mL of 0.1% solution of natural and synthetic glycerin (purity 99.5%). No indication of sensitisation was observed following challenge with further 0.05 mL injections of 0.1 % glycerol after a 2 week exposure-free period. However, due to a lack of detail, this study lacks the reliability to detect sensitization (OECD-SIDS, 2002).

Several human patch studies (of varying reliability) listed in the IUCLID Datasheet showed no indication of skin sensitization. Skin patch tests were conducted on workers in a foam rubber factory. No sensitising effects of a glycerol/water mixture became apparent. Based on the available information, there is no human or animal data that indicates glycerol to be a skin sensitizer (OECD-SIDS, 2002).

6.4 Dermal/Percutaneous Absorption:

6.4.1 Conclusion:

No relevant information was available following the literature searching instructions contained within the Standard Operating Procedure for Creating New Ingredient Toxicity Profiles.

6.4.2 Summary:

No relevant information was available following the literature searching instructions contained within the Standard Operating Procedure for Creating New Ingredient Toxicity Profiles.

6.5 Repeated-Dose Toxicity:

6.5.1 Conclusion:

Based on the information summarized below, this substance can be considered to produce no systemic adverse effects to rats when fed at

dose levels up to 20% in the feed (reported as 8000 mg/kg bw/day for males and 10000 mg/kg bw/day for females).

| Species / strain / sex / number | Doses / route of exposure / duration | NOAEL/NOEL (or LOAEL/LOEL) (units) | Effect and effect level | References |
|---|---|---|---|---|
| Rats/strain and sex not specified/ 22 | 5, 10 and 20% natural or synthetic glycerol (Males: equivalent to 2000, 4000 or 8000 mg/kg bw/day; Females: equivalent 2500, 5000 and 10000 mg/kg bw/day)<br><br>Dietary<br><br>2 years (1 year for the high dose group) | NOAEL: Male: 8000 mg/kg bw/day Females: 10000 mg/kg bw/day | No adverse effects were observed | (OECD-SIDS, 2002) |
| Rat/ strain not specified/ 5 females/ treatment | 5% (natural or synthetic) (equivalent to 3335 mg/kg bw/day)<br><br>Drinking water<br><br>6 months | Not specified | Mortality 1/5 (synthetic) Small thymus and spleen, calcified kidney masses | (OECD-SIDS, 2002) |
| Rat/ strain, sex and number not specified | 10 mL of 50% solution/ kg bw/day (equivalent to 6300 mg/kg bw/day)<br><br>Oral<br><br>6 months | NOAEL: 6300 mg/kg bw/day | No abnormal findings | (OECD-SIDS, 2002) |
| Rat/ strain, sex and number not specified | 1-20% solution (equivalent to 667-13340 mg/kg bw/day)<br><br>Drinking water<br><br>3 months | Not specified | At 20%: Mortality 2/12 rats at top dose; decreased initial growth and development (recovery) | (OECD-SIDS, 2002) |
| Rat/ strain, sex and number not specified | 10 mL of 20% solution/kg bw/day (equivalent to 2520 mg/kg bw/day)<br><br>Oral<br><br>50 days | NOAEL: 2520 mg/kg bw/day | No abnormal findings | (OECD-SIDS, 2002) |
| Rat/ strain not specified/ 20 males/ treatment | ~1260 mg/kg bw/day<br><br>Gavage<br><br>44 days | NOAEL: ~1260 mg/kg bw/day | No treatment related effects | (OECD-SIDS, 2002) |

| Species / strain / sex / number | Doses / route of exposure / duration | NOAEL/NOEL (or LOAEL/LOEL) (units) | Effect and effect level | References |
|---|---|---|---|---|
| Rat/ strain not specified/ 20 males/ treatment | 1, 5, 10, 20% in water (equivalent to115-2300 mg/kg bw/day)<br><br>Gavage<br><br>44 days | Not specified | Mortality 15% in all treatment groups and controls | (OECD-SIDS, 2002) |
| Rat/ strain, sex and number not specified | 20% suppl. diet (equivalent to 8824 mg/kg bw/day)<br><br>Dietary<br><br>28 days | NOAEL: 8824 mg/kg bw/day | No abnormal findings | (OECD-SIDS, 2002) |
| Rat/stain not specified/ 8 males/ treatment | ~1525 mg/kg bw/day<br><br>Gavage<br><br>21 days | Not specified | Mortality at 1525 mg/kg 5/8, decreased $O_2$ consumption | (OECD-SIDS, 2002) |
| Rat/ strain not specified/10 females/ treatment | 950, 1900 or 3800 mg/kg bw/day<br><br>Gavage<br><br>3 days | LOAEL (local effects): 950 mg/kg bw/day | GI-tract: hyperaemia, petechial haemorrhage or erosions (DR) | (OECD-SIDS, 2002) |
| Guinea pig/ strain and sex not specified/10 animals | 5 mL of 50% solution (equivalent to 6300 mg/kg bw/day)<br><br>Oral<br><br>30-40 days | Not specified | All animals died; decreased red blood cells | (OECD-SIDS, 2002) |
| Dog/strain and sex not specified/ 3 animals | 35%<br><br>Dietary<br><br>50 weeks | Not specified | Decreased body weight gain | (OECD-SIDS, 2002) |
| Dog/ strain and sex not specified/ 1-2/ treatment | 950, 1900 or 3800 mg/kg bw/day<br><br>Gavage<br><br>3 days | LOAEL (local) 950 mg/kg bw | GI-tract: hyperaemia, petechial haemorrhage or erosions (DR) | (OECD-SIDS, 2002) |

| Species / strain / sex / number | Doses / route of exposure / duration | NOAEL/NOEL (or LOAEL/LOEL) (units) | Effect and effect level | References |
|---|---|---|---|---|
| Rabbits/ strain, sex and number not specified | 4.0 mL/kg bw (corresponds to 5040 mg/kg bw/day)<br><br>Dermal<br><br>45 weeks (8 hours/day, 5 days/week) | NOEL: 5040 mg/kg bw/day | No effects noted | (OECD-SIDS, 2002) |
| SD rats 15/sex/treatment | 0, 33, 165 or 662 mg/m$^3$<br><br>Inhalation (nose-only)<br><br>13 weeks (5 days/week, 6 hours/day) | NOAEC (local irritant effects): 165 mg/m$^3$<br><br>NOAEC (systemic): 662 mg/m$^3$ | Local irritation to the upper respiratory tract above 165 mg/m$^3$. No systemic treatment related effects were observed. | (OECD-SIDS, 2002) |
| Sprague Dawley rats (10/sex/group) | 0, 1000, 1930 or 3910 mg/m$^3$<br><br>Inhalation (nose-only)<br><br>2 weeks (5 days/week, 6 hours/day) | NOEC: 3910 mg/m$^3$ | No systemic effects were seen at the highest dose tested | (OECD-SIDS, 2002) |

### 6.5.2 Summary:

With respect to repeated oral exposure, no studies conducted to current OECD guidelines were available. Based on the available studies of better quality, a 2-year dietary study (1 year for the high dose group) conducted on 22 rats at levels of 5, 10 or 20% natural or synthetic glycerol in diet (males equivalent to 2000, 4000 or 8000 mg/kg bw/day; females equivalent to 2500, 5000 or 10000 mg/kg bw/day) was selected as key study. The authors concluded that no adverse effects were observed at up to 10000 mg/kg bw/day (OECD SIDS, 2002). A number of other studies are available in the table 6.5.1. It can be concluded that repeated oral exposure by gavage to glycerol does not induce adverse effects other than local irritation of the gastro-intestinal tract. The lowest effect value was 950 mg/kg bw/day, found in a 3-day study with rats (OECD-SIDS, 2002).

In a dermal study conducted prior to GLP standards and OECD test guidelines, there were no effects noted in rabbits dosed 8 hours/day, 5

days/week for 45 weeks with dose levels as high as 4.0 ml/kg (corresponds to 5040 mg/kg/day using a density of 1.2611 g/cm$^3$ at 20 ℃, a dose of 4.0 ml/kg) (OECD-SIDS, 2002).

In a subchronic study, Sprague-Dawley rats (10/sex/treatment) were exposed nose-only to a respirable aerosol of glycerol for 2 weeks (5 days/week, 6 hours/day). Mean exposure concentrations attained were 0, 1000, 1930 or 3910 mg/m$^3$. Only minimal to mild squamous metaplasia of the epithelium of the epiglottis was observed. The frequency of animals with mild metaplasia was greatest at the highest exposure concentration (3910 mg/m$^3$). No systemic effects were seen at the highest dose tested (OECD-SIDS, 2002).

In a further 90 day study, nose-only exposure of rats (SD 15/sex/treatment) 6h/day, 5d/w for 13 weeks to a respirable aerosol (MMAD <2 micrometres) of glycerol at measured concentrations of 0, 33, 165 and 662 mg/m$^3$ lead no treatment related effects. The NOAEC for local irritant effects to the upper respiratory tract is 165 mg/m3 and 662 mg/m$^3$ for systemic effects (OECD-SIDS, 2002).

## 6.6 Mutagenicity/Genotoxicity:

### 6.6.1 Conclusion:

Non-mutagenic/Non-genotoxic according to *in vitro* Ames, HGPRT, chromosome aberration, sister chromatid exchange and unscheduled DNA synthesis assays, as well as *in vivo* chromosome aberration and dominant lethal assays (OECD-SIDS, 2002)

### 6.6.2 Overview:

| Assay Type | Test Article | Species / strain / sex / number / cell line | Dose / route of exposure / duration | Metabolic Activation | Results (Positive or Negative) | Comments (Method and GLP compliance) | Ref. |
|---|---|---|---|---|---|---|---|
| *in vitro* bacterial | | | | | | | |
| Ames test | Glycerol | *Salmonella typhimurium* TA1535, TA1537, TA98 and TA100 | 100, 333.3, 1000, 3333, 10000 µg/plate | With and without metabolic activation (rat and hamster S9) | Negative | Non GLP and OECD | (OECD -SIDS, 2002) |

| Assay Type | Test Article | Species / strain / sex / number / cell line | Dose / route of exposure / duration | Metabolic Activation | Results (Positive or Negative) | Comments (Method and GLP compliance) | Ref. |
|---|---|---|---|---|---|---|---|
| Ames test | Glycerol | *Salmonella typhimurium* TA 98, TA 100, TA 1535, TA 1537, TA 1538 | 200-1000 ug/plate | With rat S9 | Negative | Non GLP and OECD | (OECD -SIDS, 2002) |
| *in vitro* mammalian | | | | | | | |
| HGPRT assay | Glycerol | CHO cells | 100-1000 ug/mL | With and without | Negative | Non GLP and OECD No cytotoxicity observed | (OECD -SIDS, 2002) |
| Chromosome aberration test | Glycerol | Chinese hamster ovary | 100, 200, 400, 600, 800 and 1000 ug/mL | With metabolic activation (S9) | Negative | Non GLP and OECD | (OECD -SIDS, 2002) |
| Sister chromatid exchange assay | Glycerol | CHO cells | 200-1000 ug/mL | With and without (rat S9) | Negative | Non GLP and OECD | (OECD -SIDS, 2002) |
| Unscheduled DNA synthesis | Glycerol | Rat hepatocytes | 100-1000 ug/mL | Not specified | Negative | Non GLP and OECD | (OECD -SIDS, 2002) |
| *in vivo* | | | | | | | |
| Chromosome aberration test | Glycerol | Rat, 10 males (strain not reported) | 1000 mg/kg bw in water or isotonic salt solution (dosing volume 2 mL)<br><br>Single injection in the abdomen | Not applicable | Negative | Did not induce a statistically significant increase in chromosomal aberrations compared to controls | (OECD -SIDS, 2002) |
| Dominant lethal assay | Glycerol | Male rats (strain and number not reported | 10, 100 and 1000 mg/kg bw<br><br>Method of administration not reported | Not applicable | Negative | A dose related increase was seen in post implantation loss but was considered not statistically significant compared to controls | (OECD -SIDS, 2002) |

6.7 Carcinogenicity:

6.7.1 Conclusion:

Non-carcinogenic according to a chronic carcinogenicity study where glycerin was administered for up to 2 years in the diet of rats and according to the OECD-SIDS Expert Panel (OECD-SIDS, 2002)

6.7.2 Summary:

5%, 10%, 20% natural glycerol and synthetic glycerol were administered to rats in the diet for 12-24 months. The treatment period at the 20% level was 1 year. No increase in tumour formation was observed compared to controls. The report authors concluded that glycerol does not initiate tumour development in the rat (OECD-SIDS, 2002).

A weak promotion effect on the incidence of lung tumour formation was reported in male ddY mice administered glycerol (5% in drinking water) for 1-20 weeks after a single s.c. injection with 4-nitroquinoline 1-oxide (4-NQO) (OECD-SIDS, 2002). However, no increase in the number of tumour bearing mice relative to controls was observed when conducted glycerol alone (in drinking water) (OECD-SIDS, 2002). The OECD SIDS Expert Panel concluded that the data does not raise concern for carcinogenic potential (OECD-SIDS, 2002).

6.8 Reproductive / Developmental Toxicity:

6.8.1 Conclusion:

Non-reproductive toxic/non-developmental toxic according to a multigenerational study using glycerin administered by gavage to rats and according to developmental toxicity studies using glycerol administered by gavage during organogenesis to gravid rats, mice and rabbits (OECD-SIDS, 2002).

Maternal toxicity NOAEL (Rat, gavage) = 2000 mg/kg bw/day (OECD-SIDS, 2002)
Developmental/reproductive NOAEL (Rat, gavage) = 2000 mg/kg bw/day (OECD-SIDS, 2002)

6.8.2 Summary:

Glycerol (20% solution in water) was administered to male and female rats (10/treatment) daily by gavage during the 8 weeks before mating. Exposure in females continued throughout pregnancy or until weaning of the F1 generation. No effects were found on reproductive efficiency of the parents, nor were adverse effects observed in F1 and F2 generation. The report authors established a NOAEL of 2000 mg/kg bw/day (OECD-SIDS, 2002).

Intratesticular administration of glycerol decreased spermatogenesis, leading to complete loss of spermatogenic cells in rats, but did not affect sexual behaviour. It was noted in the SIDS report that this is not a relevant route of exposure (OECD-SIDS, 2002).

Glycerol was administered to rats, mice and rabbits by gavage at dose levels up to 1310, 1280 and 1180 mg/kg bw, respectively, during the organogenesis phase of gestation. No maternal toxicity or teratogenic effects were observed at the highest dose levels. A NOAEL of 1180 mg/kg bw/day was derived (OECD-SIDS, 2002).

6.9 Toxicokinetics:

6.9.1 Conclusion:

No bioaccumulation potential based on study results (OECD-SIDS, 2002)

6.9.2 Summary:

Glycerol was rapidly absorbed in the intestine and the stomach, distributed over the extracellular space and excreted in humans and animals. Glycerol is phosphorylated to alpha-glycerophosphate by glycerol kinase predominantly in the liver (80-90%) and kidneys (10-20%) and incorporated in the standard metabolic pathways to form glucose and glycogen. Glycerol kinase is also found in intestinal mucosa, brown adipose tissue, lymphatic tissue, lung and pancreas. Glycerol may also be combined with free fatty acids in the liver to form triglycerides (lipogenesis) which are distributed to the adipose tissues.

The turnover rate is directly proportional to plasma glycerol levels (OECD-SIDS, 2002).

6.10 Photo-Induced Toxicity:

6.10.1 Conclusion:

No relevant information was available following the literature searching instructions contained within the Standard Operating Procedure for Creating New Ingredient Toxicity Profiles.

6.10.2 Summary:

No relevant information was available following the literature searching instructions contained within the Standard Operating Procedure for Creating New Ingredient Toxicity Profiles.

6.11 Human Data (other than human skin irritation/sensitisation data considered above):

A $LD_{Lo}$ value of 1428 mg/kg bw was reported in humans. However, further details were not available and the reliability of this data is unknown (OECD-SIDS, 2002).

No significant differences in sperm quality parameters were reported in 64 male workers in glycerol manufacture (OECD-SIDS, 2002).

## *7.0 No-Observed-Adverse-Effect Level (NOAEL) and Rationale:*

7.1 Conclusion:

An oral NOAEL of 8000 mg/kg bw/day can be assigned based on a 2-year repeated dose study in rats where no effects were observed at the highest dose tested (20% glycerin; equivalent to 8000 mg/kg bw/day in males and 10000 mg/kg bw/day in females) (OECD-SIDS, 2002).

## *8.0 Further Relevant Information:*

According to 21CFR § 182.1320, glycerin is generally recognized as safe when when used in accordance with good manufacturing practices (21 CFR, 2012).

### *9.0 References:*

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