Classification Submitted

Methoxyethanol (CAS: 109-86-4, EC: 203-713-7)

Current listed classification and risk phrase(s) under directive 67/548 and subsequent amendments and adaptations	**Harmonised classification indicated in regulation1272/2008 Annex VI.** **CLP signal word and pictogram,** **CLP Hazard class and statement codes**	**Classification as indicated by the available data that was included in the IUCLID dossier submission (according to regulation 1272/2008). Signal word, pictogram, Hazard class and statement codes ***
R10 Repro cat 2: R60, R61 Xn: R20/21/22	Flam liq 3: H226 Rep 1B: H360FD Acute tox 4: H332, H312, H302	Flam liq 3: H226 Rep 1B: H360FD Acute tox 4: H332, H312, H302 STOT (SE) cat 1: H370 STOT (RE) cat 2: H373
Flammable May impair fertility. May cause harm to the unborn child. Harmful by inhalation, in contact with skin and if swallowed.	Flammable liquid and vapour. May damage fertility or the unborn child. Harmful if inhaled. Harmful in contact with skin, Harmful if swallowed.	Flammable liquid and vapour. May damage fertility or the unborn child. Harmful if inhaled. Harmful in contact with skin, Harmful if swallowed. Causes damage to immune system. May cause damage to thymus through prolonged or repeated exposure.
		

* This proposal was submitted alongside the current harmonised classification.

Justification :

Physicochemical properties

Flashpoint greater than 23C but less than 60C.

Classification for reprotoxic effects

RATS

Methoxyethanol when administered to SD rats over 2 generations and dosed via drinking water was toxic to reproduction. The top 0.1% dose almost completely inhibited reproduction in the F0 generation and the mid dose 0.03% significantly reduced the number of live pups borne; other

adverse changes were seen at this dose on male testes and sperm. The lowest dose 0.01% (equivalent daily dose ~10mg/kg) showed minor changes to sperm density and testicular lesions, but these could not be clearly attributed to treatment with a clear dose response relationship and therefore not considered significant adverse effects. In a repeat of the experiment which used a different litter to form the parents for the F2 generation (litter 2 versus litter 5), the high dose 0.024%(20mg/kg) significantly reduced the number of pups borne live and the number of male pups borne live. These effects persisted into the second generation. The cross over trial showed that effects were on the males only. The mid dose group 0.012% (11mg/kg)) produced no adverse effects apart from an increase in pup weights, the significance of which was unclear. Many other studies have been performed over short time frames to non-standard methods to further investigate and have confirmed clear effects on males (reduced testes weight, reduced fertility, adverse effects on sperm – multiple abnormal parameters, reduced pregnancy rates, increased post-implantation loss, and fetal death) and females (estrus cycle effects.) Males are clearly more sensitive than females.

When administered to SD rats by inhalation, methoxyethanol was toxic to reproduction at an exposure of 300ppm. Males were more sensitive than females with infertility being caused by testicular atrophy and impairment of sperm production. The NOAEL was 100 (316mg/m3) ppm. In another single generation study, male and female rats exposed to 25ppm exhibited no effects on fertility or overt effects on development. Measurable neurochemical changes were observed in the pups from exposed males but the relevance of these findings to risk assessment is unclear. In a third study where rats (male and female) were administered methoxyethanol by inhalation prior to mating, complete infertility in males resulted following exposure to 300ppm with associated degenerative changes in the testes germinal epithelium of rats. These effects appeared to be substantially, but not completely, reversible following exposure cessation. A similar exposure produced evidence of general toxicity in females but no adverse effects on fertility. Further short term studies in males exposed by inhalation confirmed adverse effects on the testes (weight, sperm damage.)

A single short term study is available for the dermal route of exposure. Methoxyethanol when administered to rats by dermal exposure (occluded and non-occluded) for 7 days was toxic to reproduction. The effects were temporary, at least at the lower doses examined. The effects seen were inhibition of spermatid and spermatozoa production, atrophy of the testes and epididymides and consequential loss in fertility. Effects were seen at the lowest doses tested (625mg/kg/day for the occluded test and 1250mg/kg/day for the non-occluded test. However, the effects seen at this dose were reversible resulting in a NOAEL after 15 weeks recovery time of 625mg/kg/day for occluded animals and 5000mg/kg/day for non-occluded animals.

MICE

Methoxyethanol was administered to 3 different strains of mice (CD1, C57B1/6 and C3H over 2 generations via drinking water. There was clear evidence of toxicity to reproduction in all three strains. The most sensitive effect was a reduction in the number of females becoming pregnant and delivering live pups. The top 0.3% dose was severely toxic in all strains. In the CD1 and C3H mice, the middle dose had few detectable effects on the F0 animals but significantly reduced the reproductive success of the F1 animals. In C57B1/6 mice, the middle dose was toxic, reducing pup numbers and increasing levels of abnormal sperm. The lowest dose 0.03%, equivalent to 53-64mg/kg/day was

without adverse effect in all CD1 and C3H and can be regarded as a NOAEL. In the third strain, the lowest dose 0.03%, equivalent to 53mg/kg/day reduced seminal vesicle weights and sperm counts in the F1 generation. However, the effects were not large (~10% change from controls) which suggests that the NOAEL is not much lower than this dose. Other oral studies in mice at higher doses confirmed these effects. No studies have been carried out in mice by other routes of exposure

OTHER SPECIES

Methoxyethanol when administered to male rabbits for 13 weeks via drinking water produced a marked inhibition of normal spermatogenesis. The effect is marked with a NOAEL of 12.5mg/kg and a LOAEL of 25mg/kg. The effect is very specific with no clear effects on sperm morphology and no effect on the ability of the sperm that remain to fertilize a female rabbit. No other adverse effects that could be attributed to treatment were observed at the LOAEL. A gavage study in guinea pigs also confirmed adverse sperm effects at the lowest dose tested of 200mg/kg.

There is clear evidence in animals of adverse effects on fertility. Classification is warranted.

Classification for developmental effects

RAT (ORAL)

Methoxyethanol when administered in a liquid diet to pregnant female rats during GD7-18 produced both teratogenic and embryotoxic effects. The most sensitive effect being embryotoxicity, manifest as a slight but significant reduction in pup weight of 12-15% at the lowest dose tested of 0.006% (equivalent to 26mg/kg/day.) The no effect level for teratogenic effects was 0.006% and for maternal toxicity 0.025% (73mg/kg/day). This study was used as the key study as the route of exposure is more relevant than gavage.

Methoxyethanol when administered by gavage to pregnant female rats during GD6-15 produced embryotoxic, manifest as a slight but significant reduction in the number of live pups per litter. The no effect level was 12.5mg/kg. At higher dose, more severe effects were seen with total resorptions occurring at 100mg/kg.

A study specifically designed to assess the developmental effects of methoxyethanol in the heart showed no adverse effects on this organ when given to pregnant rats over two different parts of the organogenesis period. A slight prolongation of gestation was observed at the dose used (25mg/kg) and a slight change in a biomarker for cellular growth was seen but the biological significance of this, particularly for risk assessment, is unclear. A similar study confirmed the severe developmental effects of methoxyethanol in the absence of maternal toxicity. The most sensitive effects were offspring viability (manifest as no litters) and reduced pup body weight. Pregnancy length also increased. The inhibition of Orthinine Decarboxylase (ODC) activity in the heart was found to be closely associated with the developmental effects, and whilst there is no evidence to suggest causality, this was proposed by the study authors as a biomarker for developmental effects. In another study focussing on the heart, doses which produced adverse changes to litter parameters such as pup body weight, also produced teratogenic effects with heart defects the most sensitive effect. The clear no effect level for developmental effects was 25mg/kg although it could be argued that this is a LOAEL because of the incidence of hydronephrosis at this level. There were also clear reprotoxic effects at 50mg/kg and evidence of biological if not statistically significant effects at

25mg/kg. Overall, whilst effects remained small, there was multiple evidence to suggest that the no effect level for reprotoxic and possibly developmental effects was below the lowest level tested of 25mg/kg. In the final study of this type, severe effects on reproductive outcome in the absence of maternal toxicity were again demonstrated. In addition to producing physical abnormalities, reduced litter sizes and reduced survival rates, offspring surviving to 8 weeks of age showed a persistent intraventricular delay cardiac abnormality, albeit in the absence of any visible morphological changes; the consequences of this aberration are unknown and the implications unclear. A no effect level was not established as effects were seen at the lowest dose tested (50mg/kg).

A study specifically designed to assess certain serum chemistry parameters relevant to development confirmed the marked developmental and reprotoxic effects of methoxyethanol in the absence of maternal toxicity. At a dose which produced adverse changes to litter parameters such as survival and pup body weight, there is also evidence for teratogenic effects with heart defects the most sensitive effect. The clear no effect level for maternal toxicity was 50mg/kg whilst developmental effects developmental effects were seen at this dose (NOAEL50mg/kg). Changes were observed in the serum levels of calcium and vitamin D that could be attributed to treatment but these changes were considered secondary to the loss of litters.

A single dose of methoxyethanol given by gavage to pregnant female rats on GD13 was capable of inducing digit malformation and dismorphogenesis of limb bud developments as well as depressing fetal body weight growth. Lower doses which caused dismorphogenesis soon after treatment did not result in visible malformations at the end of term suggesting that recovery could result from these lower insult levels. The biologically and statistically significant no effect level was less than 50mg/kg.

RAT (INHALATION)

Methoxyethanol when inhaled at 25ppm by pregnant female rats caused overt effects on development. However, a measurable deficit was recorded in one of six behavioural tests and neurochemical changes were observed for pups from exposed females. The relevance of these findings, particularly the neurochemical changes, to risk assessment is unclear.

Methoxyethanol when administered by inhalation to pregnant female rats during GD6-15 was not teratogenic but produced slight fetotoxicity or variations in the highest dose group, manifest as a slight but significant increase in skeletal variations. Slight effects were seen on dam erythrocyte parameters, but the biological significance of these was questionable. A clear no effect level for developmental effects was observed at a dose of 10ppm and below.

RAT (DERMAL)

In an OECD guideline and GLP prenatal toxicity study, 2-Methoxyethanol was applied dermally (6hrs/day) to pregnant Wistar rats in doses of 0.05; 0.1 and 0.3 ml/kg body weight/day to the intact shaven dorsal skin using an occlusive dressing on GD6-15. Control animals were treated with water. The two higher doses elicited clear signs of maternal toxicity (reduced food consumption, impaired body weight gain (corrected), although the lower dose induced no signs of maternal toxicity. Severe Embryo-/fetotoxicity was demonstrated in the intermediate and high dose group manifest by

increased post-implantation losses and at all three dose levels by reduced fetal weights. A clearly increased incidence of different soft tissue variations, retardations and unclassified observations were also seen in the mid and high dose groups, although observations in the latter were greatly restricted by the very small number of offspring produced at this dose. Teratogenic effects were seen at all three doses, manifest through increased incidence of various malformations. NOAEL (maternal effects) 0.05ml/kg. NOAEL (teratogenicity) <0.05ml/kg

Methoxyethanol when administered by occluded dermal application to pregnant female rats showed teratogenic potential according to the criteria of the screening study used. The no effect level was 3% in 10ml physiological saline and a clear dose response relationship was seen. In a separate study, when administered as a single un-occluded dermal application to pregnant female rats on GD12 showed clear teratogenic and embryotoxic effects with multiple malformations in fetuses and a reduction in fetal body weight observed. The clear no effect level seen was a dose of 250mg/kg.

Methoxyethanol when administered as a single un-occluded dermal application of 2000mg/kg to pregnant female rats on showed clear teratogenic effects with multiple malformations in fetuses and a reduction in fetal body weight observed. Administration over a window of .GD10-14 produced these anomalies, although GD14 was the least sensitive and GD12-13 the most sensitive. Treatment on GD11-12 produced predominantly soft tissue anomalies whilst treatment on GD12-13 produced predominantly external and skeletal malformations.

Values obtained by the dermal route do not establish the true NOAEL and a route to route extrapolation is therefore preferred to derive the DNEL.

RABBIT

Methoxyethanol when administered by inhalation to pregnant female rabbits during GD6-18 produced severe and extensive teratogenicity at an exposure of 50ppm. Significant but not severe maternal toxicity was also seen, manifest as a decrease in body weight gain but this is unlikely to be a primary cause of the malformations seen. An increase in resorptions was seen at 10ppm relative to concurrent controls, but as these were within the range of historic controls, they were not attributed to treatment. No other effects were seen at this exposure, hence the NOAEL was 10ppm.

MONKEY

Methoxyethanol when administered by gavage to pregnant female monkeys during GD20-45 produced embryotoxicity, manifest as an increase in the number of abortions seen. Treatment at the lowest dose tested of 12mg/kg was attributed by the authors to cause death of primate embryos at a rate of 23% of total pregnancies and 100% at 36mg/kg. The embryonic death rate should be treated semi-quantitatively however as the small number of animals used precluded meaningful statistical treatment of the results. The results cannot unequivocally be related to treatment.

MOUSE

Methoxyethanol when administered by gavage to pregnant female mice during GD7-14 results in toxicity and teratogenicity in the absence of marked maternal toxicity. The most sensitive effects were skeletal variations and retardation of ossification, which was seen at the lowest dose tested of

32.5mg/kg. A single dose of methoxyethanol given by gavage to pregnant female mice on GD11 was capable of inducing digit malformations. The biological and statistically significant no effect level was 100mg/kg.

Methoxyethanol when administered by inhalation to pregnant female mice during GD6-15 was not teratogenic but produced slight fetotoxicity or variations in the highest dose group, manifest as a slight but significant increase in skeletal extra lumbar ribs and unilateral testicular hyperplasia. No effects were observed at a dose of 10ppm.

There is clear evidence in animals of developmental toxicity effects in the absence of maternal toxicity. Classification is warranted.

Classification for acute toxicity effects

A number of oral acute toxicity studies are available. Some are quite old but a significant number are available that are judged sufficiently reliable for the purposes of hazard assessment. A number of studies are available in rats (multiple species), both male and female, both fasted and non-fasted animals. Values obtained are reasonably consistent, ranging from 2257mg/kg in fasted animals to 3930 in non-fasted animals. A reliable study in mice produced an LD50 of 3930mg/kg in fasted animals and 4150mg/kg in non fasted animals. These are the two species normally used for acute toxicity classification by the oral route. Lower values are available for the guinea pig and rabbit. The sole value for the rabbit could not be judged for its reliability, but the value for the guinea pig of 950mg/kg (male and female) was judged reliable based on the detail provided in the publication.

In a study designed to assess inter-laboratory variation of the OECD acute inhalation toxicity study, a number of different rat strains were exposed to 2 -methoxyethanol vapour in the concentration range of 25 -33mg/l (average 29mg/l). No deaths resulted when the animals were exposed to this concentration for 1 -3 hours. From these results it was possible to predict that the LC50 is likely to be greater than 20mg/l. In another study designed to assess testes effects following acute exposure, male rats were exposed to a number of concentrations of methoxyethanol in the range 150ppm up to saturated vapour pressure for a period of 4 hours. No deaths were observed at any concentration. However, the study did note adverse effects on the testes of animals exposed to 625ppm and above of methoxyethanol, producing a NOAEC of 300ppm (0.95mg/l). The study did not provide a true LC50 and as such the results are only of partial use for classification and labelling purposes, but they can be used to derive a NOAEC for risk assessment purposes with appropriate safety factors. It can also be concluded that the LC50 is greater than 5000ppm (15.8mg/l). In an acute toxicity range finder study by the inhalation route, male rats were exposed to a number of concentrations of methoxyethanol for a period of 4 hours. All animals tolerated and exposure of 12.4mg/l but 60% mortality was seen at 17.8mg/l, suggesting that the LC50 fell within this range.

In an acute dermal toxicity study, male rabbits were exposed to 2 -methoxyethanol. The LD50 was established as 3939mg/kg. Sub-lethal effects were seen at lower doses including anorexia, slight depression, cyanosis, ataxia, soft faeces, and at higher doses salivation, nasal discharge, iritis, significant depression, laboured breathing, and prostration. A second study in rabbits produced a much lower LD50 of 1340ml/kg. Only basic details are reported in the study but it is considered that the result cannot be excluded from the overall evaluation of the acute dermal toxicity of this substance.

In conclusion, For the oral route, based on the results of the two species normally used, the substance does not warrant classification for acute toxicity in accordance with the current EU guidelines. However, the result from the guinea pig cannot be completely excluded which suggests that classification as harmful is appropriate. For the inhalation route, methoxyethanol does not appear to be particularly toxic, with the majority of studies (in rats only) indicating that classification is not required. However, one study indicated an LC50 of approximately 16mg/l. Based on this result, methoxyethanol falls marginally within the category where classification as harmful by the inhalation route is required. Limited and mixed results are currently available for the dermal route and in only one species (rabbit). However, the lowest reliable value available indicates that classification as harmful is warranted.

Classification for repeat dose effects

ORAL ROUTE

All of the available studies consistently indicate that the rat is more sensitive than the rabbit. In a well conducted drinking water study, rats were exposed to methoxyethanol at concentrations ranging from 750 -6000ppm for a period of 90 days. At this dose, both sexes also showed a significant reduction in thymus weight, both relative and absolute. Bone marrow cellular depletion, splenic atrophy and/or capsular fibrosis and thymic atrophy were apparent in both sexes from doses of 135 -165mg/kg upwards.

Numerous other sub-acute studies are available that consistently support the above results. None of them establish LOAELs below 71mg/kg. These studies consistently report reduction in thymus weight in the absence of body weight effects and reversible effects on markers for immune system function. Adverse effects on white blood cell population are also reported.

In a well conducted drinking water study, mice were exposed to methoxyethanol at concentrations up to 10000ppm for a period of 90 days. A NOAEL was established in the study for males at the lowest dose tested of 2000ppm, equivalent to 295mg/kg, based on testicular degeneration and increased hematopoiesis in the spleen at the next dose tested. However, a NOAEL was not established for female mice, since adrenal gland hypertrophy and increased hematopoiesis in the spleen occurred at the lowest concentration administered (equivalent to 492mg/kg).

DERMAL ROUTE

Limited data is available by the dermal route. A study examined the sub-acute percutaneous toxicity of methoxyethanol in rats. Animals were subjected to daily doses of 100 or 1000mg/kg under both occluded and non-occluded conditions for a period of 28 days. The only effect seen at the lower dose was reduced body weight gain and food intake under occluded conditions. At the higher dose, significant toxicity was observed with adverse effects body weight reduction, on the testes, haematology and the bone marrow. Only the first two were seen under non-occluded conditions.

The only other data is from studies which used much higher dose levels. These confirmed the effects on body and organ weights (testes, spleen) as well as on the blood (haematology) and that effects are more severe for exposure under occluded conditions, as would be expected for a volatile substance. A short term study that only examined male reproductive toxicity and used an exposure of 7 days, established a NOAEL under non-occluded conditions of 1250mg/kg.

INHALATION ROUTE

In a sub-chronic 13 week study, both male and female rats and rabbit were exposed by inhalation to methoxyethanol vapour in concentrations of 30, 100 and 300ppm. No rats died prior to scheduled sacrifice, but some rabbits in the 100 and 300ppm exposure groups died or were sacrificed when moribund during the study. Body weights as well as thymus and testicular weights of rats and rabbits in the 300ppm group were reduced as a result of the exposures. Hematologic changes occurred in rats and rabbits exposed to 300ppm. Concentrations of total protein, albumin and globulins in serum of rats (but not rabbits) in the 300ppm group were lower than for controls. Gross lesions in rats and rabbits exposed to 300ppm included decreased size of thymus in both sexes, decreased abdominal fat, and small flaccid testes in males. In addition there was decreased lymphoid tissue in some rabbits, as well as a slight-to-moderate decrease in size of testes in 4 of 5 rabbits in the 100ppm group and in 2 of 5 rabbits exposed to 30ppm. The only effects attributed to exposure to 30ppm methoxyethanol in this study were slight microscopic changes in testes of 1 of 5 male rabbits.

In a sub-acute inhalation toxicity study, male and female rats and mice were exposed to methoxyethanol vapour for 9 days over an 11 day period at concentrations up to 1000ppm. In rats at 1000ppm, adverse effects were seen on body weight gain, peripheral blood counts, bone marrow, testes and lymphoid tissue. Similar, albeit less marked, effects were seen at 300ppm, including thymus weight reduction and reduced red and white blood cell counts. The only significant change seen in the lowest 100ppm dose group was a reduction in white blood cell counts. Only a partial analysis was made in the mice. At 1000ppm, adverse effects were seen in both sexes on thymus and male testes. Female liver weight was also significantly reduced. The only significant change seen in the lowest 300ppm dose group was reduced thymus weight in females. The study confirmed the results from the oral studies that mice appear to be less sensitive than rats to the toxic effects of methoxyethanol.

Based on the considerations above, classification for specific organ toxicity by repeated exposure needs to be considered. Using the above data it is possible to conclude that a category STOT 2 classification would again be appropriate for only the oral route. The following phrase would be appropriate "May cause damage to organs (thymus) through prolonged or repeated exposure".

Classification for immunotoxic effects

Treatment of mice with relatively large doses of methoxyethanol (500 -1000mg/kg) caused a decrease in thymic cellularity and atrophy of the cortex. Thymic markers (CD4 +/CD8 +, Thy+,PNA+), immature thymocytes are relatively decreased. There were also increases in response to other ex-vivo immunological assays (eg. Lympho-proliferative response to concanavalin A.) Overall, the study indicated that methoxyethanol at high doses selectively depletes immature thymocytes

All four strains of mice treated with methoxyethanol for 10 days at doses of 50 -400mg/kg were comparatively resistant to adverse effects on the humoral immune system as quantified using an antibody response to TNP-LPS assay. In another study, treatment of mice with methoxyethanol for 10 days at doses of 50 -400mg/kg had no immunosuppressive effects.

Exposure of mice to methoxyethanol for two weeks as doses up to 1000mg/kg resulted in a significant reduction in thymus weight (NOAEL=250mg/kg) but no reduction in the effectiveness of

the humoral or cell mediated immune system when examined in a number of in vitro assays. No adverse effect was seen in a functional assay either

Treatment of rats acutely with methoxyethanol for 2 days significantly suppresses the antibody response to TNP-LPS. The study did not establish a NOAEL since effects were seen at the lowest dose tested (50mg/kg). Benchmark dose analysis of the results indicates that the NOAEL was in the range 25 -30mg/kg. Treatment of rats for 10 days at doses of 25 -200mg/kg caused significant suppression of the antibody response to TNP-LPS in all four strains tested. Statistically, a no effect level of 25mg/kg was established although the results suggest that the biologically significant no effect level could be lower than this.

Treatment of rats with methoxyethanol by oral gavage for 10 days at doses of 50 -200mg/kg causes significant suppression of immune system, as quantified by a number of assays. The most sensitive changes were lymphoproliferative reduced response to certain mitogens, enhanced PFC response to SRBC and IL2 reduced production at all dose levels. Other assays or the same ones with different mitogens or antibody stimulants were less sensitive or produced negative results. A decrease in thymus weight in the absence of body weight change was also seen at all doses.

Treatment of rats with methoxyethanol by oral gavage for 10 days at doses of 50 -400mg/kg causes significant suppression to the humoral and specific cell mediated immune system. The most sensitive changes were reduced lymphoproliferative response to a number of mitogens where effects were seen at all doses. A decrease in thymus weight in the absence of body weight change was also seen at al doses.

Oral treatment of rats with a single dose of methoxyethanol as low as 125mg/kg results in a visible increase in the number of thymic apoptotic cells within 3 hours. Prior treatment with phenobarbital reduced the level of thymic toxicity which is likely to be due to a reduction in the capacity of the animal to metabolise methoxyethanol to the active metabolite toxicant methoxyacetic acid.

Treatment of rats with methoxyethanol by dermal exposure for 4 days at doses of 150 -1200mg/kg causes significant suppression of the specific cell mediated immune system and the humoral immune system in particular. The no effect level for suppression of the latter was 150mg/kg. A decrease in thymus weight in the absence of body weight change was also seen at higher doses. Effects from dermal exposure mirror those from oral exposure clearly indicating that methoxyethanol is toxic by the dermal route.

In conclusion, 2-methoxyethanol does appear to be toxic to the immune system in both mice and rats. The evidence suggests that effects are only seen at quite high oral doses in mice (LOAEL=500mg/kgbw/day) but that clear suppression of the immune system of rats was seen at oral doses as low as 50mg/kgbw/day. For classification under the CLP regulation 1272/2008, since there is clear evidence for immunosuppressive effects in rats after as few as 2 exposures, classification for specific target organ toxicity for a single dose exposure by the oral route seems appropriate. Since the dermal study only used a four day exposure, this also seems appropriate to consider as a 'single' rather than a 'repeat dose' exposure. The LOAEL for the oral route is 50mg/kgbw/day whilst for the dermal route it is 300mg/kgbw/day. These would trigger a category 1 classification for both routes. There is no data for the inhalation route, but there is no reason to suspect that the same toxicity would not be manifest following dosing by this route, so the hazard phrase should not be route

specific. A classification of STOT (single exposure) H370 "Causes damage to organs (immune system)" is therefore recommended.