

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

DODINE (N-dodecylguanidine acetate)

Chemical Code # 245, Tolerance # 172

5/27/99

I. DATA GAP STATUS

Combined, rat:	No data gap; no adverse effect
Chronic toxicity, dog:	No data gap; no adverse effect
Oncogenicity, mouse:	No data gap; possible adverse effect
Reproduction, rat:	No data gap; no adverse effect
Teratology, rat:	No data gap; no adverse effect
Teratology, rabbit:	No data gap; no adverse effect
Gene mutation:	No data gap; no adverse effect
Chromosome effects:	No data gap; no adverse effect
DNA damage:	No data gap; no adverse effect
Neurotoxicity:	Not required at this time.

Toxicology one-liners are attached.

All record numbers through 168931 were examined.

** indicates an acceptable study.

Bold face indicates a possible adverse effect.

indicates a study on file but not yet reviewed.

File name: T169273

Leung, 5/27/99

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

** 172-065; 164839; "Chronic Toxicity and Carcinogenicity Study of Dodecylguanidine Acetate (Dodine) in the Sprague-Dawley Rat by Dietary Administration" (M. Dange, Rhone-Poulenc Agro, Centre de Recherche, France, Study # SA 95083, 9/10/98). Dodine Technical (Batch # 1174, 98.6% purity) was administered in the diet at 0, 200, 400 or 800 ppm to 60 Sprague-Dawley rats/sex/dose for 2 years with 10 additional rats/sex/dose designated for interim sacrifice after 52 weeks (M: 0, 10.2, 20.3, or 41.9 mg/kg/day, respectively; F: 0, 13.2, 26.5, or 53.5 mg/kg/day, respectively, for weeks 1 - 101). No treatment-related clinical signs or effect on the mortality rate were reported. Reduced mean body weights were noted in high dose males (90% of control, $p < 0.05$, weeks 1 to 37 and weeks 85 and 89) and females (85% of control, $p < 0.05$, weeks 1 to 101) were noted with occasionally decreased in food consumption. In addition, reduced mean body weight was also observed in mid dose females (90% of control, $p < 0.05$, weeks 89 and 101). No test-article related changes in hematology, clinical chemistry, urinalyses, ophthalmology, necropsy and histopathology were observed. **No adverse effects.** NOEL (M/F) = 200 ppm (M: 10.2 mg/kg/day, F: 13.2 mg/kg/day; based on reduced body weight). **Acceptable.** (Leung, 2/19/99).

CHRONIC TOXICITY, DOG

172-037 157656 831 "52-Week Toxicity Study in Dogs with Dodine" by J.A. Trutter, Corning Hazleton Inc., Vienna, VA (study #CHV 656-192; 12/9/96). 4 beagles/sex/dose received Dodine Technical (batch #1174; 98.6% Dodine) in gelatin capsules by the oral route at 0, 2, 10 or 20 mg/kg/day, 7 days/wk, for at least 52 wks. Observations for mortality/moribundity were made 2x/day, and for pharmacotoxic signs 1x/day. Body wts & food consumption were recorded weekly. Ophthalmoscopy was performed before treatment & during wk 52. Hematology, serum chemistry & urinalyses were performed on fasted dogs during wks 26 & 52. Gross pathology, organ wts & histopathology were performed after euthanasia at 52 wks. All animals survived to euthanasia. Clinical signs included diarrhea (HD), emesis before or just after dosing (MD/HD females) and salivation (MD/HD). Body weight appeared unaffected by dosing. Individual animals (1 MD female, wks 3-14; 1 HD male, wks 3-7; 1 HD female, wks 2-33 & 36-53; their food consumption values were excluded from mean calculations during these times) had to be maintained on supplemental feeding due to low feed intake during the early weeks of dosing (this was interpreted as evidence that an MTD had been reached). Overall food consumption appeared somewhat elevated in HD males (mean weekly consumption at ascending doses: 1.8, 1.8, 1.8, 1.9* kg; * $p < 0.05$). This may have been incidental. Mean food efficiency was generally similar among the dose groups, though the HD dogs exhibited sporadically lower values in both sexes. Ophthalmoscopy did not reveal abnormalities. Hematology revealed elevated mean WBC counts in HD females at 26 & 52 wks ($p < 0.05$ at wk 52). Also, segmented neutrophils were significantly elevated in wk 26 HD females. One HD female showed a high leukocyte pattern (8 segmented neutrophil, lymphocyte & monocyte counts). Serum chemistry revealed elevated mean aspartate aminotransferase in wk 26 HD males ($p < 0.05$) and elevated alanine aminotransferase in wk 26 & wk 52 HD males. Urinalyses revealed slightly elevated epithelial cells & specific gravity in wk 26 HD females and sperm in wk 26 HD males. Gross necropsy, organ wt determinations & histopathology did not reveal test article-related abnormalities. **No adverse effects. NOEL (M) = 10 mg/kg/day (low feed intake); NOEL (F) = 2 mg/kg/day (low feed intake). **Acceptable.** (Rubin, 11/21/97)

ONCOGENICITY, MOUSE

**** 172-066; 164840;** “78-Week Dietary Oncogenicity Study with Dodine in Mice” (K. D. Williams, Covance Laboratories Inc., Madison, WI, Study # 6224-220, 10/9/98). 70 Crl:CD-1(ICR)BR mice/sex/dose were fed diets containing 0, 200, 750, or 1500 ppm Dodine Technical (Lot # 1174, 98.6% purity) for 78 weeks. 10 mice/sex/dose group were sacrificed at 52 weeks (interim sacrifice) and the remaining animals were designated for termination after 78 weeks. No test material-related decrease in survival were noted in either sex. Six high dose females died or were sacrificed in moribund condition during week 44. Cause of death was due to 6-fold error in test diet preparation. Reduced body weight and food consumption were noted in 1500 ppm males and females and 750 ppm females. Macroscopic examination revealed slightly increased incidence of masses in the liver at terminal sacrifice in animals given 1500 ppm. **Possible adverse effect:** Histopathology indicated significantly increased incidence of combined hepatocellular adenoma and carcinoma in females dosed at 1500 ppm, but neither was statistically different from control when considered alone. Males did not exhibit any statistical differences in the incidence of hepatocellular adenoma, hepatocellular carcinoma or combined adenoma and carcinoma. NOEL (M/F) = 200 ppm (M: 24 to 38 mg/kg/day, F: 31 to 47 mg/kg/day; based on reduced body weight and food consumption); **Acceptable** (Leung, 2/23/99).

REPRODUCTION, RAT

****172-040 157659 834** “Two-Generation Reproduction Study with Dodine in Rats” by S.M. Henwood, Corning Hazleton Inc., Madison, WI (project #HWI 6224-218; 12/17/96). 30 F0 rats/sex/dose were exposed *via* the diet to Dodine (lot #1174; 98.6% pure) at 0, 200, 400 or 800 ppm for 10 wks before mating & throughout mating, gestation & lactation until F1 necropsy. F1 animals were exposed for at least 10 wks following weaning & throughout mating, gestation & lactation until F2 necropsy. Observations for mortality/moribundity were made 2x/day. Male body wts were determined weekly. Female wts were determined weekly during pre-mating & mating, on gestation days 0, 7, 14 & 20 & on lactation days 0, 4, 7, 14 & 21. Food consumption was measured over similar periods. Estrous cycles were monitored through vaginal smears. The presence of sperm in the vaginal smear or copulatory plugs was evidence of mating. Litters were observed daily and culled to 4/sex on day 4. Live pups were examined and weighed on days 7, 14 & 21. After weaning 1/sex were randomly selected from each F1 litter for mating to produce the F2 generation (30 matings/dose). On lactation day 21, 10 pups/sex/dose (F1 & F2) were necropsied. Parental males were necropsied after mating, parental females after litter weaning. Histology was conducted on a range of tissues from control & HD animals. Semen was evaluated for each sacrificed male. Despite the deaths among F0 animals of 1 control female & 1 LD male (wks 9 & 7), and among F1 animals of 1 MD male (wk 11), there were neither Dodine-related deaths nor clinical observations through the F2 generation. Wt change was statistically suppressed at the HD in both F0 sexes by wk 1, with a wt difference maintained throughout the pre-mating period. An effect was not observed during gestation or lactation. Wt change in F1 parentals was similar to F0, though suppression did occur during gestation. F1 MD females also showed suppressed wt gain. Suppressions in food consumption were noted in both sexes in the F0 and F1 generations, primarily at the HD, but also occasionally at the MD. Reproductive parameters, estrous cycles & semen were unaffected by exposure. F1 & F2 pup wts were suppressed at the HD and, less often, at the MD. The lower parental terminal body wts at the HD & MD were associated w/lower absolute organ wts, lower organ-to-brain wt ratios & higher organ-to-body wt ratios for some organs. Necropsies & histopathologic analyses did not reveal abnormalities. **No adverse effects.** Reproductive NOEL > 800 ppm. Developmental NOEL = 200 ppm (\pup wt). Parental NOEL = 200 ppm (\body wt/food consumption). **Acceptable.** (Rubin, 12/9/97)

TERATOLOGY, RAT

****172-038, -063 157657, 158707 833** “Dodine: Teratogenicity Study in Rats” by J.A. Wilson & K.P. Hazelden, Inveresk Research International, Tranent, Scotland (project #437766; 7/10/89). 25 mated female Sprague-Dawley rats/dose were dosed w/Dodine (batch #92/88/2;

95.3% Dodine) 1x/day by oral gavage between gestation days (GD) 6-16 inclusive. Doses were 0, 10, 45 or 90 mg/kg/day, administered as a suspension in distilled water at 10 ml/kg. Viability checks were conducted twice daily. Clinical signs were recorded daily, w/particular attention paid to the 1st 1-1.5 hr after dosing. Body wts were recorded on GD 0, 6, 9, 13, 17 & 20. Food consumption was recorded daily from day 4. Rats were euthanized on GD 20 and the thoracic & abdominal cavities necropsied. The reproductive tract was removed & weighed and the number of corpora lutea & the number & position of uterine implant sites were determined. Numbers of live & dead fetuses were counted and individual live fetal weights recorded. Approximately half of the fetuses were fixed in alcohol, examined for visceral abnormalities and the skeletons stained & examined. The other half were fixed in Bouin's fluid, sexed and examined for soft tissue abnormalities by free-hand sectioning. There were no maternal deaths. Salivation or staining after dosing in 4/25 HD dams may have been treatment-related. Necropsy/histopath revealed reddened lungs in 2/25 HD dams (one of those exhibited dark red foci) with evidence of hemorrhage or congestion. 11/23 HD dams & 6/23 MD dams lost weight during GD 6-9. Mean weight gain for the remaining HD dams was lower than control, resulting in a mean weight loss overall. Mean weight gains for GD 6-9 were, at ascending doses, 15.1, 15.1, 8.6 & -1.0* g, *p<0.001. Mean weight gains for GD 6-17 were 76.7, 72.9, 74.5 & 61.0*, *p<0.001. Total mean food consumption was reduced at GD 6-10 at the top two doses (147.2, 141.1, 127.2 & 102.6 g/rat/day for that period). Pregnancy performance, fetal weight and the appearance of fetal abnormalities/variant were unaffected by exposure to Dodine. **No adverse effects.** Maternal NOEL = 10 mg/kg/day (reduced weight gain & food consumption). Developmental NOEL > 90 mg/kg/day. **Acceptable.** (Rubin, 11/25/97)

TERATOLOGY, RABBIT

172-039, -063 157658, 158707 833 "Dodine: Teratogenicity Study in Rabbits" by C. McCay & K.P. Hazelden, Inveresk Research International, Tranent, Scotland (project #437745; 7/19/89). 16 (control, LD & MD) or 20 (HD) mated female New Zealand White rabbits/dose were treated w/Dodine (batch #92/88/2; 95.3% Dodine) 1x/day by oral gavage between gestation days (GD) 6-18 inclusive. Doses were 0, 10, 40 or 80 mg/kg/day, administered as a suspension in distilled water (4 ml/kg). Viability checks were conducted twice daily. Clinical signs were recorded daily, w/particular attention paid to the 1st 1-2 hr after dosing. Body wts were recorded on GD 6, 9, 12, 15, 19, 22, 26 & 29, and food consumption daily from day 4. Rats were euthanized on GD 29 and the thoracic & abdominal cavities necropsied. The reproductive tract was removed & weighed, the number of corpora lutea & the number & position of uterine implant sites were determined, and ocular exams conducted. Live & dead fetuses were counted and individual live fetal weights recorded. **b of the fetuses were fixed in alcohol, examined for visceral abnormalities and the skeletons stained & examined. The remainder were fixed in Bouin's fluid and examined for soft tissue abnormalities by free-hand sectioning. Deaths, HD: 3 killed *in extremis* (days 11 & 15); MD: 1 found dead (day 8). 3 of these 4 deaths were considered due to accidents during dosing as they were associated w/breathing difficulties & lung pathology. 2 abortions (days 20/21) & 1 death @ the HD were considered Dodine-related as they were associated w/weight loss, reduced food consumption, softened/liquid GI contents and, in one doe, stomach irregularities. Other Dodine-related clinical signs included cold ears, emaciation, dirty/foul smelling ano-genital region, splayed forelimbs, all occurring at the HD, & one doe w/liquid cecal contents at the MD. Other possibly Dodine-related necropsy findings included fluid-distended colon, pitted/scarred kidneys & foci on kidneys, with the latter 2 findings occurring at the MD. While minor mean wt loss occurred at the HD at GD 6-9, no differences from control occurred over the dosing period if aborting does are excluded from calculation. Mean food consumption was suppressed at the HD, particularly during the 1st few treatment days, an effect largely due to suppressions in the 2 does fated for abortion and 1 doe not fated to survive. Neither pregnancy parameters (including fetal weight) nor the appearance of fetal abnormalities indicated a treatment effect. Maternal NOEL = 10 mg/kg/day (clinical signs & necropsy findings). Developmental NOEL > 80 mg/kg/day. **Acceptable.** (Rubin, 12/1/97)

GENE MUTATION

172-041 157660 842 "Evaluation of Dodine Tech. 95% for Mutagenic Activity in the Ames Assay" by M.I. Willems, Civo Institutes TNO, Zeist, The Netherlands (report #V.81.102/210064-7; 3/81). The histidine-dependent *Salmonella typhimurium* tester strains TA 1535, TA 1537, TA 1538, TA 98 & TA 100 were exposed in triplicate KS9 microsomes to Dodine Technical (lot #51-24-3; 95% pure) at 0 (solvent control: methanol), .06, .19, .56, 1.67 or 5.0 Fg/plate for 3 days at 37EC. This dose range was established by a preliminary toxicity test in which bacterial lawn growth was inhibited at 10 Fg/plate. Despite the ability of the positive controls to induce reversion to histidine independence, no concentration of Dodine could generate similar behavior regardless of the absence or presence of a microsomal activating system. Dodine is not considered to be mutagenic in this system under the conditions tested. **Unacceptable** (no individual plate counts; inadequate justification for concentrations used). (Rubin, 12/11/97)

172-043 157663 842 "An Investigation into the Possible Induction of Point Mutation at the HGPRT Locus of Chinese Hamster Ovary Cells by Dodine" by P.B. Davis, Division of Technology for Society TNO, Delft, The Netherlands (report #R 85/105; 5/10/85). 24 hr after seeding 3.5×10^6 cells/175 cm² flask, Dodine (code #KG8507; 98% pure) at doses of 0 (solvent control: 0.8% ethanol), 2.5, 5, 10, 15 or 20 Fg/ml (-S9 activating microsomes) or 0, 5, 10, 15, 20, 25 or 30 Fg/ml (+S9) was added for a period of 5 hr. Dosing was established by a preliminary cytotoxicity test. After washing and a passage/expression period, the cells were exposed to the selective agent (10 FM 6-thioguanine) at a density of 20,000 cells/ml (10 ml/petri dish; 10 petri dishes/exposure). Mutant frequencies were determined as the ratio of the survivors of the 6-TG exposure ÷ the number of clonable cells. Despite the ability of the positive controls (-S9: 0.4 Fl/ml ethyl methanesulphonate; +S9: 2 & 5 Fl/ml dimethyl nitrosamine) to increase the number of survivors of 6-TG exposure, survival frequencies among cultures exposed to Dodine were not clearly different from control values. Dodine is not considered to be mutagenic in this system under the conditions tested. **Acceptable. (Rubin, 12/15/97)

CHROMOSOME EFFECTS

172-042 157661 843 "Chromosome Analysis of Cultured Human Lymphocytes Treated *in Vitro* with Dodine" by J.W.G.M. Wilmer, Civo Institutes TNO, Zeist, The Netherlands (report #V85.164/250209; 4/85). Lymphocytes prepared from a healthy male volunteer were exposed to Dodine (batch KG 8507; 98% pure) for 24 hr (-S9) or 2 hr (+S9) at doses of 0 (solvent control: ethanol), 0.37, 1.11, 3.33 or 10 Fg/ml (-S9), or 0, 0.56, 1.67, 5 or 15 Fg/ml (+S9). These dose levels were established in a preliminary study which showed clear toxicity at and above 4.94 Fg/ml, KS9. 100 well-spread metaphases/duplicate culture (25/slide) were analyzed for chromosome aberrations. Despite the ability of the positive controls (-S9: 30 Fg/ml methyl methane sulphonate; +S9: 20 Fg/ml cyclophosphamide) to induce chromosome aberrations, no concentration of Dodine could generate similar behavior regardless of the absence or presence of a microsomal activating system. Dodine is not considered to be clastogenic in this system under the conditions tested. **Acceptable. (Rubin, 12/12/97)

DNA DAMAGE

**172-044 157667 844 "Mutagenicity Test on Dodecylguanidine Acetate [Dodine], Technical *In Vivo* Mammalian Micronucleus Assay" by H. Murli, Hazleton Washington, Inc., Kensington, MD (project #14710-0-455; 4/14/92). 15 mice/sex/dose (20/sex/dose at the HD; extra animals were dosed at the HD to supply cells in the event of death) were treated orally by gavage with Dodecylguanidine Acetate [Dodine] (lot #303/90; -94% pure) at doses of 100, 200 or 400 mg/kg in corn oil (10 ml/kg). At 24, 48 & 72 hr after dosing the animals were euthanized (negative & positive controls were harvested at 24 hr only), the bone marrow harvested, the coded slides scored for micronuclei and for the polychromatic (PCE) to normochromatic (NCE) cell ratio. 1000 PCEs/animal were scored. Positive controls (treated w/80 mg/kg cyclophosphamide) were euthanized at 24 hr only. Deaths: one HD male @ 6 hr post dose and one HD male (secondary group) prior to the 24-hr harvest. Distended abdomens were noted in 1

MD & 1 HD male prior to the 48-hr harvest and in 1 HD male prior to the 72-hr harvest. Despite the ability of the positive control compound to increase the % micronucleated PCEs/1000/animal, no such ability was forthcoming from the test article. Neither the positive controls nor the test article showed any clear differences from controls in the PCE/NCE ratio. Dodecylguanidine Acetate [Dodine] is not considered to induce micronuclei in this system under the conditions tested. **Acceptable.** (Rubin, 12/15/97)

NEUROTOXICITY

Not required at this time.

SUBCHRONIC STUDIES

172-036 157655 822 "A 21-Day Dermal Toxicity Study in Rats with CT-334-87" by C.S. Auletta, Bio/dynamics, Inc., East Millstone, NJ (project #4932-88; 7/7/89). CT-334-87 (no lot #; 35% Dodine; a clear peach-colored liquid) was administered in aqueous dilutions to 5 rats/sex/dose on a clipped upper dorsal area 5 days/week, 6 hr/day, for 3 weeks (15 applications). Doses were 0 (controls received vehicle, 2 ml/kg), 12.5, 25 & 50 mg/kg/day. The test site was covered by a polyethylene patch & adhesive bandaging. Conventional clinical observations (including skin irritation exams, systemic toxicity, hematology, clinical chemistry, organ weights, necropsy & histopathology) were conducted. All animals survived to euthanasia. HD animals gained somewhat less weight than controls, though there was no clear dose dependence (at ascending doses, male wk 0-3 gains = 82, 87, 81, 75 g, female = 35, 24, 29, 22 g). Food consumption in wk 2 HD females was statistically depressed compared to controls (140, 127, 146, 120*; *p<0.05). No test article-dependent pharmacotoxic signs were observed. Mean total WBC counts were somewhat higher than controls for HD males (16.7, 13.3, 16.7, 22.7 x10³/FI) & HD/MD females (8.9, 9.2, 12.2 & 15.9), though the male data at the HD were largely influenced by one rat. HD males showed a suppression of total blood protein (6.2, 6.1, 6.1, 5.9 g/dl) and albumin (3.5, 3.5, 3.5, 3.2* g/dl; *p<0.01) and an elevation of serum glutamic pyruvic transaminase (32, 38, 34, 42* IU/dl; *p<0.01). HD female mean liver weight and liver:body weight ratio were elevated, though no liver pathology was evident upon histopathology. Dermal irritation exams revealed erythema, atonia, desquamation, fissuring & superficial necrosis at all doses with a marked dose dependence for incidence & severity. Edema, exfoliation, eschar & necrosis were observed only at the HD (**possible adverse dermal effect**). All of these lesions were also seen at necropsy (in addition, eschar was seen in 1 LD male). HD histopath revealed inflammatory cell accumulation, hyperkeratosis, parakeratosis, squamous cell hyperplasia, necrotic epithelium, erosions/ulcers & chronic inflammation. Dermal NOEL (M/F) < 12.5 mg/kg/day (skin effects). Systemic NOEL (M/F) = 50 mg/kg (no systemic effects at HDT). **Supplemental.** (Rubin, 11/19/97).

ANIMAL METABOLISM

**172-045 157670 851 "Disposition and Metabolism of ¹⁴C-Labeled Dodine in Rats (Preliminary and Definitive Study)" by V. Reddy *et al*, Midwest Research Institute, Kansas City, MO (project #9938-F; 9/10/92). ¹⁴C-Dodine (a mixture of ¹⁴C-Dodine [lot #910225, specific activity 56.5 mCi/mmol; >99% pure] and unlabeled Dodine [lot #FF1/88, 99.8% pure]) was administered orally as a corn oil suspension (4 ml/kg) to 6 groups of rats: Group 1, 1/sex, single dose, 27.5 & 28.5 (M & F) mg/kg; Group 2, 1/sex, single dose, 397.1 & 415.0 mg/kg; Group 3, 5/sex, single dose, 36.2 & 36.6 mg/kg; Group 4, 5M/6F, 14 daily doses of 40 mg/kg Dodine followed by a single dose of ¹⁴C-Dodine, 37.5 & 37.4 mg/kg; Group 5, single dose, 377.2 & 375.4 mg/kg. Due to low aqueous solubility, i.v. dosing was not attempted. Rats were fasted overnight prior to radiolabel dosing. For Groups 1 & 2 (the preliminary study), air, urine & feces were collected @ 4, 8, 12, 24, 48 & 72 hr postdose and the animals sacrificed @ 72 hr. For Groups 3-5, urine & feces were sampled at -24, 4, 8, 12, 24, 48, 72, 96 & 120 hr, and the animals sacrificed after 120 hr. A range of tissues was sampled for radioactivity. Metabolite determination for urine & feces was done using HPLC, TLC, MS & enzyme hydrolysis. The

preliminary study showed that, at the low dose (Group 1), most of the label was eliminated by 72 hr, but at the high dose (Group 2) 72 hr was insufficient. Consequently the definitive study was run out to 120 hr. Since less than 1% of the total dose was excreted through expired air, this parameter was not measured in the definitive study. Group 3: urinary elimination (cumulative % of dose), M/F, 24 hr=36.35/35.15, 48 hr=39.19/39.43, 120 hr=40.55/42.42; fecal, 24 hr=47.88/34.66, 48 hr=56.46/50.74, 120 hr=59.69/55.14; total, 24 hr=84.23/69.81, 48 hr=95.66/90.17, 120 hr=100.25/97.56. Group 4: urinary, 24 hr=39.94/38.34, 48 hr=43.49/42.41, 120 hr=45.35/45.00; fecal, 24 hr=42.22/29.41, 48 hr=52.99/49.93, 120 hr=56.18/53.74; total, 24 hr=82.16/67.74, 48 hr=96.48/92.34, 120 hr=101.52/98.74. Group 5: urinary, 24 hr=11.94/10.03, 48 hr=24.43/20.17, 120 hr=41.91/43.11; fecal, 24 hr=7.18/4.76, 48 hr=17.94/14.52, 120 hr=50.50/47.53; total, 24 hr=19.12/14.80, 48 hr=42.38/34.69, 120 hr=92.42/90.74. These data show that elimination was virtually complete by 24 hr for both LD groups, but required 120 hr at the HD. Recovery from blood & tissues ranged from 0.62-3.34%. The majority of the urinary label resided in 4 metabolite peaks (hydroxydodecyl guanidine, intermediate β oxidation products, urea & unidentified). One major peak (parent Dodine) appeared in feces. **Acceptable.** (Rubin, 12/11/97)