

the first 4 weeks of treatment and weekly thereafter for clinical signs of toxicity. Individual bodyweights and food consumption were measured on a weekly basis for the first 26 weeks of treatment and every 2 weeks thereafter. Fundoscopic and biomicroscopic examinations were conducted on the control and 5% groups during weeks 1, 13, 26, 52, 78, and 103. Clinical chemistry and haematological samples were collected at weeks 13, 25, 39, and 51. After 104 weeks, ophthalmoscopic examinations, haematology, clinical chemistries and organ weight data revealed no changes which could be attributed to the feeding of gellan gum. Survival of male treated rats was poor when compared to controls whereas female treated rats exhibited better survival than their concurrent controls. Male rats, fed gellan gum at the 3.8 and 5.0% dietary levels, exhibited lower body weights after 76 weeks. The initial bodyweights were 5.2 and 3.4% lower than the control values for the 3.8 and 5.0% dietary levels, respectively. It was concluded that in spite of the initial body weight deficit, the growth pattern for these treated groups was identical to that of the control. In addition, this effect was not seen in either the females or any other species tested. There is no basis to suggest that the lower body weights, observed in the male rats, are indicative of toxicity. Organs and tissues as those listed in the mouse study were examined for histopathological changes at study termination. There were no neoplastic or non-neoplastic changes that could be associated with the feeding of gellan gum. The authors concluded that gellan gum is non-carcinogenic to Sprague-Dawley rats.

For chronic toxicity study on dogs, diets containing 0, 3, 4.5, and 6% gellan gum were fed to groups of 5 Beagle dogs per sex for a period of 52 weeks. The dogs were observed daily for clinical signs of toxicity and were measured for body weights and food consumption. Ophthalmoscopic examinations were performed during pretreatment and after 12, 24, 29, and 51 weeks. Hematology and clinical chemistry were measured during pretreatment and after 6, 13, 25, 39, and 50 weeks. After 52 weeks all animals were killed and grossly examined. All animals survived treatment. Food intake was higher in the treated groups compared to the controls. There were no adverse effects associated with the feeding of gellan gum to beagle dogs for a period 1-year.

6. *Animal metabolism.* The adsorption, distribution, and excretion of gellan gum was studied using a dually radiolabeled (^3H and ^{14}C)

preparation. The use of dual labeling allowed simultaneous quantitation of both polysaccharide and "protein" fractions of gellan gum.

One male and one female Sprague-Dawley rat were gavaged with single doses of the $^3\text{H}/^{14}\text{C}$ -gellan gum (ca. 960 mg/kg; ca. 4 μCi). Expired air was collected 24 hours after dosing. Less than 0.55% of the given radioactivity was detected as ^{14}C .

Four male and three female Sprague-Dawley rats were dosed with single gavage dose of $^3\text{H}/^{14}\text{C}$ -gellan gum (ca. 870 mg/kg; 2.9 - 4.1 μCi ^{14}C ; 0.7 - 0.9 μCi ^3H). Urine and feces were collected for 7 days, at which time the animals were sacrificed and their tissues analyzed for residual radioactivity. Females excreted 86.8% and 1.9% of the given ^{14}C in the feces and urine, respectively. Males excreted 86% of the dosed ^{14}C in the feces and 3.3% in the urine. Females excreted 4.1% of the dosed ^3H in their urine and 100.1% in their feces, while males excreted 3.6% of the total ^3H in their urine and 99.6% in their feces. In all animals, the activities of ^3H in tissues (blood, brain, liver, kidney, lung, muscle, skin, heart, and carcass) were too low to be quantitated accurately. Tissue and carcass radioactivity for ^{14}C averaged 3.8% of dose for male rats and 3.0% of dose for female rats. A male and four female Sprague-Dawley rats were gavaged with about 1 g/kg of radiolabeled gellan gum and blood samples collected from the tail vein at different time intervals over a 7-day period. Data were reported as ^{14}C dmp/mL blood (^3H dmp/mL blood was not reported). The peak level of radioactivity, which amounted to about 0.4% of the administered radioactivity, occurred about 5 hours after dosing.

Gellan gum was shown to be poorly absorbed and did not cause any deaths in rats which received a single large dose (5 g/kg bwt) in the diet or by gavage.

7. *Metabolite toxicology.* Gellan gum is a polysaccharide polymer composed of D-mannopyranose with D-glucopyranose and 6-deoxy-L-mannopyranose, calcium, potassium, and sodium salt. Gellan gum metabolizes into simple non-toxic sugars and their salts.

8. *Endocrine disruption.* Gellan gum does not belong to a class of chemicals known or suspected of having adverse effects on the endocrine system. There is no evidence that gellan gum has any effect on endocrine function in developmental or reproduction studies. Furthermore, histological investigation of endocrine organs in chronic dog, rat, and mouse studies did not indicate that

the endocrine system is targeted by gellan gum.

C. Aggregate Exposure

1. *Dietary exposure.* As a minor formulation component, there is no reasonable expectation that gellan gum will appear in diet.

i. *Food.* Gellan gum is approved in the U.S. under 21 CFR 172.665 as a food additive, stabilizer, and thickener in batters, breadings, coatings, glazes, gravies, and sauces for meat and poultry products. As a minor formulation component, there is no reasonable expectation that gellan gum will appear in food from pesticide uses.

ii. *Drinking water.* As a minor formulation component, there is no reasonable expectation that gellan gum will appear in water.

2. *Non-dietary exposure.* The only non-dietary exposure to gellan gum will be exposure through treating and handling of treated seeds and application of formulations containing gellan gum.

D. Cumulative Effects

The potential for cumulative effects of gellan gum and other substances that have a common mechanism of toxicity has also been considered. Gellan gum is a high-molecular-weight polysaccharide gum produced by a pure-culture fermentation of a carbohydrate with *Sphingomonas elodea*. There is no reliable information to indicate that toxic effects produced by gellan gum would be cumulative with those of any other chemical including another pesticide. Therefore, CP Kelco believes it is appropriate to consider only the potential risks of gellan gum in an aggregate risk assessment.

E. Safety Determination

1. *U.S. population.* The occupational exposure to gellan gum in pesticide formulations during distribution and storage will be limited to: Workers involved in the transportation of gellan gum to customers; and those involved in the loading and off-loading of the product containers from commercial carriers and during opening of drums containing gellan gum. However, the potential for worker exposure is expected to be well controlled and limited if worker-safety procedures are routinely practiced. The potential opportunity for human exposure to gellan gum is expected to be limited to clean-up activities during routine maintenance, or following an accidental spill or release. Exposures occurring during these activities would typically be minimized by the accommodations made in equipment design and