ATTACHMENT 5

Comparative assessment of the allergenicity of cottonseed meal from Bollgard™ and non-transgenic indian hybrid cotton in a guinea pig model.

Monsanto Company
Biotech Regulatory Science
Final Report

REPORT NO.: MSL-15763

DATE: 12/5/98

TITLE: **Comparative assessment of the allergenicity of cottonseed meal from Bollgard™ and non-transgenic Indian hybrid cotton in a guinea pig model**

AUTHOR: **Richard E. Goodman**

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The addition of cottonseed meal to the diet at 10% w/w produced an immediate decrease in body weight gain and lower weights when compared to controls. For example, by day 21 body weights of animals fed the non-transgenic raw cottonseed meal diets, MECH-1 and MECH-3, were significantly less ($p<0.001$) than animals fed the control diet (Table I). Weight gains in the MECH-1 and MECH-3 groups were on average only 22% compared to the control group. These animals also exhibited clinical signs including reduced fecal pellet production, soft stools and rough coats.

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Abstract
(continued)

Table I
Mean Body Weights (g) of Guinea Pigs

Diets	Day 0	Day 21	Day 28	Day 49
Control	333	444	484	551
Control / MECH-1 Bt[1]	332	443	473	529
MECH-1	333	355 *	405 *	443 *
MECH-3	333	359 *	402 *	466 #

[1] This group did not receive cottonseed meal in the diet from day 1 through day 28 and MECH-1 Bt from day 28-49. Significantly different from control: * $p<0.001$, # $p<0.01$.

On day 21, all animals were fed commercial diet for the next seven days to determine whether the animals would recover body weight. In addition, feed samples were analyzed for vitamin C, mycotoxins and Cry1Ac; results showed that the feed provided to the MECH-1 Bt group for the first 21 days did not contain Cry1Ac, subsequently it was determined that this group inadvertently had been fed control diet. Between days 21 and 28, MECH-1 and MECH-3 groups gained weight at a rate similar to controls, except that one animal in the MECH-1 group died and one in the MECH-3 group was moribund and subsequently euthanized.

On day 28, remaining animals were fed their intended diets. Body weight gains were again decreased in cottonseed meal fed groups from days 29 to 35, whereas gains were lower or similar to control gains from days 36-49. Failure of the animals to thrive on 10% cottonseed meal indicated probable compromised health status of these animals. The study was terminated without performing PCA assays on day 49.

In conclusion, results demonstrate that guinea pigs have decreased body weight gains and clinical signs (reduced fecal pellet size and abundance, soft stools and rough coat) when fed a nutritionally balanced diet containing 10% cottonseed meal (MECH-1 and MECH-3). Although a direct comparison of gains and signs between the MECH-1 Bt and MECH-1 and MECH-3 groups was not possible, the results show that guinea pigs fed diets with 10% (w/w) cottonseed meal have significant decreases in body weights and gains by day 21. Since weight gain for MECH-1 and MECH-3 groups were on average 22% of the weight gain of the control group during the first 21 days of this study, the likelihood that the animals would produce a reliable immune response was doubtful. Thus it was concluded that feeding guinea pigs 10% cottonseed meal for a 60 day sensitization period to accurately measure relative allergenic activity of the test diets was not possible.

Study Title

Comparative assessment of the allergenicity of cottonseed meal from Bollgard™ and non-transgenic Indian hybrid cotton in a guinea pig model

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Study Report
December 5, 1998

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Laboratory Project ID
97-01-00-02

Study Number: 97-01-00-02

Title: Comparative assessment of the allergenicity of cottonseed meal from Bollgard™ and non-transgenic Indian hybrid cotton in a guinea pig model

Study Author : Richard E. Goodman

Contributors: Larry R. Holden, Joan L. Lee, Gyula Holleschak, Terry Kaempfe, James D. Astwood

Record Retention: All study specific raw data, protocols and final reports will be retained at Monsanto, St. Louis, except the raw data developed at Ralston Analytical Labs, for analysis of the raw cottonseed meal, which is retained at the Ralston Analytical Laboratory, 824 Gratiot, St. Louis, MO 63102. Actual dietary composition, other than the cottonseed, is proprietary and is held at the Richmond, IN facility of Purina TestDiet, 1050 Progress Dr., Richmond, IN 47374.

Sample Retention: Any study samples which are to be retained will be stored at Monsanto, St. Louis.

Signatures of Report Approval:

Richard E Goodman 12/5/98
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Protein Characterization and Safety Center

Andrew J. Reed December 5. 1998
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ABBREVIATIONS

cry1Ac	Class I (Lepidopteran-specific) crystal protein gene
Cry1Ac	Class I (Lepidopteran-specific) crystal protein from *Bacillus thuringiensis* var. *kurstaki*
CSM	cottonseed meal
DHL	DHL Worldwide Express
g	gram
mg	milligram
µg	microgram
ml	milliliter
µl	microliter
FcγR	High affinity IgG1a receptor
i.c.	intracardiac
i.d.	intradermal
IgE	antibody isotype IgE
MAHYCO	Maharashtra Hybrids Seeds CO. Ltd.
MECH-1	MAHYCO cotton hybrid #1
MECH-3	MAHYCO cotton hybrid #3
MECH-1 Bt	Transgenic MAHYCO cotton hybrid #1 with Cry1Ac and NPTII
nptII	neomycin resistance, selectable marker gene (Neomycin phosphotransferase II gene
NPTII	neomycin resistance protein (amino-glycoside-3'-phosphotransferase II)
SAS®	SAS® statistical analysis software
SDS-PAGE	sodium dodecylsulfate-polyacrylamide gel electrophoresis
SLI	Springborn Laboratories, Inc.
w/v	weight to volume
w/w	weight to weight

1. SUMMARY

A study was conducted using guinea pigs to assess the relative allergenic activity of cottonseed meal from transgenic cotton, containing the Cry1Ac Lepidopteran specific insecticidal protein from *Bacillus thuringiensis*, compared to non-transgenic cotton. Young adult female Hartley-derived albino guinea pigs were fed diets containing no cottonseed meal (control diet) or diets containing 10% (w/w) cottonseed meal made either from non-transgenic cottonseed (MECH-1 and MECH-3) or transgenic cottonseed (MECH-1 Bt) containing Cry1Ac. The diets were to be fed for approximately 60 days and a passive cutaneous anaphylaxis assay (PCA) would be done to compare the antigen specific IgG1a reaginic antibody response of all groups. However, by day 21 guinea pigs fed cottonseed meal-containing diets gained significantly less weight compared to controls and failed to thrive. As a result, all groups were fed commercial guinea pig diet from day 21 to day 28; guinea pigs subsequently were fed their intended diets from day 28 to day 49 at which time the study was terminated.

The addition of cottonseed meal to the diet at 10% w/w produced an immediate decrease in body weight gain and lower weights when compared to controls. For example, by day 21 body weights of animals fed the non-transgenic raw cottonseed meal diets (MECH-1 and MECH-3) were significantly less ($p<0.001$) than animals fed the control diet (Table I). Weight gains in the MECH-1 and MECH-3 groups were on average only 22% compared to the control group. These animals also exhibited clinical signs including reduced fecal pellet production, soft stools and rough coats.

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2. INTRODUCTION

Bollgard™ (a registered trademark of Monsanto Co.) cotton contains the *cry1Ac* gene encoding the Cry1Ac Lepidopteran specific insecticidal protein that was originally isolated from *Bacillus thuringiensis* var. *kurstaki*. The *cry1Ac* gene was transferred into cotton along with the marker gene, *nptII*, which expresses the neomycin phosphotransferase II (NPTII) protein. Monsanto Company and Maharashtra Hybrids Seeds CO. Ltd. (MAHYCO) have crossed Bollgard cotton with Indian cotton (MECH-1) to incorporate the *cry1Ac* gene into Indian cotton hybrids to provide protection against Lepidopteran insect pests in India.

2.1 Background

Various *Bacillus thuringiensis* formulations have been safely used for more than thirty years to control insect pests in a variety of crops, ornamentals and trees (reviewed in Entwistle et al., 1993). As literature searches indicate, this use has not led to any documented cases of allergic responses to the insecticidal proteins. Cry1Ac is insecticidal only to lepidopteran larvae when ingested. Cry1Ac acts by binding to a lepidopteran larval specific mid-gut membrane receptor and after activation in the highly basic gut fluid, inducing perforation of the gut. Cry1Ac has no adverse biological effect on non-target species including mammals. More detailed background information is presented in MSL-15740 (Goodman and Holden, 1998). Searches of the literature and studies that we have performed (Astwood, 1995a; Ream, 1994; Ream, 1993; Fuchs et al., 1993; Astwood, 1995b) indicate that there is no evidence that would implicate either Cry1Ac or NPTII proteins as allergens. In addition, there is no evidence that any of the transgenic cotton materials are more allergenic than non-transgenic cotton.

The current study was performed in response to the request from the Indian Department of Biotechnology to further assess in a guinea pig model, the relative allergenic activity of transgenic Indian Bollgard cottonseed compared to non-transgenic Indian cottonseed. The basis for the assay is that Hartley guinea pigs develop reaginic antibodies, predominantly IgG1a, in response to a wide range of antigens (Sarlo et al., 1994, Zhou et al., 1998). Antigen specific antibody concentrations or titers may be measured by passive cutaneous anaphylaxis (PCA). Since the primary concern for increasing the allergenicity of agricultural products is the risk associated with consumption, the logical route of sensitization is including the test material in the diet of naïve guinea pigs (Pahud and Schwarz, 1984). However, no animal model has been validated and shown to be an accurate predictor of the allergenic activity of a range of clinically relevant allergens (Metcalfe et al., 1996).

Guinea pigs do not normally consume cottonseed or cottonseed meal. There are no known reports establishing safe levels of consumption of cottonseed meal in this species. A primary concern regarding the use of any animal species to test cottonseed meal is the ability to tolerate gossypol. Gossypol is a polyphenolic compound that is known to be more toxic to monogastric species than to ruminants (Abraham and Hron, 1992). There is little data concerning the safety levels for guinea pigs, but the acute LD_{50} may be as low as 280 mg/kg, nearly ten fold lower than the level that is safe for rats (Abou-Donia, 1989). If that number is valid, a 400 g guinea pig would be expected to consume around 20 g of feed per day, or 2 g of cottonseed meal. Assuming

1% of the cottonseed weight is gossypol (Nida et al., 1996), the animal would consume 20 mg of gossypol, or approximately 12 to 15% of the LD_{50} dose, on a daily basis for 60 days. It is not clear what effect that level of consumption would have on the animals. Based on reports in the literature for domestic pigs, it is reasonable to assume that there could be serious health effects in guinea pigs due to chronic ingestion of cottonseed. Therefore, one objective of these studies was to assess whether guinea pigs would tolerate extended feeding of raw, full-fat cottonseed meal (CSM) at 10% of the diet.

2.2 Purpose

The purpose of this study was to assess the relative allergenicity of Indian Bollgard cottonseed meal compared to conventional cottonseed meal using a PCA assay by comparing the reaginic antibody response of Hartley guinea pigs fed either transgenic or non-transgenic cottonseed meal.

3. EXPERIMENTAL DESIGN

Prior to the initiation of this study, a similar study using the Brown Norway rat as a test animal was initiated under Study Protocol # 98-01-36-01. The overall design of the current study (protocol amendment request submitted to the Dept. of Biotechnology by Dr. Muzumdar, Appendix 7.1) was to sensitize Hartley guinea pigs to cottonseed proteins by feeding different groups of animals cottonseed meal from transgenic (MECH-1 Bt) and non-transgenic (MECH-1 and MECH-3) hybrid cotton. A non-cottonseed diet was included as an additional control. Serum from all animals would then be tested for the production of cotton specific IgG1a by the *in vivo* method of PCA. Ten animals were assigned to each feeding group, non-cottonseed control, and 10% cottonseed meal diets of MECH-1 Bt, MECH-1 (non-transgenic) and MECH-3 (non-transgenic). At the end of the study, serum was to be collected from each animal, and used in a cross-over PCA assay designed to compare the relative reactivity of serum from each sensitization group and similarly dosed challenge groups. Skin reaction sizes were to be scored for comparison between hybrid extracts, doses and diets. This design allows direct comparison of each cottonseed test extract material while reducing the influence of animal to animal variation.

3.1 Materials

a. Cottonseed. Seed of transgenic cotton (MECH-1 Bt) and non-transgenic cotton (MECH-1, MECH-3) were harvested, acid delinted by MAHYCO and shipped via DHL, through U.S. Customs to Monsanto Company.

b. Raw cottonseed meal (CSM). Cold (-20°C) delinted cottonseed lots were weighed and ground to a moderately fine powder in the presence of liquid nitrogen, using a commercial/industrial Waring blender. Powdered meals were stored frozen (-20°C), with permeable covers and mixed occasionally over one day to allow the N_2 to sublimate from the meal. The ground cottonseed meals were maintained frozen (-20°C). Proximate analysis was conducted on ground, whole cottonseed meal of all three hybrids. Raw, ground seed of the three hybrids was used in the manufacture of the feed for the guinea pigs.

c. Defatted cottonseed meal. Samples of raw CSM of each of the three hybrids were defatted by three serial extractions of each ground meal in six volumes of hexane (HPLC, UV spectrophotometry grade) at 45°C to 50°C with mixing for 15 minutes. The hexane was removed by filtration after each extraction. Residual hexane was removed by evaporation at room temperature under vacuum. Defatted samples were used for protein gel electrophoresis, for immunoassay of Cry1Ac in the CSM and for production of challenge doses for the passive cutaneous anaphylaxis (PCA) assays.

d. Cottonseed meal analysis. Samples of raw cottonseed meal (not defatted) were submitted to Ralston Analytical Labs for analysis of gossypol content and for proximate analysis.

e. Guinea pig diet pellet formulation. Dr. Dorrance Haught, primary animal nutritionist of Purina TestDiet in St. Louis, MO, formulated three diets based on standard, commercial Purina Laboratory Guinea Pig Diet 5025. These were a control diet containing no cottonseed meal and three feed sensitization diets containing full-fat, ground, raw, transgenic MECH-1 Bt, non-transgenic MECH-1 and non-transgenic MECH-3 cottonseed. The percentage of cottonseed in the cottonseed containing diets was equal to 10% of the bulk weight of the diet. All four diets were balanced with approximately equal composition of total protein, lipid, carbohydrate and fiber. The other major plant material sources were soybeans, corn, oats, sugar beet, wheat and alfalfa. The diets contained fish meal and domestic animal meat. The exact proportion of components in the diets is proprietary (Purina) except for the concentration of cottonseed meal.

f. Guinea pig diet pellet manufacture. Four test diets were manufactured at Purina TestDiet, Richmond, IN. Each diet was manufactured as two individual batches, dried and packed into three containers (boxes) for

shipment to Springborn laboratories. Retention samples were submitted to Monsanto.

g. Cry1Ac detection assay. A qualitative immuno-detection assay was used to measure Cry1Ac protein in seed samples and dietary pellets using a Cry1Ac specific monoclonal antibody and detection system. This assay was used to demonstrate that the MECH-1 Bt test materials contained the transgenic protein and that non-transgenic materials did not.

3.2 Animals

Guinea pigs. Nulliparous, non-pregnant female Hartley guinea pigs between 300 g total body weight (approximately 5 to 7 weeks of age) were purchased from Charles Rivers Laboratories, Raleigh, NC by Springborn Laboratories. Animals were acclimated on control diet (Purina 5026) with food and deionized water provided *ad libitum*. All animals were marked with uniquely numbered ear tags. Animals were stratified by body weight and assigned to the feeding groups to minimize average weight differences.

3.3 Feeding Exposure

Springborn Laboratories Inc., of Spencerville, OH conducted these studies. Protocols and results are included in the Final Report from Springborn (SLI Study # 3044.697), Appendix 7.2. Following acclimation, the animals were fed from box #2 of each of the appropriate dietary boxes for the first 21 days of the study (July 24, 1998 to August 14, 1998). As will be discussed in the results, on day 21 it became evident that the two non-transgenic CSM diets were not being consumed at a rate that would maintain the health status of the animals. All animals of the study were placed on commercial guinea pig diet for the next seven days to allow recovery of the health status of the animals, and to provide an opportunity to perform analyses of all diets. At day 28 of the study analytical results were equivocal, but most of the animals were gaining weight at a rate equal to the control diet growth rate. At day 28 all animals were returned to the scheduled dietary treatment, however feed was supplied from box #1 of each diet instead of box #2. In addition, on day 31, all animals were placed on water bottles with supplemented vitamin C to help ensure sufficient vitamin C intake for those animals that were not consuming adequate diet. Within one week after re-starting the treatment diets, all three CSM dietary groups were gaining significantly less weight than the control diet group and the MECH-1 Bt group lost an average of 5% body weight. On day 49 the study was terminated and all animals were euthanized due to the questionable health status and potential confounding effect on that might have on the immune system and study results.

3.4 Statistical Methods

Analysis of body weight data was performed at Monsanto using SAS® (SAS Institute Inc., Cary, NC), by a one-way analysis of variance. Springborn Laboratories, Inc., performed separate data analyses which are presented in the final report, Appendix 7.2.

4. RESULTS/OBSERVATIONS

4.1 Cottonseed Meal Analyses

Cottonseeds were ground in liquid nitrogen (N_2) at Monsanto in preparation for feed, analytical work and for the passive cutaneous anaphylaxis assay. Samples of the ground meal were transferred by courier to Ralston Analytical Labs, St. Louis, MO for analysis. Data from the individual analyses (Appendix 7.3) are summarized in Table II.

Table II. Summary data of Ralston Analytical proximate analysis of cottonseed meal samples, reported as percents of meal.

Cottonseed meal analysis	MECH-1 Bt	MECH-1	MECH-3
Moisture %	8.36	7.73	8.76
Protein % [1]	23.0	23.1	23.6
Ammonia %	0.14	0.13	0.14
Fat % [2]	13.8	14.5	14.3
Crude Fiber %	19.4	19.5	18.0
Ash %	4.28	3.92	4.21
Gossypol % [3]	0.48	0.52	0.40

[1] Protein measured by the protein combustion-IR method; [2] Fat determined by soxhlet extraction with ether; [3] free gossypol determined by HPLC

4.2 Transgenic Protein Expression in Seeds

Seed samples from the cottonseed hybrids provided by MAHYCO were ground and extracted in neutral buffer, then tested using a Cry1Ac specific solid phased immunoassay. The MECH-1 Bt seed sample was the only that tested positive for the Cry1Ac protein.

4.3 SDS-PAGE Band Patterns

The banding patterns of the CSM extracts in colloidal blue stained gel indicated that there were no obvious differences in the extracted proteins of the three CSM preparations (MECH-1 Bt, MECH-1 or MECH-3).

4.4 Feed Manufacture

Purina TestDiet manufactured the guinea pig feeding pellets based on the Purina 5025 guinea pig diet. A control diet was made using the same components as the test article diets, but without CSM. To manufacture the CSM diets, portions of components of the proprietary feed were replaced with raw, full-fat cottonseed meal such that 10% of the bulk of the diet was from either MECH-1 Bt, MECH-1 or MECH-3. The ingredient mix of the other components were adjusted to provide approximately equal levels of protein, lipid, carbohydrate and fiber in each diet, as summarized in Table III. The exact formulation was determined by the Purina TestDiet Nutritionist, based on the proximate data for the cottonseed meal provided by the Ralston Analytical Labs assay. Historical data of composition of the individual ingredients were used to formulate the diets. Contents included corn, oats, alfalfa, sugar beet pulp, wheat germ, wheat middlings, soybean meal, fish meal, meat meal, brewer's yeast, micro-nutrients, calcium carbonate, sodium chloride, whey, DL-methionine, tallow, molasses, choline chloride and water. Diets were made sequentially, with the last completed on June 5, 1998, shipped directly to Springborn Laboratories. Retention samples were shipped to Monsanto.

Table III. Calculated dietary composition, percent of total mass, calculated values estimated from proximate analysis of cottonseed meal and historical data of other components.

	Control	10% MECH-1 Bt[2]	10% MECH-1[2]	10% MECH-3[2]
Protein[1]	19.3	20.1	20.1	20.1
Fat (Soxhlet)[1]	4.3	4.3	4.3	4.3
Crude Fiber[1]	13.0	13.8	13.8	13.7
Starch[1]	17.3	12.8	12.8	12.8
Ash[1]	8.1	7.6	7.6	7.6

[1] percent by weight; [2] cottonseed meal, raw, full-fat

4.5 Feed Analysis Prior to Study Initiation

Samples of all diets were submitted to Ralston Analytical Laboratories. Proximate analysis, iron, vitamin C and free gossypol determinations were performed on samples from boxes #1 and #2 of each diet. Pesticide residue analyses were performed on samples from box #2 of each diet. Diets were manufactured approximately one month prior to sampling. Values for each box of feed used in this study were determined (Table IV). Two values were lower than the other diets. Although low, vitamin C at 754 ppm in box#1 of MECH-3 was still approximately three times greater than the minimum required for guinea pigs. The protein concentration of the sample from box #2 of MECH-3 (13.8%) was lower than other samples. New samples were

submitted and analyzed in duplicate (17.2% and 17.4%), indicating that the protein concentration in this diet was sufficient. The concentration of free gossypol in all diets was low and was not expected to cause toxic effects. Values for pesticide residues were below the limits of detection.

Table IV. Measured analytical values one month after manufacture. Samples were analyzed by Ralston Analytical Laboratories.

Box #1 of each[3]	Control	10% MECH-1 Bt[2]	10% MECH-1[2]	10% MECH-3[2]
Moisture	10.8	8.00	8.98	13.0
Protein[1]	19.9	20.6	20.1	20.1
Fat (Soxhlet)[1]	4.78	5.25	5.46	4.63
Crude Fiber[1]	13.6	16.2	15.7	14.5
Ash[1]	7.12	7.71	7.41	7.4
Iron (ppm)	281	298	280	276
Vitamin C (ppm)	1070	1200	1100	754
free gossypol[1]	0.011	0.034	0.037	0036
Box #2 of each[4]	Control	10% MECH-1 Bt[2]	10% MECH-1[2]	10% MECH-3[2]
Moisture	7.72	10.4	11.6	12.2
Protein[1]	20.4	19.4	19.6 [19.6][7]	13.8*[17.3][7]
Fat (Soxhlet)[1]	4.79	4.56	5.66	5.44
Crude Fiber[1]	14.0	13.6	14.5	17.8
Ash[1]	7.68	7.96	7.77	8.08
Iron (ppm)	275	280	259	280
Vitamin C (ppm)	1320	1250	1230	1220
free gossypol[1]	0.01	0.011[5]	0.041	0.04
carbamates[6]	nd	nd	nd	nd
org.phosphates[6]	nd	nd	nd	nd
chlorinated pest.[6]	nd	nd	nd	nd

[1] percent by weight; [2] cottonseed meal, raw, full-fat; [3] samples from Box#1 of each diet (stored at room temperature for 30 days prior to sampling; [4] samples from Box#2 of each diet (stored refrigerated for 30 days prior to sampling); [5] note that this low free gossypol value measured for this box of feed is one of the few measurements that clearly supports the idea that box#2 of the MECH1 Bt diet did not contain cottonseed; nd, not detected; [6] broad spectrum pesticide screen, all values below the limit of detection. * Out of range protein value. [7] New sample analysis for protein only, 12/3/98 by Ralston Analytical.

4.6 Animal Body Weights Days 0 to 21

Each animal was weighed approximately weekly (Appendix 7.2). Cumulative mean percent weight gains over the 21 day feeding period (Figure 1) were compared statistically using a one-way analysis of variance. There were significant differences among weight gains between diet groups, establishing that cottonseed diets had an adverse impact on growth rates. On day 21, the Springborn Study Director notified Monsanto of the weight gain discrepancy

and early clinical observations that suggested there was a significant depression of the guinea pig growth rates with two of the cottonseed diets. Samples of dietary pellets from each box of feed were taken by Springborn and shipped to Ralston Analytical for vitamin C and mycotoxin assays. Similar samples were submitted to Monsanto for immunoassay detection of the Cry1Ac protein. On day 21 the test diet feed was removed from all cages and commercial diet (Purina 5025) was supplied *ad libitum* for the next seven days. During the seven day recovery period the animals were monitored closely. One animal from the MECH-1 group died and one animal from the MECH-3 group was euthanized because it failed to gain weight and clinical symptoms indicated that the animal was moribund. All other animals gained weight at rates approximately equal to the control group and appeared to have recovered sufficiently by day 28 to restart the study.

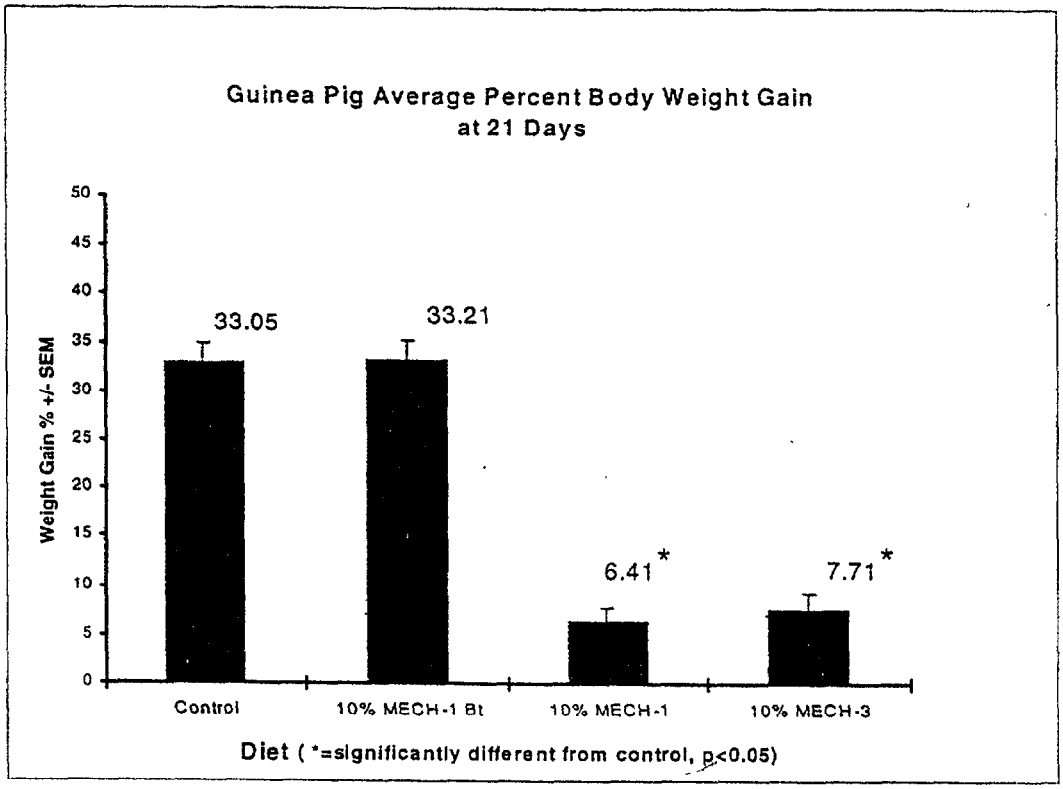

Figure 1. Average percent body weight gain at day 21 of the study. Treatment averages were compared to the control dietary group. This was the first indication that guinea pigs would not gain weight normally on 10% full-fat cottonseed meal diets. Analysis of all boxes of diet following this finding demonstrated that the 10% MECH-1 Bt group in fact had been fed control diet (without cottonseed) for the first 21 days of the study and had not received the intended cottonseed diet. No other differences were found.

4.7 Immunoassay of Cry1Ac Protein in Feed

Samples of each box of feed (3 per diet), returned by Springborn Laboratories for identity analysis were ground and extracted, and the supernatants were tested for the presence of the Cry1Ac protein. The results were as expected except that box #3 of the Control diet tested positive for Cry1Ac, and box #2 of the MECH-1 Bt diet tested negative for Cry1Ac. Subsequent testing of retention samples at Monsanto, and directly on-site at Springborn Laboratories, verified these results and indicated that the error occurred during packaging of those two boxes of diet. The results established that the MECH-1 Bt feeding group had not received CSM diet during the first 21 days of the study, but instead had received the non-cottonseed control diet, and therefore were equal to the control diet fed group during the initial feeding. When feeding of test diets was resumed at day 28, all animals were fed from box #1 of the specified diets, which tests had shown were correct regarding the presence of the transgenic cottonseed meal.

4.8 Feed Analysis Post-Day 21

Because of the lack of weight gain in the non-transgenic cottonseed fed groups, samples of all three boxes of each diet (12 in all) were sent to Ralston Laboratories for analysis of vitamin C and 19 mycotoxins. Animals were only fed from boxes #1 and #2 during this study. Lack of vitamin C, or the presence of mycotoxins were potential causes of the compromised health of the animals. Some of the mycotoxin assays were performed by Romer Laboratories, on a subcontract from Ralston. Vitamin C values were all above 1,000 ppm except box #1 of the MECH-3 diet which at 793 ppm was similar to the previous determination of 753 ppm, and well above the minimum required dietary requirement. Only one mycotoxin was measured above the level of detection. That was deoxynivalenol (vomitoxin), which was measured in all dietary boxes including control diets. Fusarium infected corn was the most likely source of this mycotoxin. The measurements of deoxynivalenol were between 0.2 and 0.3 ppm and were not considered significant as the animals fed the control diet and the MECH-1 Bt diet (box #2) had the same level of the toxin and showed no ill effects. The nutritionist at Purina was consulted along with Monsanto veterinary pathologists and there was a general agreement that the levels of deoxynivalenol were insignificant. The conclusion from this analysis was that the low weight gain, and apparent unpalatability of the cottonseed diets were not caused by a loss of vitamin C, and were not likely to have been caused by mycotoxins. Since the animals seemed to have recovered by day 28 on commercial diet and the specific cause of the weight gain reduction in CSM diets hadn't been

identified, a decision was made to restart the study using box#1 from each diet, which were demonstrated to contain the correct test articles.

4.9 Weight Gain Day 21 to Termination at Day 49

Following the seven day recovery period (day 21 to day 28) when animals were on commercial diet, the correct treatment diets were provided *ad libitum* from box #1 of each diet on day 28. Additional vitamin C was provided in drinking water at day 31 since some of the earlier clinical symptoms suggested that some of the animals had symptoms consistent with scurvy which would be attributable to inadequate dietary intake of vitamin C. On day 35 at the next body weight measurement, all three CSM feeding groups were either loosing weight, or gaining weight at a significantly lower rate than the control group. This finding indicated that all three cottonseed diets were compromised. Although the rate of weight gain increased from day 35 to day 42, the total body weight differences between the control animals (averaging around 550 g at day 42) and the two non-transgenic cottonseed groups (averaging around 450 g at day 42) indicated that the health of the cottonseed fed groups was impaired. The study was stopped and all animals were euthanized on day 49. Because of the compromised health status of the animals, the planned immunological assays (PCA) were not performed. The body weights were measured on the day of termination, day 49, and analysis indicated that although the animals were gaining weight, the animals were substantially smaller than the control animals (Figure 2).

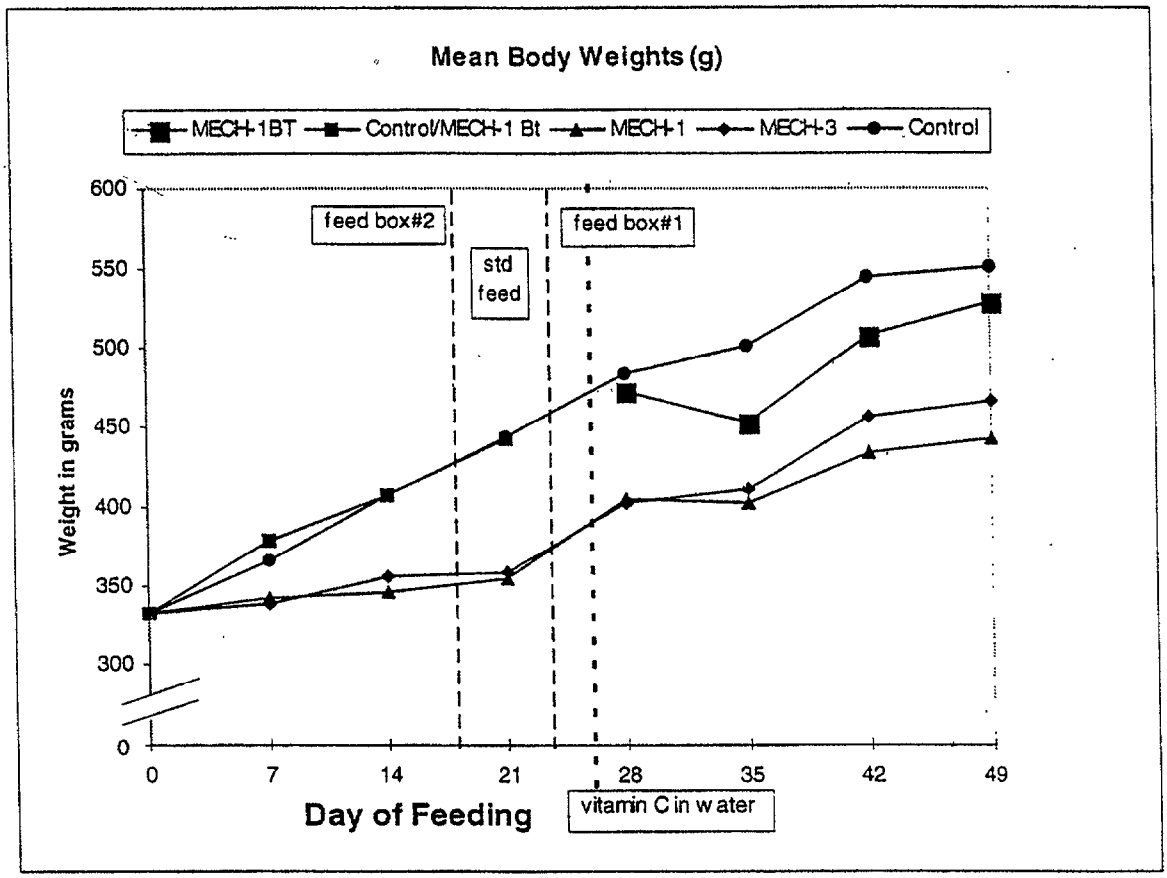

Figure 2. Mean body weights. Animals were weighed at approximately weekly intervals. Average group weights are shown. While the average weights were equal initially, at the time of termination there was approximately a 100 g difference in total body weight between non-transgenic cottonseed fed animals and controls control fed animals. The weight difference indicates a highly likelihood of significant differences in the health and immune status of the animals. All animals were euthanized on day 49 of the study and the sera was discarded. MECH-1 Bt group were unintentionally fed control diet during the first 21 days of the study and are indicated as MECH-1 Bt(CTL).

5. CONCLUSIONS/DISCUSSION

The primary conclusion of this study was that guinea pigs do not thrive on a diet containing 10% raw, full-fat cottonseed meal for an extended period of time. Assay of vitamin C levels and tests for a broad spectrum of mycotoxins failed to provide an answer regarding the cause of the unsuitable response to the cottonseed meal diets. There was evidence that the depressed weight gain was due to feed refusal. Animals fed the cottonseed meal diet gained less weight than controls, but recovered the rate of gain in seven days. However, reintroduction of the cottonseed meal diets at day 28 caused weight loss in two groups and little gain in the other. In addition, observations

indicated that some of the cottonseed meal fed animals were spilling feed, without evident consumption. As a consequence of the failure to thrive on these diets, the guinea pig model could not be used to accurately measure the relative allergenic activity of the transgenic and non-transgenic cotton hybrids.

Alternatively the Brown Norway rat model could be used to assess relative allergenicity of transgenic and non-transgenic cottonseed meal. These animals have been demonstrated to be tolerant to feeding 10% raw, full-fat cottonseed meal in the diet for sixty days (Goodman and Holden, 1998). The Brown Norway rat model has been used to evaluate potential changes in endogenous cottonseed allergens in transgenic hybrids relative to conventional cotton. No differences were found in the rat study using the same hybrids tested in this guinea pig study (Goodman and Holden, 1998).

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APPENDICES: Assessment of the allergenicity of Bollgard cottonseed proteins relative to conventional cottonseed proteins.

Appendix 7.1 Study Protocol

Amendment Request (4/17/98) for:

IV. PROTOCOL FOR ALLERGENICITY TESTING OF GENETICALLY TRANSFORMED PRODUCTS IN ANIMAL MODEL.

Submitted by Dr. P. Muzumdar, to The Department of Biotechnology, Government of India, New Dehli.

Animal Model. Unfortunately, no established animal model is available in the literature for assessing the allergenicity of genetically modified foods, however, rabbit or guinea pig could be used to detect allergenicity. Brown Norway rats (Atkinson and Miller, 1994; Atkinson, et al., 1996) have been used in experimental studies but it is yet to be accepted as an animal model by the regulatory agencies. However, this could be used to generate additional data.

Treatment Schedule: Normal adult healthy animals are kept under proper husbandry conditions with 12 hour light and 12 hour dark periods. Before the start of the experiment, animals are kept at least five days for acclimation. Animals are randomly divided into four groups, based on diet fed. The experimental group consists of ten animals, sensitized to the test protein(s) by incorporating the transgenic food stuff (crop material, variety or line) into the feeding pellets such that 10% of the total diet is from the test compound. The control groups of ten animals are fed 10% of the total diet of non-transgenic foodstuff or crop material. A negative control group of ten animals are fed a diet that does not contain the crop material. The diets are balanced as closely as possible for total protein, carbohydrate, lipid and fiber. Animals are fed for sixty days. Water is provided *ad libitum*. Sera from the treated animals are used to assess allergenicity.

Preparation of antigen/allergen: Collect the test materials in as pure form as possible, grind into a fine powder form and defat with ether (or hexane). Extract the defatted material with buffered saline, 10% wt./vol., however, this proportion can be varied depending upon the type of test compound. Mix the suspension at 20 to 25°C for 2 to 4 hours to extract the proteins from the insoluble matter. Filter through Whatman No. 1 filter paper, then through 0.45 micron or smaller pore size sterile filters. Transfer to sterile vials and lyophilize or freeze the aliquotes at -80°C.

Experimental Protocol

The following *in-vivo* immunological assays could be used for the detection of reaginic antibodies in the test sera.

In-vivo assay:

Passive Cutaneous Anaphylaxis (PCA)

Application and limitations of test: PCA is an in-vivo method usually employed to assay the specific reaginic antibody present in serum. It is a useful immunological tool to detect as little as 0.1 μg antibody protein. In this test the anaphylactic reaction is visualized as a local skin reaction.

Sex of animals: Male and/or female healthy young adult animals can be used. If females are used they should be nulliparous and non-pregnant.

Housing and feeding conditions: Where the lighting is artificial, the sequence should be 12 hours light, 12 hours dark. For feeding, conventional laboratory diets may be used

with an unlimited supply of drinking water. If guinea pigs are used, it is essential that animals receive an adequate amount of ascorbic acid.

Preparation of the animals: Animals are acclimated to the laboratory conditions for at least 5 days prior to the test. Before the test, animals are randomized and assigned to the treatment groups. Removal of hair is done by close clipping, shaving or by chemical depilation. Care should be taken to avoid abrading the skin.

Principle: PCA could be produced with the sera of the allergic host by challenging intradermally sensitized sites with intravenously injected antigen/allergen plus dye. Well-defined blue areas appear, indicating the sites of antigen-induced extravasation of fluid due to the interaction with tissue fixed reaginic antibody.

Description of test procedure: Naïve animals are shaved on the back and flanks, avoiding abrasion of skin. Unblemished skin sites are selected and cleaned with 70% alcohol. Injections are spaced approximately 2-4 cm apart. 0.1ml (or 0.05ml) of test serum is injected intradermally. Doses are usually in the ratio of 1:2:4 or 1:3:9. The doses are injected using tuberculin syringe(s). The syringe used for the intradermal injection must not leak even under heavy injection pressure. Plastic disposable sterilized tuberculin syringes are satisfactory in this respect. Glass tuberculin syringes must be checked for leaks both at the needle butt and past the piston. Needles with "short bevel" points, usually ½ inch x 26 gauge are used. 4 to 72 hours later, 1.0ml of antigen/allergen (1mg or 2mg), in sterile physiological saline, with 1% Evans blue dye is injected intravenously or intraventricularly. For the intravenous injection the piston of the syringe must be easy moving so that there is no doubt that the needle is in the vein when the smallest pressure is applied. The needle must be very sharp. For intravenous administration in guinea pigs, the vein which runs on the dorsal surface of the hind foot between the metatarsals of the outer and middle toes or ear vein or intracardiac route can be used. In rabbits, the vein running along the margin of the ear is the most useful site but other veins which are easily accessible can also be used.

Assay design: Since cottonseed proteins are known allergens, the non-transgenic control sensitized animals should produce a significant reaginic antibody response. This assay is designed to measure differences in response of animals exposed to transgenic vs. non-transgenic cottonseed proteins by injecting equal doses of sera from each group of animals into every naïve PCA test subject. That way, each animal serves as it's own control. In addition the naïve animals will receive sera from non-sensitized animals and from animals sensitized with a distinct line of cottonseed. The challenge antigen is also critical in this assay. One group of naïve animals that have been injected with serum dilutions will be challenged with the transgenic cottonseed proteins while a second group, injected with identical serum dilution samples will receive a challenge dose from the non- transgenic cottonseed. Reciprocal comparisons of the differences in reaginic responses will be used to determine if there true differences in the immune responses induced by the transgenic plant relative to the non-transgenic plant. A third group,

injected with an identical serum pattern will not be challenged with cottonseed protein, but will be injected with Evans blue dye to ensure that the extravasation is due to reaginic responses, rather than general irritation, or improper injection.

Observation: 30-60 min. later, animals are killed. The skin is opened and reflected so that the lesions can be evaluated. Measurements of diameter and the assessment of intensity are usually made. This can be postponed until all the animals have been killed but the delay is not advised and should not exceed 2 hours. The skin must not be allowed to dry. Intensity of bluing is often expressed arbitrarily as + to +++. Since the relationship between the area of response and the dose is roughly linear, the plot of mean diameter upon log dose will also be linear. A table showing both would usually be preferred. When the potency of sensitizing antibody is unknown, a wider range of doses may be useful. The highest dose should give lesions of about 15 to 20 mm. Diameter and the smallest about 5mm.

Appendix 7.2 Springborn Final Report

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS

FINAL REPORT

Study Director

Kimberly L. Bonnette, M.S., LATG

Study Completed on

November 30, 1998

Performing Laboratory

Springborn Laboratories, Inc. (SLI)
Ohio Research Center
640 North Elizabeth Street
Spencerville, OH 45887

SLI Study No.

3044.697

Monsanto Study No.

SB-98-212

Submitted to

Monsanto Company
800 N. Lindbergh Blvd.
St. Louis, MO 63167

Springborn Laboratories

STATEMENT OF NO CONFIDENTIALITY CLAIM

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA 10(d)(1)(A), (B), or (C).

COMPANY: Monsanto

COMPANY AGENT: Richard E. Goodman RE Goodman

Scientist - Biotech Reg. Sc:
TITLE

12/2/1998
DATE

COMPLIANCE STATEMENT

Kimberly L. Bonnette

Date 11/30/98

Kimberly L. Bonnette, M.S., LATG
Study Director/Author
Springborn Laboratories, Inc.

Richard E. Goodman

Date 12/2/1998

Sponsor/Submitter
Monsanto Company
Richard E. Goodman, ph D

QUALITY ASSURANCE STATEMENT

This study was inspected by the Quality Assurance Unit and reports were submitted to management and the Study Director in accordance with SLI's Standard Operating Procedures as follows:

Phase	Date
Gene Check Assay	09/23/98
Data Audit	11/24/98, 11/25/98, 11/27/98
Report Review	11/30/98
Report to Study Director and Management	11/30/98

This study was conducted in compliance with the Good Laboratory Practice Standards as described by the EPA (40 CFR Part 160) and the FDA (21 CFR Part 58.)

Anita M. Bosau, RQAP-GLP
Director of Compliance Assurance

Date 11/30/98

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SUMMARY

This study was performed to provide an assessment of the allergenic activity of transgenic and non-transgenic cottonseed meal in a guinea pig model. Animals were to be sensitized by feeding diets containing cottonseed meal for approximately sixty days, to induce cottonseed protein specific IgG_{1a}, the dominant reaginic antibody of guinea pigs. Antibody titers were to be measured by passive cutaneous anaphylaxis (PCA) following transfer of serum from sensitized animals to naive recipients. However, based on the results of the main study, in particular, the results pertaining to adverse clinical observations/reduced body weight/weight gain (possibly compromising PCA results) in conjunction with the results of the test feed analysis indicating that Group 1 did not receive test article feed through day 21, the PCA was not conducted. The main study design consisted of an untreated control group and three treatment groups with ten females in each group as follows:

Group No.	No. of Animals	Administration
1	10	NB# 6312322 (Mech1 trans) 5713C-I (10%)* [5713C-I]**
2	10	NB# 6312323 (Mech1 non-trans) 5713C-K (10%) [5713C-K]**
3	10	NB# 6312331 (Mech3 non-trans) 5713C-M (10%) [5713C-M]**
4	10	Control Diet 5713C-H [5713C-H]**

*Apparently, from day 0 - day 21, the box utilized to feed this group was mislabeled by the manufacturer and was apparently control diet (5713-H) based on analytical results of the diet. A second box utilized beginning on study day 28 was the correct diet.
**Abbreviation of the test article name.

Animals were fed the appropriate pre-made diet as received from the Sponsor ad libitum from days 0-21. Animals were returned to commercial guinea pig chow on day 21 through day 28 to allow for recovery from adverse clinical signs observed when feeding the test diets. On day 21, the animals were anesthetized with isoflurane and blood samples were obtained ocularly (via orbital sinus) to conduct clinical pathology/clinical chemistry. In addition, blood samples were collected from five stock animals in order to compare the test diet animals with completely untreated animals. Animals were returned to their respective test diets on day 28. On day 30, water was provided ad libitum in water bottles (rather than the automated watering system) and supplemented with ascorbic acid (Vitamin C, 200 mg/L). Detailed clinical observations were conducted weekly and animals were observed daily for overt clinical signs of toxicity. Individual body weights were obtained for the animals on study days 0, 7, 14, 17, 21, 24, 28, 35, 38, 42

and 49. Individual food consumption was measured three times a week during the study. On day 49, the study was terminated for both humane reasons concerning the palatability of the feed and the invalidation of Group 1 through day 21 due to the incorrect labeled feed. Gross necropsy examinations were conducted on animals that died or were euthanized for cause. No gross necropsy examinations were conducted for surviving animals.

One animal in Group 2 (Animal No. 4611) was found dead on day 27. The animals's death was associated with poor feed intake/inadequate nutrition in conjunction with body weight loss and severe adverse clinical observations. This death may have been a direct result of Vitamin C deficiency as a consequence of an inadequate intake of Vitamin C sufficient diet, although this could not be definitively determined. A second animal in Group 3 (Animal No. 4648) was removed from study on day 28 due to severe adverse signs probably caused by the above. The onset of the majority of the adverse clinical observations began on day 16 for Groups 2 and 3. These observation included: feces small in size, soft stool, rough coat, fecal stain, distended abdomen, dehydration, decreased food consumption and extremities blue in color (Vitamin C deficiency-like clinical observations possibly due to reduced feed intake). After returning to commercial guinea pig chow on day 21, the majority of the clinical observations subsided. Upon study diet restart (day 28) along with the water bottles containing added Vitamin C (day 30), adverse clinical observations began to reappear by day 30 in all test groups (Group 1, 2 and 3). Due to the severity of clinical observations causing an animal welfare concern (possible mortality) and due to an apparent lack of feed intake (probable palatability issue and/or inadequate diet), the study was terminated on day 49.

A statistically significant decrease in mean body weight was noted in Groups 2 and 3 by day 7 and continued to be decreased at days 14, 17, 21, 24 and 28. After returning to normal commercial guinea pig chow, body weight gains were similar from days 21 - 28. However, after resuming the test article diets, the body weight for Group 2 was significantly depressed by day 38 and both Groups 2 and 3 were significantly depressed by days 42 and 49. Although not significantly different, Group 1 also had a notable decrease in body weight during this time period (day 35-49).

Examination of the hematology and biochemistry data revealed significantly decreased alkaline phosphatase, chloride, phosphorus, total protein and albumin in Groups 2 and 3 and significantly decreased globulin, urea nitrogen, sodium and calcium in Group 3, only. Mean corpuscular volume and mean corpuscular hemoglobin were significantly decreased in the animals of both Groups 2 and 3. Hemoglobin and hemacrit were significantly decreased for Group 3, only. Alanine

amino transferase was significantly increased in Group 2. There was a significant increase in segmented neutrophils, lymphocytes and leukocytes for Group 3. When compared to the results of the stock animals, there were no notable differences; and, the results were only slightly outside published values for guinea pigs [1].

Based on the results of this study, the most reasonable conclusion from body weight data, observations regarding feeding and clinical symptoms is that the 10% cottonseed diets provided by the Sponsor were unpalatable, or there was an undetermined toxic response to those diets specifically. The nearly immediate weight loss in all cottonseed meal fed groups upon restarting the study on day 28 indicated that it was highly unlikely that the animals could have survived a full sixty day feeding trial on the appropriate diets. Because of the questionable health status and immune function of the surviving guinea pigs in this study, the Sponsor ordered the study terminated. Therefore, the PCA was not conducted since any results would not have been reliable utilizing serum from compromised main study animals.

I. INTRODUCTION

This study was performed to validate that the Passive Cutaneous Anaphylaxis Assay (PCA) could determine the titer of IgG_{1a} antibody present in serum of the animals fed (approximately 60 days) with test article. However, based on the results of the main study, in particular, the results pertaining to adverse clinical observations/reduced body weight/weight gain (possibly compromising PCA results) in conjunction with the results of the test feed analysis indicating that Group 1 did not receive test article feed through day 21, the PCA was not conducted. This study was performed at Springborn Laboratories, Inc., 553 North Broadway, Spencerville, Ohio. The protocol was signed by the Study Director on July 24, 1998 (GLP initiation date). The in-life phase of the study was initiated with test article administration on July 27, 1998 (day 0) and concluded with termination on September 14, 1998.

II. MATERIALS AND METHODS

A. Experimental Protocol

The study protocol and protocol amendment are presented in Appendix A.

B. Test Articles

The test articles were received from the Sponsor and identified as follows:

Sponsor's ID	Assigned SLI ID	Physical Description	Receipt Date	Expiration Date
5713C-I Lot No.: 9848-2	S98.019.3044	Brown pellets	June 9, 1998	None provided
5713C-K Lot No.: 9848-4	S98.021.3044	Brown pellets	June 9, 1998	None provided
5713C-M Lot No.: 9848-6	S98.023.3044	Brown pellets	June 9, 1998	None provided
5713C-H* Lot No.: 9848-1	V98.003.3044	Brown pellets	June 9, 1998	None provided

*Apparently, from day 0 - day 21, the box utilized to feed this group was mislabeled by the manufacturer and was apparently control diet (5713C-H) based on gene feed analytical results of the diet. A second box utilized beginning on study day 28 was the correct diet (see Appendix B for results of the gene assay).

The test articles were stored refrigerated or at room temperature. The Sponsor is responsible for any necessary evaluations related to chemical composition, strength, purity, stability and other data required by 40 CFR 160.105 and 21 CFR Part 58.105. After study completion, each box of diet was analyzed by the Sponsor at SLI using a gene feed assay (See Appendix B).

C. Retention/Analytical Samples

An approximate 20 g analytical sample of each lot of test/control article feed was taken on days 7, 14, 21 28, 35, 42 and at study termination (day 49) and stored in a -70° C freezer for possible Sponsor evaluation. An approximate 10 g retention sample of each lot of test/control article feed and each subsample was collected. These samples were stored refrigerated and serve as the retention samples for all studies conducted with the lot of test/control article feed utilized.

D. Test Article Disposition

The remaining test/control articles were dispensed of by incineration following completion of all studies with the test/control articles.

E. Method of Test Article Preparation

Each appropriate dietary test article for Groups 1, 2, 3 and 4 was fed as a pre-made diet as received from the Sponsor to each animal ad libitum. A Certificate of Analysis for each test article will be maintained by the Sponsor. On day 21, 50 g samples of each box of diet (3 boxes/test article diet) were sent to Ralston Analytical Laboratories, 824 Gratiot, St. Louis, MO 63102.

F. Animals and Animal Husbandry

1. Description, Identification and Housing

Young adult, Hartley-derived albino guinea pigs (born on 6/19/98) were received at SLI from Charles Rivers Laboratories, Inc. Raleigh, North Carolina. Upon receipt, plastic ear tags displaying unique identification numbers were used to individually identify the animals. Cage cards displaying at least the study number, animal number and sex were affixed

to each cage. The animals were housed individually in suspended stainless steel cages. All housing and care were based on the standards recommended by the Guide for the Care and Use of Laboratory Animals [2].

2. Environment

The animal room temperature and relative humidity ranges were 67-73°F and 38-80%, respectively. Environmental control equipment was monitored and adjusted as necessary to minimize fluctuations in the animal room environment. Light timers were set to maintain a 12-hour light/12-hour dark cycle and room ventilation was set to produce 10-15 air changes/hour. The room temperature and relative humidity were recorded a minimum of once daily.

3. Food

PMI Certified Guinea Pig Chow #5026 (Purina Mills, Inc.) or diet provided by the Sponsor was provided ad libitum to the animals throughout the study. The lot number of each batch of diet used during the study were recorded. The feed was analyzed and certified by the supplier for nutritional components and environmental contaminants. Dietary limitations for various environmental contaminants, including heavy metals, pesticides, polychlorinated biphenyls and total aflatoxin are set by the manufacturer. Within these limits, contaminants which may have been present were not expected to compromise the purpose of this study. Results of the dietary analyses (Certificates of Analysis) are provided by the manufacturer for each lot of diet. Certificates of Analysis from Purina Mills, Inc. are maintained by SLI. For the feed supplied by the Sponsor, Certificates of Analysis are maintained by the Sponsor.

4. Water

Municipal tap water treated by reverse osmosis was available ad libitum throughout the study. The purified water was supplied by an automatic watering system (day 0-29) or reverse osmosis water in water bottles supplemented with 200 mg/L ascorbic acid (Vitamin C, day 30-49). A Certificate of Analysis for the ascorbic acid was provided by the manufacturer and is presented in Appendix C. Monitoring of the drinking water for contaminants is conducted annually by SLI and the records are available for inspection. Within generally accepted limits, contaminants which may have been present were not expected to compromise the purpose of this study. The water meets the standards specified under the EPA National Drinking Water Regulations (40 CFR Part 141).

5. Acclimation

Upon receipt, the animals were removed randomly from the shipping cartons, examined by qualified personnel, identified with plastic ear tags and then acclimated to the laboratory conditions for a minimum of five days. The animals were observed daily for overt physical or behavioral abnormalities, general health/moribundity and mortality.

6. Animal Selection

Animals were weighed and examined in detail for adverse clinical observations. Animals determined to be suitable as test subjects were assigned to groups randomly by body weight. The animal numbers and the respective body weight values were entered into the computer. Homogeneity of groups by weight was the criteria of acceptance of the randomization. Disposition of animals not selected for study was documented in the study records.

III. EXPERIMENTAL PROCEDURES

A. Study Group Design

The main study consisted of :

Main Study Group No.	No. of Test Animals	Administration (Days 0-21 and Days 28-49)
1	10	NB# 6312322 (Mech1 trans) 5713C-I (10%)*
2	10	NB# 6312323 (Mech1 non-trans) 5713C-K (10%)
3	10	NB# 6312331 (Mech3 non-trans) 5713C-M (10%)
4	10	Control Diet 5713C-H**

*Apparently, from day 0 - day 21, the box utilized to feed this group was mislabeled by the manufacturer and was apparently control diet (5713C-H) based on analytical results of the diet. A second box utilized beginning study day 28 was the correct diet.

**In addition, stock animals were assigned to two of the diets (Group 5: four animals to 5713C-I and Group 6: four animals to 5713C-H) from days 35-44 to determine if the results would repeat utilizing new animals.

B. Dosing Procedures (Main Study)

1. Dietary Dosing

Each group of Dietary Test animals was fed the appropriate pre-made diet as received from the Sponsor ad libitum from day 0 through day 21. Due to severe adverse clinical observations/reduction in body weight/weight gain, the animals were removed from test/control diets on day 21 and resumed their appropriate test diet on days 28 - 49. During days 21-28 animals were fed PMI Certified Guinea Pig Chow #5026 in an attempt to return the animals to good health and complete the study. On day 35, eight animals were chosen from stock to determine if new animals would respond the same way as the main study animals. Therefore, four animals were designated as Group 5 and fed diet 5713C-I (Group 1 feed) and four animals were fed diet 5713C-H (10%, Group 4 feed) until day 44 (day 9).

2. Clinical Observations

The animals were checked for general health/mortality and moribundity twice daily during the study. In addition, cage-side observations were performed once daily and detailed clinical observations were performed weekly.

3. Body Weights

Individual body weights were obtained for the animals on study days 0, 7, 14, 17, 21, 24, 28, 35, 38, 42 and 49. Note: Additional body weights were collected in order to evaluate animal health.

4. Food Consumption

Individual food consumption was measured 3 times a week. Food was also added as necessary to maintain ad libitum feed. Food consumption values were used as a means to track test article usage and are not reflective of the actual amount of diet consumption. Therefore, this data was invalidated as food consumption data and will not be reported.

5. Collection of Blood Samples/Clinical Pathology

On day 21, animals were anesthetized with isoflurane and approximate 2 mL blood samples were obtained ocularly (via orbital sinus). Hematology and biochemistry parameters were evaluated (see Appendix D for methodology):

a. Hematology Parameters

erythrocyte count (RBC)
hematocrit (Hct)
hemoglobin concentration (Hgb)
mean corpuscular hemoglobin (MCH)
mean corpuscular hemoglobin concentration (MCHC)
mean corpuscular volume (MCV)
platelet count
reticulocyte count
total and differential leukocyte counts

b. Biochemistry Parameters

alanine aminotransferase (ALT)
albumin
albumin/globulin ratio (calculated)
alkaline phosphatase
aspartate aminotransferase (AST)
blood creatinine
blood urea nitrogen (BUN)
calcium
cholesterol
electrolytes (sodium, potassium, chloride)
globulin (calculated)
glucose
phosphorus
total bilirubin
total serum protein

6. Euthanasia

Animals dying on study or euthanized moribund (carbon dioxide inhalation) during the study were necropsied. Body cavities (cranial, thoracic, abdominal and pelvic) were opened and examined. On day 30, Animal No. 4648 was euthanized for cause. The proximal and distal ends of the femur and tibia were collected, processed/decalcified and evaluated by Dr. J. Dale Thurman, D.V.M., M.S., DACVP. No other tissues were retained. Following clinical observations and food consumption determination on study day 49, all surviving animals were euthanized by carbon dioxide inhalation or sodium pentobarbital and discarded.

C. Protocol Deviations

Group 1 was fed the incorrect diet (control diet 5713C-H rather than 5713C-I) during the day 0-21 interval due to a labeling error by the manufacturer. This error resulted in a compromised Group 1. There was no expiration date for feed supplied by Sponsor. The animal room relative humidity range (38-80%) exceeded the preferred range (30-70%) during this study. The method of euthanasia for surviving animals was not documented. IACUC approval of this study was not obtained prior to study initiation. On day 0, the sample of each test/control feed article was inadvertently not collected. These occurrences were considered to have had no adverse effect on the outcome of this study.

IV. ANALYSIS OF DATA

Statistical analyses were performed using a MicroVax 3100 computer. The level of significance was a minimum of 5% and tests were two-tailed. The control group data was compared to the treated data using all groups or by a group by group comparison depending on the test. Data including body weights, weight gain and clinical pathology were analyzed by one way analysis of variance. If significance was detected, a group by group comparison proceeded with Tukey-Kramer.

V. MAINTENANCE OF RAW DATA, RECORDS AND SPECIMENS

All original paper data, photographs, the final report, magnetically encoded records and any specimens were transferred to the SLI archives for a period of 7 years. The Sponsor will be contacted prior to final disposition of these items.

VI. RESULTS

A. Survival and Clinical Observations

Table 1 (Summary Data)
Appendix E (Individual Data)

One animal in Group 2 (Animal No. 4611) was found dead on day 27. The animal's death was associated with poor feed intake/inadequate nutrition in conjunction with body weight loss and severe adverse clinical observations. This death may have been a direct result of Vitamin C deficiency as a consequence of an inadequate intake of Vitamin C sufficient diet, although this could not be definitively determined. A second animal in Group 3 (Animal No. 4648) was removed from study on day 28 due to severe adverse signs probably caused by the above. The onset of the majority of the adverse clinical observations began on day 16 for Groups 2 and 3. These observation included: feces small in size, soft stool, rough coat, fecal stain, distended abdomen, dehydration, decreased food consumption and extremities blue in color (Vitamin C deficiency-like clinical observations possibly due to reduced feed intake). After returning to commercial guinea pig chow on day 21, the majority of the clinical observations subsided. Upon study diet restart (day 28) along with the water bottles containing added Vitamin C (day 30), adverse clinical observations began to reappear by day 30 in all test groups (Group 1, 2 and 3). Due to the severity of clinical observations causing an animal welfare concern (possible mortality) and due to an apparent lack of feed intake (probable palatability issue and/or inadequate diet), the study was terminated on day 49.

B. Body Weights and Weight Gain

Tables 2 and 3 (Summary Data)
Appendices F and G (Individual Data)

A statistically significant decrease in mean body weight was noted in Groups 2 and 3 by day 7 and continued to be decreased at days 14, 17, 21, 24 and 28. After returning to normal commercial guinea pig chow, body weight gains were similar from days 21 - 28. However, after resuming the test article diets, the body weight for Group 2 was significantly depressed by day 38 and both Groups 2 and 3 were significantly depressed by days 42 and 49. Although not significantly different, Group 1 also had a notable decrease in body weight during this time period (days 35-49).

C. Collection of Blood Samples/Clinical Pathology

Tables 4 and 5 (Summary Data)
Appendices H, I and J (Individual Data)

Examination of the hematology and biochemistry data revealed significantly decreased alkaline phosphatase, chloride, phosphorus, total protein and albumin in Groups 2 and 3 and significantly decreased globulin, urea nitrogen, sodium and calcium in Group 3, only. Mean corpuscular volume and mean corpuscular hemoglobin were significantly decreased in the animals of both Groups 2 and 3. Hemoglobin and hemacrit were significantly decreased for Group 3, only. Alanine amino transferase was significantly increased in Group 2. There was a significant increase in segmented neutrophils, lymphocytes and leukocytes for Group 3. When compared to the results of the stock animals, there were no notable differences; and, the results were only slightly outside published values for guinea pigs [1].

D. Gross Necropsy Observations

Appendix K (Individual Data)

Gross necropsy examinations of the animal in Group 2 (Animal No. 4611) which died on day 27 included body fat depletion, distended stomach and dark red apical lobe of the lung. The animal in Group 3 (Animal No. 4648), removed from study on day 28 due to severe adverse clinical observations/body weight loss and euthanized for cause on day 30, revealed body fat depletion, distended stomach and small intestines, mottled lungs, fluid in the abdominal cavity and foam in the trachea. A necropsy examination was not required for surviving animals. Also the proximal and distal ends of the femur and tibia appeared within normal limits to the board-certified pathologist.

E. Added Stock Animals

Appendix L (Individual Data)

Within two days post feeding, all four of the stock animals in Group 5 fed 5713C-I (same diet as Group 1) developed few feces and/or soft stools and/or feces small in size. In addition body weight loss/reduced body weight gain was observed in all four of the stock animals. No body weight loss was observed in Group 6 fed control diet (5713C-H same diet as Group 4). These results were similar to the effects observed when administering the correct test

diet to Group 1 on day 28. The observations associated with feeding this additional group of animals the cottonseed meal diet confirm the findings in the main study, that the cottonseed diets appear to be the direct cause of the health problems that occurred in feeding Groups 1, 2 and 3.

VII. CONCLUSION

Based on the results of this study, the most reasonable conclusion from body weight data, observations regarding feeding and clinical symptoms is that the 10% cottonseed diets provided by the Sponsor were unpalatable, or there was an undetermined toxic response to those diets specifically. The nearly immediate weight loss in all cottonseed meal fed groups upon restarting the study on day 28 indicated that it was highly unlikely that the animals could have survived a full sixty day feeding trial on the appropriate diets. Because of the questionable health status and immune function of the surviving guinea pigs in this study, the Sponsor ordered the study terminated. Therefore, the PCA was not conducted since any results would not have been reliable utilizing serum from compromised main study animals.

Kimberly L. Bonnette, M.S., LATG
Study Director

Date 11/30/98

VIII. REPORT REVIEW

Deborah A. Douds, M.S.
Assistant Manager of Acute Toxicology

Date 11/30/98

Joseph C. Siglin, Ph.D., DABT
Director of Toxicology

Date 11/30/98

IX. REFERENCES

1. Terrel, L. A., D.V.M., M.S. and D. J. Clemons, D.V.M., M.S., The Laboratory Guinea Pig, ed. M. A. Suckow, D.V.M., CRC Press LLC, 1998, pp. 21, 22 and 61-63.

2. Guide for the Care and Use of Laboratory Animals, DHHS Publication No. (NIH) 96-03, 1996.

TABLE 1

SLI STUDY NO.: 3044.697 — A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS — PAGE 1

CLIENT: MONSANTO COMPANY — SUMMARY OF SURVIVAL AND CLINICAL OBSERVATIONS (OCCURRENCE/ANIMALS AFFECTED)

----- F E M A L E -----

TABLE RANGE:	DAY 0 TO DAY 49			
GROUP:	1	2	3	4
LEVEL:	5713C-I	5713C-K	5713C-M	5713C-H
NORMAL				
-NO REMARKABLE CLINICAL OBSERVATIONS	72/10	58/10	66/10	76/10
DEAD				
-FOUND DEAD	0/ 0	1/ 1	0/ 0	0/ 0
-REMOVED FROM STUDY, BUT NOT EUTHANIZED AT THIS - TIME	0/ 0	0/ 0	1/ 1	0/ 0
-SCHEDULED EUTHANASIA	10/10	9/ 9	9/ 9	10/10
ACTIVITY				
-SALIVATION	0/ 0	0/ 0	1/ 1	0/ 0
EXCRETA				
-FEW FECES	12/ 7	33/ 9	30/ 7	10/ 7
-FECES SMALL IN SIZE	9/ 7	93/10	53/ 9	14/ 8
-SOFT STOOLS	5/ 5	8/ 5	9/ 4	13/ 8
BODY				
-URINE STAIN	3/ 3	13/ 3	4/ 3	4/ 3
-ROUGH COAT	0/ 0	44/ 9	30/ 5	0/ 0
-FECAL STAIN	15/ 8	7/ 4	2/ 1	12/ 4
-EXTREMITIES APPEAR BLUE IN COLOR	0/ 0	12/ 3	5/ 1	0/ 0
-DISTENDED ABDOMEN	0/ 0	24/ 4	7/ 2	0/ 0
-DEHYDRATION	0/ 0	2/ 1	2/ 1	0/ 0
-HAIRLOSS	0/ 0	1/ 1	0/ 0	0/ 0
EYES				
-DARK MATERIAL AROUND EYE(S)	0/ 0	0/ 0	1/ 1	0/ 0

NOTE: DATA REFLECT THE TOTAL OCCURRENCE OF EACH CLINICAL FINDING OVER THE NUMBER OF ANIMALS EXHIBITING THE FINDING.

TABLE 1

SLI STUDY NO.: 3044.697 — A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS — PAGE 2

CLIENT: MONSANTO COMPANY — SUMMARY OF SURVIVAL AND CLINICAL OBSERVATIONS (OCCURRENCE/ANIMALS AFFECTED)

----- F E M A L E -----

TABLE RANGE:	DAY 0 TO DAY 49			
GROUP:	1	2	3	4
LEVEL:	5713C-I	5713C-K	5713C-M	5713C-H
QUALT FOOD/WATER				
-DECREASED FOOD CONSUMPTION	4/ 3	41/ 9	15/ 6	4/ 4
-DECREASED WATER CONSUMPTION	4/ 4	29/ 5	8/ 2	2/ 2

NOTE: DATA REFLECT THE TOTAL OCCURRENCE OF EACH CLINICAL FINDING OVER THE NUMBER OF ANIMALS EXHIBITING THE FINDING.

(22)

SLS STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

TABLE 2
A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
SUMMARY OF BODY WEIGHT DATA (GRAMS)

----- F E M A L E -----

		GROUP:	4	1	2	3
		LEVEL:	5713C-H	5713C-I	5713C-K	5713C-M
DAY	0	MEAN	333	332	333	333
		S.D.	10.3	10.8	11.1	10.4
		N	10	10	10	10
DAY	7	MEAN	366	379	342**	339**
		S.D.	16.4	16.3	21.0	8.9
		N	10	10	10	10
DAY	14	MEAN	408	408	346#	356#
		S.D.	23.6	18.7	25.3	11.3
		N	10	10	10	10
DAY	17	MEAN	421	419	346#	345#
		S.D.	27.9	27.3	22.2	11.2
		N	10	10	10	10
DAY	21	MEAN	444	443	355#	359#
		S.D.	29.6	31.2	22.2	13.6
		N	10	10	10	10
DAY	24	MEAN	461	452	373#	381#
		S.D.	31.4	27.4	34.3	25.8
		N	10	10	10	10
DAY	28	MEAN	484	473	405#	402#
		S.D.	36.0	29.1	31.6	32.8
		N	10	10	9	10

SIGNIFICANTLY DIFFERENT FROM CONTROL: ** = P<0.01 # = P<0.001

SLS STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

TABLE 2
A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
SUMMARY OF BODY WEIGHT DATA (GRAMS)

----- F E M A L E -----

		GROUP:	4	1	2	3
		LEVEL:	5713C-H	5713C-I	5713C-K	5713C-M
DAY	35	MEAN	501	453	403#	411#
		S.D.	47.5	45.2	49.7	25.6
		N	10	10	9	9
DAY	38	MEAN	525	479	416#	437#
		S.D.	43.4	40.0	60.5	33.2
		N	10	10	9	9
DAY	42	MEAN	545	508	434#	456#
		S.D.	41.9	31.7	58.4	28.4
		N	10	10	9	9
DAY	49	MEAN	551	529	443#	466**
		S.D.	51.7	48.1	54.7	32.8
		N	10	10	9	9
DAY	56	MEAN				
		S.D.				
		N				
DAY	60	MEAN				
		S.D.				
		N				

SIGNIFICANTLY DIFFERENT FROM CONTROL: ** = P<0.01 # = P<0.001

SLS STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

TABLE 3
A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
SUMMARY OF BODY WEIGHT GAIN DATA (GRAMS)

----- F E M A L E -----

		GROUP:	4	1	2	3
		LEVEL:	5713C-H	5713C-I	5713C-K	5713C-M
DAY 0 TO 7		MEAN	33	47*	9#	6#
		S.D.	8.8	7.5	16.6	6.2
		N	10	10	10	10
DAY 7 TO 14		MEAN	42	29*	4#	17#
		S.D.	9.5	9.6	11.1	10.7
		N	10	10	10	10
DAY 14 TO 21		MEAN	35	35	9#	3#
		S.D.	13.4	14.5	11.9	14.9
		N	10	10	10	10
DAY 21 TO 28		MEAN	40	30	50	43
		S.D.	19.2	7.0	14.6	24.0
		N	10	10	9	10
DAY 28 TO 35		MEAN	17	-19	-3	-1
		S.D.	29.5	33.3	30.1	20.0
		N	10	10	9	9
DAY 35 TO 42		MEAN	44	55	31	45
		S.D.	28.9	26.5	24.8	28.5
		N	10	10	9	9
DAY 42 TO 49		MEAN	6	21	9	10
		S.D.	16.5	21.2	16.9	14.8
		N	10	10	9	9

SIGNIFICANTLY DIFFERENT FROM CONTROL: * = P<0.05 # = P<0.001

SLS STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

TABLE 4
A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
SUMMARY OF HEMATOLOGY DATA

----- F E M A L E -----

		GROUP:	4	1	2	3
		LEVEL:	5713C-H	5713C-I	5713C-K	5713C-M
ERYTHROCYTES	10*6/CMM					
DAY 21		MEAN	5.05	4.80	5.03	4.77
		S.D.	0.232	0.279	0.323	0.313
		N	10	10	10	10
HEMOGLOBIN	G/DL					
DAY 21		MEAN	14.3	13.7	13.4	13.0**
		S.D.	0.68	0.84	0.69	0.95
		N	10	10	10	10
HEMATOCRIT	%					
DAY 21		MEAN	43.1	41.5	40.9	39.0**
		S.D.	1.87	2.64	2.10	2.89
		N	10	10	10	10
MEAN CORPUS VOL	FL					
DAY 21		MEAN	85.3	86.5	81.4#	81.8**
		S.D.	2.41	1.96	2.11	1.30
		N	10	10	10	10
MCH	PG					
DAY 21		MEAN	28.2	28.5	26.7#	27.2**
		S.D.	0.89	0.38	0.65	0.55
		N	10	10	10	10
MCHC	G/DL					
DAY 21		MEAN	33.1	33.0	32.8	33.3
		S.D.	0.35	0.44	0.47	0.47
		N	10	10	10	10

SIGNIFICANTLY DIFFERENT FROM CONTROL: ** = P<0.01 # = P<0.001
NOTE: THE MEANS AND STANDARD DEVIATIONS WERE CALCULATED USING NONROUNDED VALUES.

TABLE 4
A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
SUMMARY OF HEMATOLOGY DATA

----- F E M A L E -----

		GROUP:	4	1	2	3
		LEVEL:	5713C-H	5713C-I	5713C-K	5713C-M
PLATELETS	10*3/CMM					
DAY 21		MEAN	556	454	493	470
		S.D.	119.7	103.9	119.5	90.6
		N	10	10	10	10
SEGD NEUTROPHILS	% WBC					
DAY 21		MEAN	30	36	55**	62#
		S.D.	10.4	17.8	18.8	17.1
		N	10	10	10	10
LYMPHOCYTES	% WBC					
DAY 21		MEAN	68	61	44*	36#
		S.D.	9.8	18.8	18.8	16.4
		N	10	10	10	10
MONOCYTES	% WBC					
DAY 21		MEAN	1	1	2	2*
		S.D.	0.7	0.9	1.0	1.2
		N	10	10	10	10
BASOPHILS	% WBC					
DAY 21		MEAN	0	0	0	0
		S.D.	0.3	0.3	0.0	0.0
		N	10	10	10	10
EOSINOPHILS	% WBC					
DAY 21		MEAN	2	2	0	1
		S.D.	1.3	2.0	0.3	0.7
		N	10	10	10	10

SIGNIFICANTLY DIFFERENT FROM CONTROL: * = P<0.05 ** = P<0.01 # = P<0.001
NOTE: THE MEANS AND STANDARD DEVIATIONS WERE CALCULATED USING NONROUNDED VALUES.

TABLE 4
A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
SUMMARY OF HEMATOLOGY DATA

----- F E M A L E -----

		GROUP:	4	1	2	3
		LEVEL:	5713C-H	5713C-I	5713C-K	5713C-H
NON-SEGD NEUTRO.	% WBC					
DAY 21		MEAN	0	0	0	0
		S.D.	0.0	0.0	0.0	0.0
		N	10	10	10	10
NUCLEATED RBC'S	% WBC					
DAY 21		MEAN	0	0	0	0
		S.D.	0.0	0.0	0.0	0.0
		N	10	10	10	10
RETICULOCYTES	% RBC					
DAY 21		MEAN	1.8	2.1	1.6	1.2
		S.D.	0.70	0.97	0.74	0.58
		N	10	10	10	10
LEUKOCYTES	10*3/CMM					
DAY 21		MEAN	6.44	7.09	12.00*	14.22**
		S.D.	0.989	2.671	5.043	6.187
		N	10	10	10	10

SIGNIFICANTLY DIFFERENT FROM CONTROL: * = $P<0.05$ ** = $P<0.01$
NOTE: THE MEANS AND STANDARD DEVIATIONS WERE CALCULATED USING NONROUNDED VALUES.

SLS STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

TABLE 5
A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
SUMMARY OF BIOCHEMISTRY DATA

----- F E M A L E -----

		GROUP:	4	1	2	3
		LEVEL:	5713C-H	5713C-I	5713C-K	5713C-H
ALK PHOS'TASE	IU/L					
DAY 21		MEAN	180	181	123#	124#
		S.D.	31.3	33.4	20.4	28.4
		N	10	10	10	10
UREA NITROGEN	MG/DL					
DAY 21		MEAN	21	19	19	12#
		S.D.	0.9	1.5	2.0	2.6
		N	10	10	10	10
CALCIUM	MG/DL					
DAY 21		MEAN	11.38	11.09	11.16	10.72**
		S.D.	0.318	0.551	0.401	0.313
		N	10	10	10	10
CHLORIDE	MMOL/L					
DAY 21		MEAN	114	113	110*	108#
		S.D.	2.5	2.2	3.1	2.2
		N	10	10	10	10
CHOLESTEROL	MG/DL					
DAY 21		MEAN	45	50	38	34
		S.D.	11.1	7.9	12.3	8.1
		N	10	10	10	10
CREATININE	MG/DL					
DAY 21		MEAN	0.39	0.39	0.40	0.38
		S.D.	0.038	0.071	0.110	0.072
		N	10	10	10	10

SIGNIFICANTLY DIFFERENT FROM CONTROL: * = $P<0.05$ ** = $P<0.01$ # = $P<0.001$
NOTE: THE MEANS AND STANDARD DEVIATIONS WERE CALCULATED USING NONROUNDED VALUES.

SLS STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

TABLE 5
A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
SUMMARY OF BIOCHEMISTRY DATA

----- F E M A L E -----

		GROUP:	4	1	2	3
		LEVEL:	5713C-H	5713C-I	5713C-K	5713C-M
ASP. AMINOTRANS.	IU/L					
DAY 21		MEAN	54	72	84	89
		S.D.	19.2	46.7	23.4	28.1
		N	10	10	10	10
POTASSIUM	MMOL/L					
DAY 21		MEAN	5.11	5.16	4.96	4.71
		S.D.	0.643	0.423	0.373	0.466
		N	10	10	10	10
SODIUM	MMOL/L					
DAY 21		MEAN	141	140	140	138**
		S.D.	1.6	1.8	2.8	1.8
		N	10	10	10	10
PHOSPHORUS	MG/DL					
DAY 21		MEAN	7.1	6.6	5.7#	5.5#
		S.D.	0.80	0.59	0.64	0.55
		N	10	10	10	10
TOTAL BILIRUBIN	MG/DL					
DAY 21		MEAN	0.47	0.50	0.54	0.56
		S.D.	0.105	0.080	0.135	0.063
		N	10	10	10	10
TOTAL PROTEIN	G/DL					
DAY 21		MEAN	4.90	4.73	4.52*	4.04#
		S.D.	0.264	0.212	0.385	0.263
		N	10	10	10	10

SIGNIFICANTLY DIFFERENT FROM CONTROL: * = P<0.05 ** = P<0.01 # = P<0.001
NOTE: THE MEANS AND STANDARD DEVIATIONS WERE CALCULATED USING NONROUNDED VALUES.

TABLE 5
A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
SUMMARY OF BIOCHEMISTRY DATA

----- F E M A L E -----

		GROUP:	4	1	2	3
		LEVEL:	5713C-H	5713C-I	5713C-K	5713C-M
A/G RATIO						
DAY 21		MEAN	1.05	1.08	1.04	1.08
		S.D.	0.090	0.077	0.104	0.071
		N	10	10	10	10
GLUCOSE	MG/DL					
DAY 21		MEAN	149	149	146	147
		S.D.	13.2	24.7	9.9	14.7
		N	10	10	10	10
GLOBULIN	G/DL					
DAY 21		MEAN	2.40	2.28	2.22	1.95#
		S.D.	0.190	0.119	0.288	0.150
		N	10	10	10	10
ALAN. AMINOTRANS	IU/L					
DAY 21		MEAN	33	34	68**	57
		S.D.	5.1	9.3	38.6	16.2
		N	10	10	10	10
ALBUMIN	G/DL					
DAY 21		MEAN	2.50	2.45	2.30*	2.09#
		S.D.	0.146	0.151	0.138	0.145
		N	10	10	10	10

SIGNIFICANTLY DIFFERENT FROM CONTROL: * = P<0.05 ** = P<0.01 # = P<0.001
NOTE: THE MEANS AND STANDARD DEVIATIONS WERE CALCULATED USING NONROUNDED VALUES.

APPENDIX A

Protocol and Amendment

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS

Springborn Study No. 3044.697
Monsanto Study No. SB-98-212

Springborn Laboratories, Inc. (SLI)
Ohio Research Center
640 North Elizabeth Street
Spencerville, Ohio 45887

Kimberly L. Bonnette, M.S., LATG
Study Director

For

Monsanto Company
800 N. Lindbergh Blvd.
St. Louis, MO 63167

SLI Study No. 3044.697

TABLE OF CONTENTS

I. PURPOSE

The purpose of the study is to determine by Passive Cutaneous Anaphylaxis Assay the titer of IgG_{1a} antibody present in the serum of animals fed test article (approximately 60 days).

II. RESPONSIBILITIES

A. Sponsor

Monsanto Company
800 N. Lindbergh Blvd.
St. Louis, MO 63167

B. Sponsor's Representative

Terry Kaempfe
Phone: (314) 694-1318
Fax: (314) 694-4028
E-mail: terry.kaempfe@monsanto. com

C. Study Monitor

Rick Goodman, Ph.D.
Phone: (314) 737-5314
Fax: (314) 737-6189
E-mail: richard.e.goodman@monsanto.com

D. Testing Location

Springborn Laboratories, Inc.
Ohio Research Center
553 North Broadway
Spencerville, OH 45887
Telephone: (419) 647-4196
FAX: (419) 647-6560

D. Personnel Responsibilities

1. Kimberly L. Bonnette, M.S., LATG
   Study Director/Manager of Acute Toxicology
   E-mail: kbonnett@springborn.com

2. George A. Douds, M.S.
   Alternate Contact/Assistant Toxicologist

3. Deborah A. Douds, M.S.
   Assistant Manager of Toxicology

4. Robert C. Springborn, Ph.D.
   Chairman, President and CEO

5. Malcolm Blair, Ph.D.
   Vice President and Managing Director

6. Joseph C. Siglin, Ph.D., DABT
   Director of Toxicology

7. Rusty E. Rush, M.S., LAT, DABT
   Associate Director of Toxicology

8. J. Dale Thurman, D.V.M., M.S., DACVP
   Director of Pathology

9. Anita M. Bosau, RQAP-GLP
   Director of Compliance Assurance

III. PROPOSED STUDY SCHEDULE

A.	Initiation of In-Life Phase:	July 1998
B.	Completion of In-Life Phase:	August 1998
C.	Audited Report Date:	6 Weeks Following Sponsor's Approval for Study Termination

IV. TEST ARTICLE IDENTIFICATIONS

A. Test Articles

1. Main Study/PCA Assay

Phase	Sponsor Identifications	SLI Identification Nos.
Dietary Dosing (Group 1)	NB# 6312322 (Mech1 trans) 5713C-I (10%)	S98.019.3044
Dietary Dosing (Group 2)	NB# 6312323 (Mech1 non-trans) 5713C-K (10%)	S98.021.3044
Dietary Dosing (Group 3)	NB# 6312331 (Mech3 non-trans) 5713C-M (10%)	S98.023.3044
Dietary Dosing (Group 4)	Control Diet 5713C-H	V98.003.3044
PCA IC* Dosing	***	***
PCA IC Dosing	***	***
PCA IC Dosing	***	***
PCA ID** Dosing	Histamine	S98.007.3044
PCA IC Dosing	Evans blue (crystals from Sigma)	S98.012.3044
PCA ID/IC Dosing	Sterile Saline	V98.006.3044

*Intracardial, **Intradermal, ***To be added by protocol amendment.

2. Characteristics

The Sponsor is responsible for any necessary evaluations related to chemical composition, strength, purity, stability and other data required by 40 CFR 160.105 and 21 CFR Part 58.105. Any special storage conditions for the test/control articles will be supplied by the Sponsor. The Sponsor has requested that the bulk feeds be maintained refrigerated (~4°C) and smaller amounts (subsamples) removed weekly or as necessary (to be maintained refrigerated) for dispensation.

3. Handling Precautions

Safety data regarding the test/control articles should be provided by the Sponsor [Material Safety Data Sheet (MSDS) or equivalent, if available]. Technical personnel are required to read this information prior to handling

the test/control articles. Any question concerning this information should be referred to the Study Director.

Additional safety and handling information may be provided by the Study Director and/or Sponsor. Minimum safety requirements include safety glasses, impervious gloves, and laboratory wear. An MSDS shall also be available for any chemical entities utilized in the conduct of this study.

B. Analytical/Retention Samples

An approximate 20 g analytical sample of each lot of test/control article feed (Groups 1-4) will be taken on days 0, 7, 14, 21, 28, 35, 42, 49, 56 and at termination and stored in a -70°C freezer for possible Sponsor evaluation. An approximate 10 g retention sample of each test/control article feed will also be collected from each bulk test/control article and from each subsample. The sample will serve as the retention sample for all studies conducted with the lot of test article utilized.

C. Test/Control Article Disposition

All remaining test/control articles will be returned to the Sponsor following completion of all studies with the test/control articles unless otherwise instructed by the Sponsor.

D. Method of Dosage Preparation for Injection Animals

1. Main Study

a. Dietary test/control article (day 0 through day 60 ± 2 days)

Each appropriate dietary test/control article for Groups 1, 2, 3 and 4 will be fed in a premade diet as received from the Sponsor to each animal ad libitum. The Sponsor will provide analysis to be included in the final report. The method of preparation may be provided by the Sponsor, documented in the raw data and presented in the final report.

2. PCA Assays

a. Histamine for PCA Assay

Histamine will be administered intradermally at a 1:10 dilution in sterile saline or as directed by the Sponsor. The test article will be prepared and/or dispensed fresh on the day of dosing. The method of preparation will be documented in the raw data and presented in the final report.

b. Sterile Saline

Sterile saline may be administered intradermally as received (if requested) and may be dispensed on the day of dosing. The method of preparation will be documented in the raw data and presented in the final report.

c. Evans blue

An Evans blue solution of 6% w/v in sterile saline will be prepared for use on each day of the PCA Assay. The method of preparation will be documented in the raw data and presented in the final report.

d. PCA Challenge Solutions

To be determined and added by protocol amendment.

V. TEST SYSTEM

A. Justification of the Test System

1. The guinea pig is the preferred species for immunological testing by various U.S. and International regulatory agencies.

2. The Hartley-derived albino guinea pig has been shown to be sensitive to the hyperallergenic effects of a variety of drugs and chemicals. Therefore, this species and strain is a reasonable alternative to larger mammals for dermal sensitization testing of drugs and chemicals for human safety assessment.

3. The Hartley-derived albino guinea pig has been used extensively for dermal sensitization testing. Thus, data from this study may be compared and contrasted to other studies performed in Hartley-derived albino guinea pigs.

4. Historical information concerning Hartley-derived albino guinea pigs is available at SLI and in the published literature.

5. Healthy, outbred Hartley-derived albino guinea pigs may be obtained from reliable, USDA approved and regulated suppliers.

6. The laboratory guinea pig may be safely handled and manipulated by trained technical personnel.

B. Justification of the Route of Exposure and Number of Animals

1. Feeding was selected as a potential route of human exposure of the antigen being evaluated.

2. Since Hartley-derived albino guinea pigs are PVR antibody free, the response should be specific for the antigen.

3. The number of animals used on this study will be the minimum number to ensure scientifically meaningful results and to allow for adequate practice for the future studies to be conducted.

C. Description

1. Species

Guinea Pig

2. Strain

Hartley-derived albino, VAF

3. Source

Charles River Laboratories, Inc. or another USDA approved supplier

4. Age and Body Weight Range

Young adult, Main Study Animals will weigh approximately 250 g to 500 g (on day 0) and PCA animals approximately 250 to 500 g (on the day prior to dosing).

5. Number of Animals/Sex on Study

All female guinea pigs

40 Main study animals (10 per test group; 4 groups)

A maximum of 90 animals will be utilized for the PCA assay. The actual number will be documented in a protocol amendment.

D. Method of Identification

Plastic ear tags displaying unique identification numbers will be used to individually identify the animals. Cage cards displaying at least the study number, animal number, and sex will be affixed to each cage.

E. Animal Husbandry

1. Housing

The animals will be housed individually in suspended stainless steel cages. All housing and care will be based on the standards recommended by the Guide for the Care and Use of Laboratory Animals [1].

2. Environment

The environmental conditions for the animal room will be set to maintain room temperature and relative humidity ranges of 70 ± 7°F and 50 ± 20%, respectively. Environmental control equipment will be monitored and adjusted as necessary to minimize fluctuations in the animal room environment. Light timers will be set to maintain a 12-hour light/12-hour dark cycle and the room ventilation will be set to produce 10-15 air changes/hour. The room temperature and relative humidity will be recorded a minimum of once daily.

3. Food

PMI Certified Guinea Pig Chow #5026 (Purina Mills, Inc.) or diet provided by the Sponsor will be provided ad libitum to the animals throughout the study. The lot number and expiration date of each batch of diet used during the study will be recorded. The feed is analyzed and certified by the supplier for nutritional components and environmental contaminants. Dietary limitations for various environmental contaminants, including heavy metals, pesticides, polychlorinated biphenyls and total aflatoxin are set by the manufacturer. Within these limits, there are no contaminants reasonably expected in the diet which would interfere with the conduct of the study. Results of the dietary analyses (Certificates of Analysis) are provided by the manufacturer for each lot of diet. These will be maintained in the laboratory records. Feed that is outside the ranges set for the above mentioned criteria will not be utilized by the testing facility.

4. Water

Municipal tap water following treatment by reverse osmosis will be available ad libitum throughout the study. The purified water will be supplied by an automatic watering system. Monitoring of the drinking water for contaminants will be conducted annually by the testing laboratory and the records will be available for inspection. Levels of contaminants which may be present are not expected to compromise the purpose of the study. The water meets the standards specified under the EPA National Drinking Water Regulations (40 CFR Part 141).

F. Acclimation

Upon receipt, the animals will be removed randomly from the shipping cartons, examined by qualified personnel, identified with plastic ear tags, and then acclimated to the laboratory conditions for a minimum of 5 days. The animals will be observed daily for overt physical or behavioral abnormalities, general health/moribundity and mortality.

G. Animal Selection

At least 42 animals will be weighed and examined in detail for adverse clinical signs. Animals determined to be suitable as test subjects will be assigned randomly to groups. The animal numbers and the respective body weight

values will be entered into the computer. Homogeneity of groups by weight will be the criteria of acceptance of the randomization. Disposition of animals not selected for study will be documented in the study records.

VI. EXPERIMENTAL DESIGN AND PROCEDURES

A. Study Group Design

This study will consist of a Main Study and a PCA assay:

Main Study Group No.	No. of Test Animals	Administration
1	10	NB# 6312322 (Mech1 trans) 5713C-I (10%)
2	10	NB# 6312323 (Mech1 non-trans) 5713C-K (10%)
3	10	NB# 6312331 (Mech3 non-trans) 5713C-M (10%)
4	10	Control Diet 5713C-H
PCA Assay Group No.*	No. of Test Animals*	Administration*
*To be determined and added by protocol amendment.		

B. Rationale for Dosage Level Selection

Levels chosen were considered acceptable for determination of titer to the antigen administered based on preliminary work.

C. Dosing Procedures (Main Study)

1. Dietary Dosing (Groups 1-5)

   Each group of Main Study Test animals will be fed the appropriate premade diet as received from the Sponsor ad libitum from day 0 through day 60 (± 2 days).

2. Clinical Observations

The animals will be checked for general health/mortality and moribundity twice daily during the study. In addition, cage-side observations will be performed once daily and detailed clinical observations will be performed weekly. The detailed weekly observations will include, but not be limited to, evaluations of the skin and fur; eyes and mucous membranes; respiratory, circulatory, autonomic and central nervous system; somatomotor activity and behavioral pattern. Particular attention will be directed to observations of tremors, convulsions, lethargy, other signs of central nervous system depression, salivation and diarrhea.

3. Body Weights

Individual body weights will be obtained for all Main Study test animals (Groups 1, 2, 3 and 4) on day 0, 7, 14, 21, 28, 35, 42, 49 and 56 and prior to blood collection (termination).

4. Food Consumption

Individual food consumption will be measured at least weekly (or more frequently as determined by the Sponsor) on the same day as body weights. Food consumption may be reported as g/animal/day.

5. Collection of Blood Samples

On day 60 (± 2 days), Main Study test animals (Groups 1, 2 ,3 and 4) will be anesthetized with isoflurane and blood samples will be obtained intracardially (approximately 2 mL or as much as possible up to 10mL-terminal blood collection). Blood collected for serum separation will be allowed to clot. Serum will be harvested according to the Standard Operating Procedures of the Test Facility for preparation of serum specimens. Each serum sample for PCA will be heat inactivated at approximately 56°C for 30 minutes. Approximately 200 uL or up to one-half of each of the serum samples will be collected for return to the Sponsor for possible analysis. All serum samples will be stored frozen (with minimal freeze-thaw if possible).

6. Unscheduled Deaths and Euthanasia

Any animals dying or euthanized moribund during the study will be necropsied. The animals will be euthanized by carbon dioxide inhalation or an intraperitoneal injection of sodium pentobarbital. Body cavities (cranial, thoracic, abdominal and pelvic) will be opened and examined. No tissues will be retained.

7. Scheduled Euthanasia

Immediately following the blood collection, all surviving animals will be euthanized by carbon dioxide inhalation or an intraperitoneal injection of sodium pentobarbital. A gross necropsy examination will be conducted for surviving animals at the discretion of the Sponsor (e.g., adverse clinical observations) in which case limited tissues may be collected and retained in 10% buffered formalin for possible future evaluation.

D. PCA Study Procedures

1. Preliminary Procedures

Within 14 days of Main Study blood collection, the animals will be clipped using a No. 40 size blade from the neck to the rump and down both sides onto the abdomen. When clipping, care will be taken not to abrade the skin. In addition, the back of the animals may be depilated: Neet Hair Remover or other appropriate depilatory agent will be placed on the test sites and surrounding areas and left on for a sufficient time to remove hair but no more than fifteen minutes. The depilatory will then be thoroughly removed with a stream of warm water. The animals will be dried with a towel. Test sites will be delineated on the day prior to dosing. The animals will be individually weighed on the day prior to dosing. Note: PCA assay may be conducted by splitting groups and dosing over more than one day if needed, depending upon the final number of PCA animals required.

2. Serum Preparation - Dilutions

On the day of dosing, serum samples from the Main Study animals will be allowed to thaw at less than 37°C. Each serum tube will be gently mixed prior to removing the sample aliquots. Samples (0.5 mL/serum sample or less, if possible) from each of ten animals in each Main Study group

(1-4) will be diluted individually for ID dosing. Dilutions of the serum will be made by mixing measured aliquots of the sera with measured volumes of sterile saline to provide the final ratios. The following dilutions will be utilized for dosing:

Group	Dilution*	Diluent
Group 1		Sterile Saline
Group 2		Sterile Saline
Group 3		Sterile Saline
Group 4		Sterile Saline
*To be determined and added by protocol amendment.		

Any change in dilutions requested for use by the Sponsor will be documented in the raw data and presented in the final report. All dilutions will be used on the day that they are prepared, and the time between preparation and injection will be minimized as much as possible.

3. Intradermal Injection Sites

On the day of dosing, animals selected for the PCA Study will be injected intradermally with up to 24 injections. Intradermal injection sites and injections will be determined and added by protocol amendment.

Changes to the dosing regime may be made by the Sponsor not to exceed 24 injection sites. The final dosing regime will be documented in the raw data.

Each injection site area may be re-identified with indelible ink. In addition, a PCA assay record will be used to identify each PCA test animal by identification number and will specify which individual serum samples are tested on that animal and the location (left dorsal surface or right dorsal surface). In each case, the test sera will be injected in close proximity to the shoulder and each successive dilution will be injected in a more posterior position.

A 1 cc tuberculin syringe and an attached 26 or 27 gauge intradermal needle will be utilized.

4. PCA Challenge

Approximately four hours (± 30 minutes) after the intradermal injections, a challenge dose using 1 mL of the appropriate PCA challenge solution (note: an additional 1 mL of PCA solution may be injected if needed) per animal will be injected intracardially using a 3 cc disposable syringe and a 22 gauge, 3/4 or 1 inch needle (or other appropriate size). The animals will be lightly anesthetized with isoflurane to expedite handling at challenge. Note: Histamine and Sterile Saline (if utilized) will be injected intradermally approximately 15 minutes after PCA challenge.

5. Challenge Evaluation

Approximately twenty minutes (± 15 minutes) after PCA challenge (intracardial injection of compounds and dye), the animals will be euthanized by carbon dioxide inhalation or an intraperitoneal injection of sodium pentobarbital. The skin will be removed, inverted, photographed (with e.g. a clear ruler) and examined for areas of bluing (the diameter of which will be measured). In addition, the thoracic cavity of each PCA animal will be examined specifically to observe heart and lungs. Also, it will be noted if the musculature of the back is a bluish discoloration.

6. Clinical Observations

Any unusual observations and mortality will be recorded. The animals will be observed for general health/mortality twice daily (once in the morning and once in the afternoon).

7. Body Weights

Individual body weights will be obtained for all PCA Study animals on the day prior to dosing.

8. Unscheduled Deaths and Euthanasia

Any animals dying or euthanized moribund during the study will be necropsied. The animals will be euthanized by carbon dioxide inhalation or an intraperitoneal injection of sodium pentobarbital. Body cavities (cranial, thoracic, abdominal and pelvic) will be opened and examined. No tissues will be retained.

VII. PROTOCOL AMENDMENT

Alterations to this protocol may be made as the study progresses. No changes in the protocol will be made without the specific consent of the Sponsor's Representative. A protocol amendment will be prepared and signed by the Study Director, SLI Quality Assurance and Sponsor's Representative for any such changes.

VIII. DATA REPORTING

One unbound copy of the draft report (if requested) and three copies of the final report (two bound and one unbound) will be submitted to the Sponsor. The final report will include all information necessary to provide a complete and accurate description and evaluation of the experimental procedures and results.

The report will include at least the following information and data:

- Table of Contents
- Regulatory Compliance
- Summary
- Introduction
- Experimental Design and Test Procedures
- Presentation and Discussion of Results
- Conclusion
- References
- Data Tables
- Summary of Titers and Diameter of Responses
- Summary of Body Weights
- Summary of Body Weight Changes
- Summary of Food Consumption (g/animal/day)
- Individual Titers and Diameter of Responses
- Individual Clinical Signs
- Individual Body Weights
- Individual Body Weight Changes
- Individual Food Consumption (g/animal/day)

The following additional information may be presented in the appendices: protocol and any amendments, sponsor analytical chemistry report and personnel responsibilities.

IX. ANALYSIS OF DATA

The last intradermal injection site on the PCA animal to show a positive response (bluing) may be considered to be the titer of that serum sample. If the highest dilution of serum tested demonstrates a positive response, a higher dilution series of that sample may be tested (e.g., 2 or 3 dilutions higher than previously tested). The response will be recorded for each dilution. Comparisons of diameters of bluing may also be made.

Statistical analyses will be performed using MicroVax 3100 computer. The level of significance will be a minimum of 5% and tests will be two-tailed. The summary tables will indicate the level of significance detected. The control group data will be compared to the treated data using all groups or by a group by group comparison depending on the test. Data including body weights, weight gain, food consumption will be analyzed by one way analysis of variance. If significance is detected, a group by group comparison will proceed with Tukey-Kramer.

X. MAINTENANCE OF RAW DATA, RECORDS AND SPECIMENS

All original data, magnetically encoded records, photographs, specimens and reports from this study are the property of the Sponsor. These materials shall be available at SLI to facilitate auditing of the study during its progress and prior to acceptance of the final report. All original paper data, the final report, magnetically encoded records, and any specimens will be transferred to the SLI archives for a period of 7 years. The Sponsor will be contacted prior to the final disposition of these items.

XI. REGULATORY COMPLIANCE

A. Guidelines

This study may be submitted to and will be performed in general compliance with the U.S. EPA and FDA Guidelines.

B. Good Laboratory Practices

This study will be performed in general compliance with the principles of the Good Laboratory Practice Standards as described by the EPA (40 CFR Part160) and FDA (21 CFR Part 58).

XII. QUALITY ASSURANCE

The study will be inspected at least once during the in-life phase by the Springborn Laboratories, Inc., Quality Assurance Unit to assure compliance with Good Laboratory Practice Standards, SLI's Standard Operating Procedures and for conformance with the protocol and protocol amendments. The final report will be audited prior to submission to the Sponsor to ensure that it completely and accurately describes the test procedures and results of the study.

XIII. USDA ANIMAL WELFARE COMPLIANCE STATEMENT

This study will comply with all applicable sections of the Final Rules of the Animal Welfare Act regulations (9 CFR) and the Public Health Service Policy on Humane Care and Use of Laboratory Animals (OPRR, NIH, 1986). Wherever possible, procedures used in this study have been designed to avoid or minimize discomfort, distress and pain to animals. All methods are described in this study protocol or in written laboratory standard operating procedures. These procedures are based on the most currently available technologies concerning proper laboratory animal use and management. Methods of euthanasia used during the study are in conformance with the above referenced regulations and the American Veterinary Medical Association Panel on Euthanasia [3]. This study design has been reviewed and approved by Springborn Laboratories, Inc. Institutional Animal Care and Use Committee (IACUC) for a maximum of 150 animals.

This study is being conducted to evaluate the potential immunological effect of the test article and is not expected to produce undue pan or distress in the animals. Following dosing, the Study Director will be notified by the technician if severe local reactions occur, if the animals exhibit overt clinical indications of pain/distress post-dose or if delayed severe skin or clinical changes subsequently develop. If severe responses are noted, the Study Director will contact the Facility Veterinarian and Sponsor to consider an appropriate course of action. In the event that the Sponsor cannot be contacted, the Study Director and/or Facility Veterinarian may authorize treatment or euthanasia of the animals.

XIV. DECLARATION OF INTENT

This study will be listed on the SLI Quality Assurance Master Schedule for the U.S. Environmental Protection Agency and US Food and Drug Administration.

XV. PROTOCOL APPROVAL

The Sponsor's signature below documents for the Study Director that there are no generally accepted non-animal alternatives for this study, and that this study does not unnecessarily duplicate any previous experiments.

Kimberly L. Bonnette, M.S., LATG
Manager of Acute Toxicology (SLI)

Date: 7/24/98

Quality Assurance Unit (SLI)

Date: 7/24/98

Malcolm Blair, Ph.D.
Vice President and Managing Director (SLI)

Date: 7/27/98

Terry Kaempfe, B.S.
Monsanto Company
Sponsor's Representative
(Principal Investigator)

Date: 7/24/98

Rick Goodman, Ph.D.
Monsanto Company
Study Monitor

Date: 7/24/98

XVI. REFERENCES

1. Guide for the Care and Use of Laboratory Animals, DHHS Publication No. (NIH) 96-03, 1996.

2. 1993 Report of the American Veterinary Medical Assoc. Panel on Euthanasia, JAVMA, Vol. 202, No. 2, pp. 229-249, January 15, 1993.

PROTOCOL APPENDIX A

Figure 1*

Intradermal Injection Sites

*To be determined and added by protocol amendment.

SLI Study No. 3044.697
Monsanto Study No. SB-98-212

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS

PROTOCOL AMENDMENT NO. 1

1) PART TO BE CHANGED/REVISED (EFFECTIVE NOVEMBER 30, 1998 AND SEPTEMBER 10, 1998):

I. Purpose

CHANGE/REVISION:

Change the first sentence to read as follows:

This study was performed to provide an assessment of the allergenic activity of transgenic and non-transgenic cottonseed meal in a guinea pig model. Animals were to be sensitized by feeding diets containing cottonseed meal for approximately sixty days, to induce cottonseed protein specific IgG_{1a}, the dominant reaginic antibody of guinea pigs. Antibody titers were to be measured by passive cutaneous anaphylaxis following transfer of serum from sensitized animals to naive recipients. However, since the results of the main study were considered to be compromised, the Passive Cutaneous Anaphylaxis Assay was not conducted.

REASON FOR CHANGE/REVISION:

Requested by the Sponsor based on apparent poor nutritional status of the animals fed the test diets (probable inadequate diet and/or palatability issue) confirmed by severe adverse clinical observations (Vitamin C deficiency-like indications) and severe reduction in body weight/body weight gain. In addition, the feed for Group 1 (fed days 0-21) was apparently mislabeled control diet (Group 4) from the manufacturer based on the Gene Feed Assay Results.

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS

PROTOCOL AMENDMENT NO. 1

2) PART TO BE CHANGED/REVISED (EFFECTIVE SEPTEMBER 10, 1998):

IV.A. Test Articles

CHANGE/REVISION:

Replace Section 1 to read as follows:

1. Main Study

Phase	Sponsor Identifications	SLI Identification Nos.
Dietary Dosing (Group 1)	NB# 6312322 (Mech1 trans) 5713C-I (10%)	S98.019.3044
Dietary Dosing (Group 2)	NB# 6312323 (Mech1 non-trans) 5713C-K (10%)	S98.021.3044
Dietary Dosing (Group 3)	NB# 6312331 (Mech3 non-trans) 5713C-M (10%)	S98.023.3044
Dietary Dosing (Group 4)	Control Diet 5713C-H	V98.003.3044

REASON FOR CHANGE/REVISION:

PCA dosing was omitted as requested by the Sponsor based on reasons stated previously.

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS

PROTOCOL AMENDMENT NO. 1

3) PART TO BE CHANGED/REVISED (EFFECTIVE AUGUST 24, 1998):

IV.A.2. Characteristics

CHANGE/REVISION:

On day 28, the subsamples of the bulk feed will be stored at room temperature rather than refrigerated to reduce potential condensation. In addition, the Sponsor evaluated a sample from each box of diet (3 boxes per diet) on site using a Gene Feed Assay to be described in the final report.

REASON FOR CHANGE/REVISION:

Requested by the Sponsor.

4) PART TO BE CHANGED/REVISED (EFFECTIVE AUGUST 17, 1998):

IV.B. Analytical/Retention Samples

CHANGE/REVISION:

Replace this section with the following:

An approximate 20 g analytical sample of each lot of test/control diet will be taken on days 7, 14, 21, 28, 35, 42 and at study termination (day 49) and stored at approximately -70°C for possible Sponsor evaluation. An approximate 10 g retention sample of each test/control diet will also be collected from each lot of test/control diet and from each subsample. These samples will be stored refrigerated and will serve as the retention samples for all studies conducted with these lots of test/control diets utilized.

REASON FOR CHANGE/REVISION:

To specify the sample collection days due to early termination of the study.

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS

PROTOCOL AMENDMENT NO. 1

5) PART TO BE CHANGED/REVISED (EFFECTIVE AUGUST 17, 1998):

IV.E. Method of Test Article Preparation for the Main Study

CHANGE/REVISION:

Add the following:

On day 21, an approximate 50 g sample of each box of diet (3 boxes/diet) was sent to Ralston Analytical Laboratories, 824 Gratiot, St. Louis, Missouri, 63102 for analysis.

REASON FOR CHANGE/REVISION:

Due to significant adverse clinical observations/reduced body weight, the feed was analyzed to determine any feed deficiencies.

6) PART TO BE CHANGED/REVISED (EFFECTIVE AUGUST 26, 1998):

IV.E.3. Food Effective

CHANGE/REVISION:

Change the seventh sentence to the following:

These dietary analyses will be maintained by the Sponsor.

REASON FOR CHANGE/REVISION:

The Sponsor will present these analyses under a separate cover.

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY
IN GUINEA PIGS

PROTOCOL AMENDMENT NO. 1

7) PART TO BE CHANGED/REVISED (EFFECTIVE AUGUST 26, 1998):

IV.E.4. Water

CHANGE/REVISION:

Add the following to this section:

The purified water will be supplied by an automatic watering system (days 0-29) or reverse osmosis water supplemented with 200 mg/L ascorbic acid (Vitamin C) in water bottles (days 30-49).

REASON FOR CHANGE/REVISION:

Requested by the Sponsor.

8) PART TO BE CHANGED/REVISED (EFFECTIVE AUGUST 31, 1998):

VI.A. Study Group Design

CHANGE/REVISION:

Replace the table as follows:

Main Study Group No.	No. of Test Animals	Administration (Days 0-21 and Days 28-49)
1	10	NB# 6312322 (Mech1 trans) 5713C-I (10%)
2	10	NB# 6312323 (Mech1 non-trans) 5713C-K (10%)
3	10	NB# 6312331 (Mech3 non-trans) 5713C-M (10%)
4	10	Control Diet 5713C-H
Main Study Group No.	No. of Test Animals	Administration (Days 35 - 44 only)
5*	4	NB# 6312322 (Mech1 trans) 5713C-I (10%)**
6*	4	Control Diet 5713C-H
*No Vitamin C supplement; fed/observed at the same time intervals as in the main study. **Correct diet.		

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY
IN GUINEA PIGS

PROTOCOL AMENDMENT NO. 1

REASON FOR CHANGE/REVISION:

Since there were severe adverse clinical observations/reduced body weight in the main study, any results from the serum of these animals would be considered compromised/unreliable, a PCA study was not performed. In addition, the feed for Group 1 (fed days 0-21) was apparently control diet (Group 4) mislabeled by the manufacturer based on the Gene Feed Assay results. Also, in order to confirm the effects of the diets, "normal stock animals" were fed the specified diets to observe/confirm the onset of adverse effects of this test diet.

9) PART TO BE CHANGED/REVISED (EFFECTIVE AUGUST 17, 24 AND 26, 1998):

VI.C.1. Dietary Dosing (Groups 1-4)

CHANGE/REVISION:

Replace to read as follows:

Each group of Main Study test animals will be fed the appropriate pre-made diet as received from the manufacturer ad libitum from days 0 -21 and from days 28-49. Also on day 28, remove Animal No. 4648 from study. In addition, on day 30, reverse osmosis water supplemented with 200 mg/L of ascorbic acid (Vitamin C), was provided to the animals (changing water bottles ~3 days per week, disconnecting the automatic watering system and refrigerating remaining preparation for use).

REASON FOR CHANGE/REVISION:

The test diet was stopped, restarted, then the study terminated early for reasons discussed previously. Due to severe adverse clinical observations persisting, the referenced animal was removed from study. In addition, Vitamin C was supplemented in an attempt to reduce Vitamin C deficiency-like signs.

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS

PROTOCOL AMENDMENT NO. 1

10) PART TO BE CHANGED/REVISED (EFFECTIVE AUGUST 13 and 20, 1998):

VI.C.3. Body Weights

CHANGE/REVISION:

Replace this section to read as follows:

Individual body weights will be obtained for all Main Study test animals (Groups 1, 2, 3 and 4) on days 0, 7, 14, 17, 21, 24, 28, 35, 38, 42 and 49 (study termination). Animals found dead after day 0 or euthanized moribund will also be weighed.

REASON FOR CHANGE/REVISION:

Additional body weights were conducted to determine animal health status due to significant adverse clinical observations. Also, in addition, the study was terminated early.

11) PART TO BE CHANGED/REVISED (EFFECTIVE AUGUST 17, 1998 AND EFFECTIVE NOVEMBER 30, 1998):

VI.C.4. Food Consumption

CHANGE/REVISION:

Replace the first sentence of this section as follows:

Individual food consumption will be measured three times a week. In addition, due to the amount of food spillage on this study, food consumption is not considered to be accurate and therefore will be invalidated.

REASON FOR CHANGE/REVISION:

Guinea pigs were fed more frequently than stated in the protocol in order to be fed ad libitum. In addition, food consumption was invalidated as requested by the Sponsor.

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS

PROTOCOL AMENDMENT NO. 1

12) PART TO BE CHANGED/REVISED (EFFECTIVE AUGUST 17, 1998):

VI.C.5. Collection of Blood Samples

CHANGE/REVISION:

Replace as follows:

On day 21, due to adverse clinical observations appearing particularly in Groups 2 and 3 along with significantly reduced weight gain or weight loss, the Sponsor requested the following:

Blood will be collected via the orbital sinus (under light anesthesia) from all animals along with 5 additional stock animals for comparison. The following parameters will be evaluated:

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS

PROTOCOL AMENDMENT NO. 1

Hematology Parameters	Biochemistry Parameters
Erythrocyte Count (RBC)	alanine aminotransferase (ALT)
Hematocrit (Hct)	albumin
Hemoglobin concentration	albumin/globulin ratio
Mean Corpuscular hemoglobin concentration (MCHC)	alkaline phosphatase
Mean Corpuscular volume	aspartate aminotransferase (AST)
Platelet Count	calcium
Reticulocyte Count	cholesterol
Total Differential Leukocyte Counts	blood creatinine
Mean Corpuscular hemoglobin (MCH)	globulin (calculated)
	glucose
	electrolytes (Na, K, Cl)
	phosphorus
	total bilirubin
	total serum protein
	Urea protein-Urea Nitrogen (BUN)

REASON FOR CHANGE/REVISION:

Serum was not needed for PCA as discussed previously. In addition, in order to better evaluate main study animals' health, clinical pathology was conducted on all main study animals and 5 stock animals as requested by the Sponsor.

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS

PROTOCOL AMENDMENT NO. 1

13) PART TO BE CHANGED/REVISED (EFFECTIVE AUGUST 26, 1998):

VI.C.6. Unscheduled Deaths and Euthanasia

CHANGE/REVISION:

Replace the last sentence as follows:

On day 30, Animal No. 4648 was euthanized moribund and a gross necropsy examination was performed. In addition, the proximal and distal ends of the femur and tibia were collected and the bones processed/decalcified and evaluated by a Pathologist.

REASON FOR CHANGE/REVISION:

Requested by the Sponsor in order to determine abnormalities, including growth plate separation (possibly Vitamin C deficiency-related).

14) PART TO BE CHANGED/REVISED (EFFECTIVE SEPTEMBER 10, 1998) :

VI.C.7. Scheduled Euthanasia

CHANGE/REVISION:

Replace with the following:

All animals surviving to study termination (day 49) will be euthanized by carbon dioxide inhalation or intraperitoneal injection of sodium pentobarbital and discarded without a gross necropsy.

REASON FOR CHANGE/REVISION:

As discussed previously, the study was terminated early. The Sponsor requested that surviving animals be discarded with out necropsy.

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY
IN GUINEA PIGS

PROTOCOL AMENDMENT NO. 1

15) PART TO BE CHANGED/REVISED (EFFECTIVE SEPTEMBER 10, 1998):

VI.D. PCA Study Procedures

CHANGE/REVISION:

Omit this section.

REASON FOR CHANGE/REVISION:

Based on the compromised results of the main study, PCA was not required as requested by the Sponsor.

16) PART TO BE CHANGED/REVISED (EFFECTIVE SEPTEMBER 10, 1998):

IX. Analysis of Data

CHANGE/REVISION:

Omit the first paragraph.

REASON FOR CHANGE/REVISION:

Since no PCA data was collected, this paragraph is not needed.

17) PART TO BE CHANGED/REVISED (EFFECTIVE SEPTEMBER 10, 1998):

Protocol Appendix A

CHANGE/REVISION:

Omit Figure 1.

REASON FOR CHANGE/REVISION:

Since no PCA was conducted, this Appendix is not needed.

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS

PROTOCOL AMENDMENT NO. 1

Kimberly L. Bonnette, M.S., LATG
Study Director (SLI)

Date 11/30/98

Quality Assurance Unit (SLI)

Date 11/30/98

Malcolm Blair, Ph.D.
Vice President and Managing Director (SLI)

Date 11/30/98

Terry A. Kaempfe, B.S.
Monsanto Company
Sponsor's Representative

Date 11/30/98

Rick Goodman, Ph.D.
Monsanto Company
Study Monitor

Date 11/30/98

APPENDIX B

Results of Feed Gene Assay

FEED GENE ASSAY

A gene check assay was performed at Springborn Laboratories, Inc., Spencerville, Ohio, by Richard Goodman, Monsanto Company on September 23, 1998 on the boxes of test diet listed in the results below. Approximately 5 pellets from each box were removed and placed in test tubes. The samples were then q.s. to approximately 4.0 mL with sterile saline and mixed (vortexed). The samples were allowed to rest for approximately 10 minutes. The subsequent supernate was then transferred to pre-labeled 1.5 mL tubes using sterile, disposable pipettes. A gene check immunoassay testing strip was then placed in each tube. The strips were allowed to develop for approximately 10 minutes. The strips were then photographed (which remain in the raw data).

The results of the test are as follows:

Sample	Box #	Springborn I.D.	Purina Lot No.	Results
5713C-H	1	V98.003.3044	9848-1	Negative[a]
	2	V98.003.3044	9848-1	Negative
	3	V98.003.3044	9848-1	Positive
5713C-I	1	S98.019.3044	9848-2	Positive
	2	S98.019.3044	9848-2	Negative
	3	S98.019.3044	9848-2	Positive
5713C-K	1	S98.021.3044	9848-4	Negative
	2	S98.021.3044	9848-4	Negative
	3	S98.021.3044	9848-4	Negative
5713C-M	1	S98.023.3044	9848-6	Negative
	2	S98.023.3044	9848-6	Negative
	3	S98.023.3044	9848-6	Negative

[a]Approximately eight minutes later, a second test strip was read and appeared to be positive for the BT gene; upon review of the first strip, what appeared originally as an imperfection was now clearly positive, but weak (light pink).

APPENDIX C

Certificate of Analysis
(Provided by the Manufacturer)

SLI Study No. 3044.697

SIGMA®

3050 Spruce Street
Saint Louis, Missouri 63103 USA
Telephone 800-521-8956 • (314) 771-5765
Fax 800-325-5052 • (314) 771-5757
email: sig-ald@sial.com
http://www.sigma.sial.com

SPRINGBORN LABS
640 N ELIZABETH ST
SPENCERVILLE OH 45887

CERTIFICATE OF ANALYSIS

ASCORBIC ACID, APPROX. 325 MESH USP XXIII

PRODUCT NO: A2343 CAS NO: 50-81-7

LOT NO: 096H03631 FORMULA: $C_6H_8O_6$

FORMULA WEIGHT: 176.13 STORE AT ROOM TEMPERATURE

TEST	SPECIFICATION	RESULTS
IDENTITY	PASS	PASS
SPECIFIC ROTATION	+20.5 DEG TO +21.5 DEG	+20.9 DEG
RESIDUE ON IGNITION	NMT 0.1%	PASS
HEAVY METALS	NMT 0.002%	PASS
ORGANIC VOLATILE IMPURITIES	METHOD IV TESTING	PASS
ASSAY	99.0% TO 100.5%	99.8%
NOTE		ALL RESULTS SUPPLIER DATA

QC ACCEPTANCE DATE MAY 1997

DAVID FELDKER
MANAGER, ANALYTICAL SERVICES
238/980825#1/SML1
DOCUMENT DATE: 08/25/98

APPENDIX D

Clinical Pathology Methodology

A. Blood Collection

1. Blood collection. Blood samples for hematology were collected into tubes containing K_3EDTA anticoagulant. Blood samples for biochemistry were collected into tubes containing no anticoagulant.

B. Hematology

1. Red blood cell (RBC) and white blood cell (WBC). A Coulter S Plus IV hematology analyzer is used in determining the RBC and WBC. A Coulter S-Cal kit is used to calibrate the instrument and Coulter Tri-Pack control sera are used in monitoring accuracy and precision of the instrument.

2. Hemoglobin (HGB). Hemoglobin is measured on the Coulter S Plus IV hematology analyzer. A lysing reagent lyses the RBC and converts the released HGB to a stable cyanide-containing pigment which is measured photometrically. Coulter Tri-Pack control sera are used in monitoring accuracy and the precision of the instrument.

3. Mean corpuscular (erythrocyte) volume (MCV). The MCV is measured on the Coulter S Plus IV hematology analyzer. Coulter Tri-Pack control sera are used in monitoring the precision and accuracy of the instrument.

4. Mean corpuscular (erythrocyte) hemoglobin (MCH). The MCH is computed electronically on the Coulter S Plus IV hematology analyzer using the following equation:

$$\text{MCH } (\mu\mu g) = 10 \times \frac{\text{HGB}}{\text{RBC}}$$

5. Mean corpuscular (erythrocyte) hemoglobin concentration (MCHC). MCHC is computed electronically on the Coulter S Plus IV hematology analyzer using the following equation:

$$\text{MCHC (g/dL)} = 100 \times \frac{\text{HGB}}{\text{HCT}}$$

6. Hematocrit (HCT). Hematocrit is the relative volume of erythrocytes and is computed electronically on the Coulter S Plus IV hematology analyzer using the following equation:

$$HCT\ (\%) = \frac{RBC \times MCV}{10}$$

7. Platelet count (PLT). The platelet count is determined on the Coulter S Plus IV hematology analyzer. Coulter 4C Tri-Pack control sera are used to monitor precision and accuracy of the instrument.

8. Differential leukocyte and nucleated red blood cell counts (NRBC). A Bayer Hema-tek slide stainer is used to automatically stain the slides using a combination of Wright stain, buffers and rinse solutions (Wright-Giemsa stain). One hundred white cells are counted and identified under oil immersion (100x) using the Nikon Labophot microscope. The slides are also checked for any abnormal RBC morphology. Nucleated red blood cell (NRBC) counts are counted as per 100 leukocytes. If the nucleated red blood cell count exceeds five or more in the differential count, then the WBC count from the Coulter S Plus IV must be corrected by using the following equation:

$$\frac{100}{100 + \text{Number of NRBC} \times \text{WBC count}} = \text{corrected WBC count}$$

9. Reticulocyte count using the Miller Disc Reticle method. Equal amounts of K_3EDTA blood and new methylene blue N solution are mixed, incubated and spread on a microscope slide. A light microscope with a 100x objective and a 10x ocular fitted with a miller disc reticle is used to enumerate reticulocytes and red blood cells. Approximately 300 cells are counted and the following equation is used:

$$\%\ \text{Reticulocyte} = \frac{\text{number of reticulocytes}}{\text{number of erythrocytes} \times 9} \times 100\%$$

D. Biochemistry

All biochemistry parameters are performed on the Beckman Synchron CX-5 chemistry analyzer. Synchron Control Level I and Level II are used as control sera to monitor accuracy and precision of the instrument. Listed below are the biochemistry parameters and their methodology.

1. Albumin (ALB). Beckman Albumin reagent is used to measure the albumin concentration by a timed-endpoint method. In the reaction, the albumin combines with Bromcresol Green (BCG) to form a colored product. The system monitors the change in absorbance at 600 nanometers at a fixed-time interval. This change in absorbance is directly proportional to the

concentration of albumin in the sample and is used by the Synchron CX-5 System to calculate and express the albumin concentration.

2. Alkaline phosphatase (ALP). Beckman ALP Reagent is used to measure the ALP activity by an enzymatic rate method using a 2-Amino-2-Methyl-1-Propanol (AMP) buffer. In the reaction, the ALP catalyzes the hydrolysis of the colorless organic phosphate ester substrate, p-Nitrophenylphosphate, to the yellow colored product, p-Nitrophenol, and phosphate. This reaction occurs at an alkaline pH of 10.3. The system monitors the rate of change in absorbance at 410 nanometers over a fixed-time interval. This rate of change in absorbance is directly proportional to the activity of ALP in the sample and is used by the Synchron CX-5 System to calculate and express the ALP activity.

3. Alanine aminotransferase (ALT). Beckman ALT Reagent is used to measure the ALT activity by an enzymatic rate method. In the reaction, the ALT catalyzes the reversible transamination of L-alanine and alpha-ketoglutarate to pyruvate and L-glutamate. The pyruvate is then reduced to lactate in the presence of lactate dehydrogenase (LDH) with the concurrent oxidation of b-Nicotinamide Adenine Dinucleotide (reduced form) (NADH) to b-Nicotinamide Adenine Dinucleotide (NAD). The system monitors the rate of change in absorbance at 340 nanometers over a fixed-time interval. This rate of change in absorbance is directly proportional to the activity of ALT in the sample and is used by the Synchron CX-5 System to calculate and express the ALT activity.

4. Aspartate aminotransferase (AST). Beckman AST Reagent is used to measure the AST activity by an enzymatic rate method. In the reaction, the AST catalyzes the reversible transamination of L-aspartate and alpha-ketoglutarate to oxaloacetate and L-glutamate. The oxaloacetate is then reduced to malate in the presence of malate dehydrogenase (MDH) with the concurrent oxidation of b-Nicotinamide Adenine Dinucleotide (reduced form) (NADH) to b-Nicotinamide Adenine Dinucleotide (NAD). The system monitors the rate of change in absorbance at 340 nanometers over a fixed-time interval. This rate of change in absorbance is directly proportional to the activity of AST in the sample and is used by the Synchron CX-5 System to calculate and express the AST activity.

5. Calcium (CA). Beckman Calcium Reagent is used to measure the calcium concentration by a timed-endpoint method. In the reaction, the calcium combines with Arsenazo III to form a colored product. The system monitors the change in absorbance at 650 nanometers at a fixed-time interval. This change in absorbance is directly proportional to the concentration of calcium

in the sample and is used by the Synchron CX-5 System to calculate and express the calcium concentration.

6. Cholesterol (CHOL). Beckman Cholesterol Reagent is used to measure the cholesterol concentration by a timed-endpoint method. In the reaction, the cholesterol esterase (CE) hydrolyzes cholesterol esters to free cholesterol and fatty acids. The free cholesterol is oxidized to cholesten-3-one and hydrogen peroxide by cholesterol oxidase (CO). Peroxidase catalyzes the reaction of hydrogen peroxide with 4-aminoantipyrine (4-AAP) and phenol to produce a colored quinoneimine product. The system monitors the change in absorbance at 520 nanometers at a fixed-time interval. This change in absorbance is directly proportional to the concentration of cholesterol in the sample and is used by the Synchron CX-5 System to calculate and express the cholesterol concentration.

7. Creatinine (CREA). Beckman Creatinine Reagent is used to measure the creatinine concentration by a modified rate Jaffe method. In the reaction, the creatinine combines with picrate in an alkaline solution to form a creatinine-picrate complex. The system monitors the rate of change in absorbance at 520 nanometers over a fixed-time interval. This rate of change in absorbance is directly proportional to the concentration of creatinine in the sample and is used by the Synchron CX-5 System to calculate and express the creatinine concentration.

8. Glucose (GLU). Beckman Glucose Reagent is used to measure the glucose concentration by a timed-endpoint method. In the reaction, hexokinase (HK) catalyzes the transfer of a phosphate group from adenosine triphosphate (ATP) to glucose to form adenosine diphosphate (ADP) and glucose-6-phosphate. The glucose-6-phosphate is then oxidized to 6-phosphogluconate with the concomitant reduction of b-Nicotinamide Adenine Dinucleotide (NAD) to b-Nicotinamide Adenine Dinucleotide (reduced form) (NADH) by the catalytic action of glucose-6-phosphate dehydrogenase (G6PDH). The system monitors the change in absorbance at 340 nanometers at a fixed-time interval. This change in absorbance is directly proportional to the concentration of glucose in the sample and is used by the Synchron CX-5 System to calculate and express the glucose concentration.

9. Phosphorus (PHOS). Beckman Phosphorus Reagent is used to measure the phosphorus concentration by a timed-endpoint method. In the reaction, inorganic phosphorus reacts with ammonium molybdate in an acidic solution to form a colored phosphomolybdate complex. The system monitors the change in absorbance at 340 nanometers at a fixed-time interval. This change in absorbance is directly proportional to the concentration of

phosphorus in the sample and is used by the Synchron CX-5 System to calculate and express the phosphorus concentration.

10. Total bilirubin (TBIL). Beckman Total Bilirubin Reagent is used to measure the total bilirubin concentration by a timed-endpoint Diazo method. In the reaction, the bilirubin reacts with diazo reagent in the presence of caffeine, benzoate, and acetate as accelerators to form azobilirubin. The system monitors the change in absorbance at 560 nanometers at a fixed-time interval. This change in absorbance is directly proportional to the concentration of total bilirubin in the sample and is used by the Synchron CX-5 System to calculate and express the total bilirubin concentration.

11. Total protein (TP). Beckman Total Protein Reagent is used to measure the total protein concentration by a timed-endpoint biuret method. In the reaction, the peptide bonds in the protein sample bind to cupric ions in an alkaline medium to form colored peptide/copper complexes. The system monitors the change in absorbance of 560 nanometers at a fixed-time interval. This change in absorbance is directly proportional to the concentration of total protein in the sample and is used by the Synchron CX-5 System to calculate and express the total protein concentration.

12. Sodium (Na), potassium (K), chloride (Cl). The Synchron CX-5 System determines sodium, potassium, and chloride by measuring electrolyte ion activity in solution. Measurements are made by ion selective electrodes. A precise volume of sample is mixed with a buffer solution at a ratio of 1:20 to establish a constant ionic strength and to set a constant activity coefficient for the electrodes. With constant activity established, the electrode system is calibrated to concentration values. This mixture is transported to the flow cell which houses the electrodes. Sodium, potassium, and chloride determinations are made by measuring potentials developed at the face of ion-selective electrodes.

13. Globulin (GLB). Globulin parameter is not measured directly but is calculated using the following equation:

Globulin g/dL = Total Protein - Albumin

APPENDIX E

Individual Clinical Observations

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL CLINICAL OBSERVATIONS
(POSITIVE FINDINGS)

ANIMAL NO.	CLINICAL OBSERVATIONS	DAY OF STUDY 0 1 2 3 4 5 6 7 8 9	1 0	1 1	1 2	1 3	1 4	1 5	1 6	1 7	1 8	1 9	2 0	2 1	2 2	2 3	2 4	2 5	2 6	2 7	2 8
4606 F	GROUP 1: 5713C-I (10%)																				
	FECAL STAIN												P								
4610 F	GROUP 1: 5713C-I (10%)																				
	FECAL STAIN												P								
4627 F	GROUP 1: 5713C-I (10%)																				
	SOFT STOOLS															P					
	FECAL STAIN															P					
4633 F	GROUP 1: 5713C-I (10%)																				
	SOFT STOOLS															P					
	FECAL STAIN												P			P					
4642 F	GROUP 1: 5713C-I (10%)																				
	DECREASED FOOD CONSUMPTION													P							
4643 F	GROUP 1: 5713C-I (10%)																				
	FECAL STAIN												P								
4649 F	GROUP 1: 5713C-I (10%)																				
	FEW FECES												P	P							
	SOFT STOOLS														P						
	FECAL STAIN												P								
	DECREASED FOOD CONSUMPTION													P							

GRADE CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

ANIMAL NO.	CLINICAL OBSERVATIONS	DAY OF STUDY	0	1	2	3	4	5	6	7	8	9	1 0	1 1	1 2	1 3	1 4	1 5	1 6	1 7	1 8	1 9	2 0	2 1	2 2	2 3	2 4	2 5	2 6	2 7	2 8
4602 F	GROUP 2: 5713C-K (10%)																														
	FEW FECES																							P	P						
	FECES SMALL IN SIZE																					P	P	P	P						
	DECREASED FOOD CONSUMPTION																								P						
4608 F	GROUP 2: 5713C-K (10%)																														
	FECES SMALL IN SIZE																						P								
	ROUGH COAT																							P							
4609 F	GROUP 2: 5713C-K (10%)																														
	FECES SMALL IN SIZE																		P	P	P	P	P								
	SOFT STOOLS																													P	
	ROUGH COAT																							P							
	FECAL STAIN																													P	
	DECREASED FOOD CONSUMPTION																		P	P											
4611 F	GROUP 2: 5713C-K (10%)																														
	FEW FECES																		P				P			P	P	P			
	FECES SMALL IN SIZE																		P	P	P	P	P	P	P	P	P	P			
	SOFT STOOLS																									P	P				
	ROUGH COAT																					P	P			P	P	P			
	FECAL STAIN																					P				P	P				
	EXTREMITIES APPEAR BLUE IN COLOR																									P	P	P			
	DISTENDED ABDOMEN																									P	P	P			
	DEHYDRATION																										P	P			
	DECREASED FOOD CONSUMPTION																									P	P	P			
	FOUND DEAD																												P		

GRADE CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL CLINICAL OBSERVATIONS
(POSITIVE FINDINGS)

ANIMAL NO.	CLINICAL OBSERVATIONS	DAY OF STUDY	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
4617 F	GROUP 2: 5713C-K (10%)																														
	FEW FECES									P																					
	FECES SMALL IN SIZE																			P											
	SOFT STOOLS																							P							
	ROUGH COAT												P	P	P	P	P	P													
	DECREASED FOOD CONSUMPTION												P	P																	
4620 F	GROUP 2: 5713C-K (10%)																														
	FEW FECES																P	P		P											
	FECES SMALL IN SIZE																	P	P	P				P	P	P	P	P			
	DISTENDED ABDOMEN																											P	P		
	DECREASED FOOD CONSUMPTION																P	P	P		P	P	P								
4632 F	GROUP 2: 5713C-K (10%)																														
	FEW FECES																			P											
	FECES SMALL IN SIZE																		P												
	ROUGH COAT																			P											
	DECREASED FOOD CONSUMPTION												P																		
4639 F	GROUP 2: 5713C-K (10%)																														
	FEW FECES																			P											
	FECES SMALL IN SIZE												P	P	P	P	P														
	ROUGH COAT														P	P	P	P													
	DECREASED FOOD CONSUMPTION												P	P				P													

GRADE CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL CLINICAL OBSERVATIONS
(POSITIVE FINDINGS)

ANIMAL NO.	CLINICAL OBSERVATIONS	DAY OF STUDY 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
4641 F	GROUP 2: 5713C-K (10%)																													
	FEW FECES																						P							
	FECES SMALL IN SIZE																					P								
	URINE STAIN																						P							
	ROUGH COAT																	P	P	P	P									
4645 F	GROUP 2: 5713C-K (10%)																													
	FEW FECES																P													
	FECES SMALL IN SIZE																P	P			P									
	ROUGH COAT																P													
	DECREASED FOOD CONSUMPTION																P	P												
4612 F	GROUP 3: 5713C-M (10%)																													
	FEW FECES																						P							
	URINE STAIN																						P							
4623 F	GROUP 3: 5713C-M (10%)																													
	FEW FECES																													P
	FECES SMALL IN SIZE																		P	P										P
	SOFT STOOLS																													P
	ROUGH COAT																		P	P	P									
4628 F	GROUP 3: 5713C-M (10%)																													
	FEW FECES																P	P												
	FECES SMALL IN SIZE																	P	P	P	P									
	ROUGH COAT																P	P	P	P	P									
	DECREASED FOOD CONSUMPTION																P													

GRADE CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL CLINICAL OBSERVATIONS
(POSITIVE FINDINGS)

ANIMAL NO.	CLINICAL OBSERVATIONS	DAY OF STUDY	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
4629 F	GROUP 3: 5713C-M (10%)																														
	FECES SMALL IN SIZE																		P	P	P										P
	DECREASED FOOD CONSUMPTION								P																						
4630 F	GROUP 3: 5713C-M (10%)																														
	FEW FECES																		P	P	P										
	FECES SMALL IN SIZE																			P	P										
	DECREASED FOOD CONSUMPTION								P	P																					
4646 F	GROUP 3: 5713C-M (10%)																														
	SALIVATION																				P										
	FECES SMALL IN SIZE								P						P	P															P
	SOFT STOOLS																												P	P	P
	ROUGH COAT									P	P	P	P	P	P	P	P												P	P	P
	FECAL STAIN																												P		P
	DISTENDED ABDOMEN																												P		
4648 F	GROUP 3: 5713C-M (10%)																														
	FEW FECES									P	P	P	P	P	P	P	P	P													
	FECES SMALL IN SIZE									P	P	P	P	P	P	P	P	P	P	P	P										P
	SOFT STOOLS															P	P														
	ROUGH COAT											P	P	P	P	P	P	P	P	P	P	P	P	P	P						
	EXTREMITIES APPEAR BLUE IN COLOR																	P	P	P	P	P	P	P	P						
	DISTENDED ABDOMEN																	P	P	P	P	P	P	P	P						
	DEHYDRATION																	P	P												
	DARK MATERIAL AROUND EYE(S)																	P													
	DECREASED FOOD CONSUMPTION								P	P	P				P	P	P														
	REMOVED FROM STUDY, BUT NOT EUTHANIZED AT THIS TIME[a]																														P

GRADE CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

[a] ANIMAL EUTHANIZED ON DAY 30; CLINICAL OBSERVATIONS NOTED AT THAT TIME INCLUDED FECES SMALL IN SIZE, SOFT STOOLS, ROUGH COAT, FECAL STAIN - SLIGHT, SKIN BLUE IN COLOR - EXTREMITIES, AND DISTENDED ABDOMEN - BACK BONE PROMINENT UPON HANDLING.

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL CLINICAL OBSERVATIONS
(POSITIVE FINDINGS)

ANIMAL NO.	CLINICAL OBSERVATIONS	DAY OF STUDY	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
4650 F	GROUP 3: 5713C-M (10%)																														
	FEW FECES																							P							
	FECES SMALL IN SIZE																					P	P								
	ROUGH COAT																							P							
4614 F	GROUP 4: 5713C-H																														
	FEW FECES																				P										
	FECES SMALL IN SIZE																					P									
	SOFT STOOLS																					P	P								
	FECAL STAIN																					P	P	P							
4621 F	GROUP 4: 5713C-H																														
	SOFT STOOLS																													P	
	URINE STAIN								P															P							
4622 F	GROUP 4: 5713C-H																														
	FECES SMALL IN SIZE																						P								
	DECREASED FOOD CONSUMPTION																									P					
4625 F	GROUP 4: 5713C-H																														
	SOFT STOOLS																				P	P	P								
	FECAL STAIN																					P	P	P							
4636 F	GROUP 4: 5713C-H																														
	FEW FECES																		P												
	FECES SMALL IN SIZE																		P												
	SOFT STOOLS																		P									P			

GRADE CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL CLINICAL OBSERVATIONS
(POSITIVE FINDINGS)

ANIMAL NO.	CLINICAL OBSERVATIONS	DAY OF STUDY	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
4638 F	GROUP 4: 5713C-H																														
	FEW FECES																				P	P									
	FECES SMALL IN SIZE																				P	P									
	SOFT STOOLS																				P										
	FECAL STAIN																		P												
4644 F	GROUP 4: 5713C-H																														
	FEW FECES																					P									
	FECES SMALL IN SIZE																					P									
	SOFT STOOLS																											P			
	URINE STAIN																						P								

GRADE CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

ANIMAL NO.	CLINICAL OBSERVATIONS	DAY OF STUDY	23	33	33	33	33	33	33	34	44	44	44	44	44	44	44
			90	01	23	45	56	78	89	01	23	45	67	89			
4606 F	GROUP 1: 5713C-I (10%)																
	FEW FECES					P											
	FECES SMALL IN SIZE					P											
	SOFT STOOLS									P							
	FECAL STAIN					P				P							
	DECREASED WATER CONSUMPTION					P											
	SCHEDULED EUTHANASIA														P		
4610 F	GROUP 1: 5713C-I (10%)																
	FEW FECES		P		P	P											
	FECES SMALL IN SIZE					P											
	DECREASED WATER CONSUMPTION					P											
	SCHEDULED EUTHANASIA														P		
4619 F	GROUP 1: 5713C-I (10%)																
	FECES SMALL IN SIZE					P											
	FECAL STAIN					P									P		
	SCHEDULED EUTHANASIA														P		
4626 F	GROUP 1: 5713C-I (10%)																
	URINE STAIN					P											
	FECAL STAIN														P		
	SCHEDULED EUTHANASIA														P		
4627 F	GROUP 1: 5713C-I (10%)																
	FEW FECES				P	P											
	FECES SMALL IN SIZE				P	P											
	DECREASED WATER CONSUMPTION					P											
	SCHEDULED EUTHANASIA														P		

GRADE CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL CLINICAL OBSERVATIONS
(POSITIVE FINDINGS)

ANIMAL NO.	CLINICAL OBSERVATIONS	DAY OF STUDY 2 3 3 3 3 3 3 3 3 3 4 4 4 4 4 4 4 4 4 4 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9
4633 F	GROUP 1: 5713C-I (10%)	
	FEW FECES	P P
	FECES SMALL IN SIZE	P P
	FECAL STAIN	P P
	DECREASED FOOD CONSUMPTION	P P
	SCHEDULED EUTHANASIA	P
4635 F	GROUP 1: 5713C-I (10%)	
	FECES SMALL IN SIZE	P
	SCHEDULED EUTHANASIA	P
4642 F	GROUP 1: 5713C-I (10%)	
	FEW FECES	P
	FECES SMALL IN SIZE	P
	SOFT STOOLS	P
	DECREASED WATER CONSUMPTION	P
	SCHEDULED EUTHANASIA	P
4643 F	GROUP 1: 5713C-I (10%)	
	FEW FECES	P
	URINE STAIN	P
	FECAL STAIN	P
	SCHEDULED EUTHANASIA	P
4649 F	GROUP 1: 5713C-I (10%)	
	URINE STAIN	P
	SCHEDULED EUTHANASIA	P

RADE CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL CLINICAL OBSERVATIONS
(POSITIVE FINDINGS)

ANIMAL NO.	CLINICAL OBSERVATIONS	DAY OF STUDY	2 3 3 3 3 3 3 3 3 3 4 4 4 4 4 4 4 4 4 4 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9
4602 F	GROUP 2: 5713C-K (10%)		
	SCHEDULED EUTHANASIA		P
4608 F	GROUP 2: 5713C-K (10%)		
	FEW FECES		P P P P P
	FECES SMALL IN SIZE		P P P
	SOFT STOOLS		P P
	URINE STAIN		P P
	FECAL STAIN		P P
	DECREASED FOOD CONSUMPTION		P P P P
	DECREASED WATER CONSUMPTION		P P P P
	SCHEDULED EUTHANASIA		P
4609 F	GROUP 2: 5713C-K (10%)		
	SOFT STOOLS		P
	SCHEDULED EUTHANASIA		P
4617 F	GROUP 2: 5713C-K (10%)		
	ROUGH COAT		P P P
	HAIRLOSS		P
	SCHEDULED EUTHANASIA		P
4620 F	GROUP 2: 5713C-K (10%)		
	FEW FECES		P P P P P P P
	FECES SMALL IN SIZE		P P P P P P P P P P P P P P P P P P P P
	SOFT STOOLS		P
	URINE STAIN		P P P P P P
	ROUGH COAT		P P P P P
	FECAL STAIN		P

GRADE CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

ANIMAL NO.	CLINICAL OBSERVATIONS	DAY OF STUDY	2 9	3 0	3 1	3 2	3 3	3 4	3 5	3 6	3 7	3 8	3 9	4 0	4 1	4 2	4 3	4 4	4 5	4 6	4 7	4 8	4 9
4620 F	GROUP 2: 5713C-K (10%) (CONTINUED)																						
	EXTREMITIES APPEAR BLUE IN COLOR																P	P	P	P	P	P	
	DISTENDED ABDOMEN															P	P	P	P	P	P	P	
	DECREASED FOOD CONSUMPTION				P	P												P	P	P	P		
	DECREASED WATER CONSUMPTION							P		P	P	P	P	P	P		P	P	P	P	P	P	
	SCHEDULED EUTHANASIA																					P	
4632 F	GROUP 2: 5713C-K (10%)																						
	FECES SMALL IN SIZE		P							P	P	P	P	P	P	P	P	P	P		P		
	ROUGH COAT							P						P								P	
	DISTENDED ABDOMEN																P	P	P	P	P	P	
	DECREASED FOOD CONSUMPTION																P	P	P	P	P		
	DECREASED WATER CONSUMPTION										P	P	P					P	P		P	P	
	SCHEDULED EUTHANASIA																					P	
4639 F	GROUP 2: 5713C-K (10%)																						
	FEW FECES		P	P	P	P				P	P												
	FECES SMALL IN SIZE		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P		
	ROUGH COAT										P	P	P	P		P	P	P	P	P	P		
	EXTREMITIES APPEAR BLUE IN COLOR																			P	P	P	
	DISTENDED ABDOMEN																P	P	P	P	P	P	
	DECREASED FOOD CONSUMPTION				P	P				P								P	P	P			
	DECREASED WATER CONSUMPTION									P	P	P							P				
	SCHEDULED EUTHANASIA																					P	

GRADE CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL CLINICAL OBSERVATIONS
(POSITIVE FINDINGS)

ANIMAL NO.	CLINICAL OBSERVATIONS	DAY OF STUDY 23	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49
4641 F	GROUP 2: 5713C-K (10%)																					
	FECES SMALL IN SIZE							P						P	P							
	URINE STAIN							P						P						P		
	DECREASED WATER CONSUMPTION							P														
	SCHEDULED EUTHANASIA																			P		
4645 F	GROUP 2: 5713C-K (10%)																					
	SCHEDULED EUTHANASIA																			P		
4612 F	GROUP 3: 5713C-M (10%)																					
	FEW FECES			P																		
	FECES SMALL IN SIZE			P																		
	DECREASED FOOD CONSUMPTION			P																		
	SCHEDULED EUTHANASIA																			P		
4623 F	GROUP 3: 5713C-M (10%)																					
	FECES SMALL IN SIZE													P	P							
	URINE STAIN																			P		
	SCHEDULED EUTHANASIA																			P		
4628 F	GROUP 3: 5713C-M (10%)																					
	FEW FECES							P														
	SCHEDULED EUTHANASIA																			P		

GRADE CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL CLINICAL OBSERVATIONS
(POSITIVE FINDINGS)

ANIMAL NO.	CLINICAL OBSERVATIONS	DAY OF STUDY	2 9	3 0	3 1	3 2	3 3	3 4	3 5	3 6	3 7	3 8	3 9	4 0	4 1	4 2	4 3	4 4	4 5	4 6	4 7	4 8	4 9
4629 F	GROUP 3: 5713C-H (10%)																						
	FECES SMALL IN SIZE				P	P			P														
	URINE STAIN							P														P	
	SCHEDULED EUTHANASIA																					P	
4630 F	GROUP 3: 5713C-H (10%)																						
	FEW FECES				P	P	P			P													
	FECES SMALL IN SIZE				P	P																	
	DECREASED FOOD CONSUMPTION				P	P																	
	DECREASED WATER CONSUMPTION																					P	
	SCHEDULED EUTHANASIA																					P	
4640 F	GROUP 3: 5713C-H (10%)																						
	SCHEDULED EUTHANASIA																					P	
4646 F	GROUP 3: 5713C-H (10%)																						
	FECES SMALL IN SIZE							P															
	SCHEDULED EUTHANASIA																					P	
4647 F	GROUP 3: 5713C-H (10%)																						
	FEW FECES														P								
	FECES SMALL IN SIZE														P	P							
	SCHEDULED EUTHANASIA																					P	

GRADE CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL CLINICAL OBSERVATIONS
(POSITIVE FINDINGS)

ANIMAL NO.	CLINICAL OBSERVATIONS	DAY OF STUDY	2 9	3 0	3 1	3 2	3 3	3 4	3 5	3 6	3 7	3 8	3 9	4 0	4 1	4 2	4 3	4 4	4 5	4 6	4 7	4 8	4 9
4650 F	GROUP 3: 5713C-H (10%)																						
	FEW FECES					P	P		P	P	P	P	P										
	FECES SMALL IN SIZE					P	P		P	P		P	P	P	P	P	P	P	P	P	P		
	SOFT STOOLS		P			P	P																
	ROUGH COAT								P													P	
	DECREASED FOOD CONSUMPTION																		P	P			
	DECREASED WATER CONSUMPTION								P	P	P	P	P	P						P			
	SCHEDULED EUTHANASIA																					P	
4601 F	GROUP 4: 5713C-H																						
	FEW FECES					P																	
	FECES SMALL IN SIZE					P	P																
	SOFT STOOLS		P																				
	FECAL STAIN								P														
	DECREASED FOOD CONSUMPTION					P																	
	SCHEDULED EUTHANASIA																					P	
4604 F	GROUP 4: 5713C-H							P	P														
	FECES SMALL IN SIZE								P														
	DECREASED WATER CONSUMPTION								P														
	SCHEDULED EUTHANASIA																					P	
4614 F	GROUP 4: 5713C-H																						
	FECES SMALL IN SIZE													P	P	P	P						
	FECAL STAIN								P													P	
	DECREASED FOOD CONSUMPTION													P									
	DECREASED WATER CONSUMPTION													P									
	SCHEDULED EUTHANASIA																					P	

GRADE CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

(06)

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL CLINICAL OBSERVATIONS
(POSITIVE FINDINGS)

ANIMAL NO.	CLINICAL OBSERVATIONS	DAY OF STUDY 29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49
4618 F	GROUP 4: 5713C-H																					
	SCHEDULED EUTHANASIA																					P
4621 F	GROUP 4: 5713C-H																					
	FEW FECES														P							
	FECES SMALL IN SIZE														P							
	SCHEDULED EUTHANASIA																					P
4622 F	GROUP 4: 5713C-H																					
	SOFT STOOLS		P	P																		
	SCHEDULED EUTHANASIA																					P
4625 F	GROUP 4: 5713C-H																					
	FECAL STAIN							P														
	SCHEDULED EUTHANASIA																					P
4636 F	GROUP 4: 5713C-H																					
	SCHEDULED EUTHANASIA																					P
4638 F	GROUP 4: 5713C-H																					
	URINE STAIN																					P
	FECAL STAIN							P														
	SCHEDULED EUTHANASIA																					P
4644 F	GROUP 4: 5713C-H																					
	FEW FECES					P																
	DECREASED FOOD CONSUMPTION					P																
	SCHEDULED EUTHANASIA																					P

GRADE CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX F

Individual Body Weight Data

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL BODY WEIGHT DATA (GRAMS)

DAY	0	7	14	17	21	24	28	35	38	42	49
GROUP 1: 5713C-I (10%)											
4606 F	315	352	391	389	400	421	442	372	399	469	453
4610 F	335	378	400	411	423	431	458	411	465	487	504
4619 F	333	374	396	393	419	435	451	455	477	501	524
4626 F	322	361	381	389	416	427	439	463	484	512	527
4627 F	319	370	408	418	436	457	468	435	504	522	518
4633 F	327	376	397	399	431	426	452	426	427	455	474
4635 F	340	386	408	428	451	466	484	488	492	509	537
4642 F	345	408	434	462	482	485	516	453	491	527	548
4643 F	345	395	428	455	483	494	508	525	526	554	607
4649 F	340	388	435	442	486	478	507	503	523	547	598
MEAN	332	379	408	419	443	452	473	453	479	508	529
S.D.	10.8	16.3	18.7	27.3	31.2	27.4	29.1	45.2	40.0	31.7	48.1
N	10	10	10	10	10	10	10	10	10	10	10

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL BODY WEIGHT DATA (GRAMS)

DAY	0	7	14	17	21	24	27 (FOUND DEAD)	28	35	38	42	49
GROUP 2: 5713C-K (10%)												
4602 F	344	392	403	401	399	429	-	461	448	497	515	518
4608 F	334	342	348	346	340	363	-	400	393	401	400	424
4609 F	320	334	347	332	354	385	-	400	411	448	476	471
4611 F	326	338	350	343	352	326	279	-	-	-	-	-
4617 F	343	330	330	336	352	381	-	421	448	444	453	434
4620 F	313	316	320	323	320	318	-	356	306	315	351	372
4632 F	336	334	338	334	344	354	-	369	379	375	400	390
4639 F	340	333	347	350	364	384	-	404	355	345	362	389
4641 F	328	336	312	332	341	382	-	403	434	445	453	466
4645 F	347	362	364	361	380	410	-	434	451	470	496	519
MEAN	333	342	346	346	355	373	-	405	403	416	434	443
S.D.	11.1	21.0	25.3	22.2	22.2	34.3		31.6	49.7	60.5	58.4	54.7
N	10	10	10	10	10	10		9	9	9	9	9

NOTE: THE MEAN IS NOT CALCULATED FOR ANIMALS FOUND DEAD.

DAY	0	7	14	17	21	24	28	35	38	42	49
GROUP 3: 5713C-M (10%)											
4612 F	326	336	366	359	370	395	416	424	453	459	487
4623 F	319	334	360	343	363	378	399	421	436	452	470
4628 F	316	324	340	332	352	377	393	403	410	430	454
4629 F	340	335	367	340	363	386	417	412	447	465	470
4630 F	334	338	351	340	349	385	412	413	403	421	426
4640 F	343	351	367	358	373	406	431	419	480	515[a]	517
4646 F	332	339	353	332	352	369	389	398	436	463	465
4647 F	342	352	349	356	382	418	441[b]	450	481	470	494
4648 F	347	348	367	358	340	322	321	-	-	-	-
4650 F	335	332	338	336	344	371	402	355	384	429	411
MEAN	333	339	356	345	359	381	402	411	437	456	466
S.D.	10.4	8.9	11.3	11.2	13.6	25.8	32.8	25.6	33.2	28.4	32.8
N	10	10	10	10	10	10	10	9	9	9	9

[a] ADDITIONAL WEIGHT TAKEN ON DAY 43 (501 G) TO ENSURE WEIGHT COLLECTED ON DAY 42 WAS NOT ABBERANT.
[b] ANIMAL WAS REMOVED FROM STUDY ON DAY 28, BUT WAS NOT EUTHANIZED UNTIL DAY 30 AT WHICH TIME THE BODY WEIGHT WAS 345 G.

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL BODY WEIGHT DATA (GRAMS)

DAY	0	7	14	17	21	24	28	35	38	42	49
GROUP 4: 5713C-H											
4601 F	326	355	406	405	435	452	469	496	502	521	526
4604 F	344	372	420	420	454	463	490	428	500	552	563
4614 F	328	351	381	397	412	435	445	480	498	529	499
4618 F	343	375	428	441	463	489	524	548	573	590	596
4621 F	339	389	434	452	476	493	496	543	557	573	586
4622 F	318	353	379	392	413	417	440	456	483	489	499
4625 F	347	389	439	465	464	507	545	575	582	610	628
4636 F	334	373	412	443	482	473	500	520	566	562	594
4638 F	334	366	410	414	443	462	489	509	536	544	550
4644 F	319	340	373	382	394	415	437	450	455	478	468
MEAN	333	366	408	421	444	461	484	501	525	545	551
S.D.	10.3	16.4	23.6	27.9	29.6	31.4	36.0	47.5	43.4	41.9	51.7
N	10	10	10	10	10	10	10	10	10	10	10

APPENDIX G

Individual Body Weight Gain Data

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL BODY WEIGHT GAIN DATA (GRAMS)

DAY	0-7	7-14	14-17	17-21	21-24	24-28	28-35	35-38	38-42	42-49
GROUP 1: 5713C-I (10%)										
4606 F	37	39	-2	11	21	21	-70	27	70	-16
4610 F	43	22	11	12	8	27	-47	54	22	17
4619 F	41	22	-3	26	16	16	4	22	24	23
4626 F	39	20	8	27	11	12	24	21	28	15
4627 F	51	38	10	18	21	11	-33	69	18	-4
4633 F	49	21	2	32	-5	26	-26	1	28	19
4635 F	46	22	20	23	15	18	4	4	17	28
4642 F	63	26	28	20	3	31	-63	38	36	21
4643 F	50	33	27	28	11	14	17	1	28	53
4649 F	48	47	7	44	-8	29	-4	20	24	51
MEAN	47	29	11	24	9	21	-19	26	30	21
S.D.	7.5	9.6	11.0	9.8	10.0	7.4	33.3	22.6	15.3	21.2
N	10	10	10	10	10	10	10	10	10	10

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL BODY WEIGHT GAIN DATA (GRAMS)

DAY	0-7	7-14	14-17	17-21	21-24	24-28	28-35	35-38	38-42	42-49
GROUP 2: 5713C-K (10%)										
4602 F	48	11	-2	-2	30	32	-13	49	18	3
4608 F	8	6	-2	-6	23	37	-7	8	-1	24
4609 F	14	13	-15	22	31	15	11	37	28	-5
4611 F	12	12	-7	9	-26	-	-	-	-	-
4617 F	-13	0	6	16	29	40	27	-4	9	-19
4620 F	3	4	3	-3	-2	38	-50	9	36	21
4632 F	-2	4	-4	10	10	15	10	-4	25	-10
4639 F	-7	14	3	14	20	20	-49	-10	17	27
4641 F	8	-24	20	9	41	21	31	11	8	13
4645 F	15	2	-3	19	30	24	17	19	26	23
MEAN	9	4	0	9	19	27	-3	13	18	9
S.D.	16.6	11.1	9.2	9.6	19.8	10.0	30.1	19.6	11.6	16.9
N	10	10	10	10	10	9	9	9	9	9

DAY	0-7	7-14	14-17	17-21	21-24	24-28	28-35	35-38	38-42	42-49
GROUP 3: 5713C-H (10%)										
4612 F	10	30	-7	11	25	21	8	29	6	28
4623 F	15	26	-17	20	15	21	22	15	16	18
4628 F	8	16	-8	20	25	16	10	7	20	24
4629 F	-5	32	-27	23	23	31	-5	35	18	5
4630 F	4	13	-11	9	36	27	1	-10	18	5
4640 F	8	16	-9	15	33	25	-12	61	35	2
4646 F	7	14	-21	20	17	20	9	38	27	2
4647 F	10	-3	7	26	36	23	9	31	-11	24
4648 F	1	19	-9	-18	-18	-1	-	-	-	-
4650 F	-3	6	-2	8	27	31	-47	29	45	-18
MEAN	6	17	-10	13	22	21	-1	26	19	10
S.D.	6.2	10.7	9.6	12.6	15.7	9.2	20.0	20.2	16.1	14.8
N	10	10	10	10	10	10	9	9	9	9

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL BODY WEIGHT GAIN DATA (GRAMS)

DAY	0-7	7-14	14-17	17-21	21-24	24-28	28-35	35-38	38-42	42-49
GROUP 4: 5713C-H										
4601 F	29	51	-1	30	17	17	27	6	19	5
4604 F	28	48	0	34	9	27	-62	72	52	11
4614 F	23	30	16	15	23	10	35	18	31	-30
4618 F	32	53	13	22	26	35	24	25	17	6
4621 F	50	45	18	24	17	3	47	14	16	13
4622 F	35	26	13	21	4	23	16	27	6	10
4625 F	42	50	26	-1	43	38	30	7	28	18
4636 F	39	39	31	39	-9	27	20	46	-4	32
4638 F	32	44	4	29	19	27	20	27	8	6
4644 F	21	33	9	12	21	22	13	5	23	-10
MEAN	33	42	13	23	17	23	17	25	20	6
S.D.	8.8	9.5	10.5	11.7	13.8	10.7	29.5	20.8	15.5	16.5
N	10	10	10	10	10	10	10	10	10	10

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APPENDIX H

Individual Hematology Data

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL HEMATOLOGY DATA

DAY 21

ANIMAL NO.	ERYTHRO-CYTES 10*6/CMM	HEMO-GLOBIN G/DL	HEMA-TOCRIT %	MEAN CORPUS VOLUME FL	MEAN CORPUS HMGLBN PG	MEAN CORPUS HEMO-CON G/DL	PLATE-LETS 10*3/CMM	SEGD NEUTRO-PHILS % WBC	LYMPHO-CYTES % WBC	MONO-CYTES % WBC	BASO-PHILS % WBC	EOSINO-PHILS % WBC
GROUP 2: 5713C-K (10%)												
4602 F	4.80	12.6	39.2	81.6	26.2	32.2	350	54	44	2	0	0
4608 F	5.00	13.2	40.0	79.9	26.4	33.0	310	15	83	1	0	1
4609 F	4.80	13.5	41.2	85.8	28.1	32.8	640	42	57	1	0	0
4611 F	5.30	13.9	41.2	77.8	26.2	33.7	540	67	30	3	0	0
4617 F	4.90	13.1	40.3	82.2	26.7	32.5	320	72	26	2	0	0
4620 F	4.90	13.1	40.3	82.3	26.7	32.5	580	61	36	3	0	0
4632 F	5.80	15.0	46.1	79.5	25.9	32.5	540	41	57	2	0	0
4639 F	5.20	13.9	42.5	81.7	26.7	32.7	540	57	43	0	0	0
4641 F	4.80	13.2	39.4	82.1	27.5	33.5	580	56	43	1	0	0
4645 F	4.80	12.8	39.1	81.5	26.7	32.7	530	82	17	1	0	0
MEAN	5.03	13.4	40.9	81.4	26.7	32.8	493	55	44	2	0	0
S.D.	0.323	0.69	2.10	2.11	0.65	0.47	119.5	18.8	18.8	1.0	0.0	0.3
N	10	10	10	10	10	10	10	10	10	10	10	10

DAY 21

ANIMAL NO.	NON-SEGD NEUTRO-PHILS % WBC	NUCLE-ATED RBC'S % WBC	RETICU-LOCYTES % RBC	NON-SEGD LEUKO-CYTES 10*3/CMM
GROUP 2: 5713C-K (10%)				
4602 F	0	0	0.6	10.90
4608 F	0	0	1.7	5.10
4609 F	0	0	3.2	10.60
4611 F	0	0	1.6	11.40
4617 F	0	0	1.5	23.70
4620 F	0	0	0.7	14.50
4632 F	0	0	1.1	9.20
4639 F	0	0	1.3	12.30
4641 F	0	0	1.9	7.60
4645 F	0	0	1.9	14.70
MEAN	0	0	1.6	12.00
S.D.	0.0	0.0	0.74	5.043
N	10	10	10	10

DAY 21

ANIMAL NO.	ERYTHRO-CYTES 10*6/CMM	HEMO-GLOBIN G/DL	HEMA-TOCRIT %	MEAN CORPUS VOLUME FL	MEAN CORPUS HMGLBN PG	MEAN CORPUS HEMO-CON G/DL	PLATE-LETS 10*3/CMM	SEGD NEUTRO-PHILS % WBC	LYMPHO-CYTES % WBC	MONO-CYTES % WBC	BASO-PHILS % WBC	EOSINO-PHILS % WBC
GROUP 3: 5713C-M (10%)												
4612 F	5.10	14.4	42.3	83.0	28.2	34.0	350	29	69	1	0	1
4623 F	4.70	12.7	37.6	79.9	27.0	33.8	590	42	53	4	0	1
4628 F	4.20	11.6	34.5	82.2	27.6	33.6	380	68	28	3	0	1
4629 F	4.40	11.7	35.2	80.1	26.6	33.2	430	68	30	2	0	0
4630 F	5.10	14.0	42.4	83.2	27.5	33.0	490	68	31	1	0	0
4640 F	4.80	12.8	39.1	81.4	26.7	32.8	410	69	29	2	0	0
4646 F	4.80	13.2	39.2	81.7	27.5	33.7	600	64	33	1	0	2
4647 F	4.70	12.9	39.2	83.4	27.4	32.9	550	93	7	0	0	0
4648 F	5.20	14.0	42.8	82.3	26.9	32.7	510	57	41	2	0	0
4650 F	4.70	12.4	37.7	80.3	26.4	32.9	390	62	37	1	0	0
MEAN	4.77	13.0	39.0	81.8	27.2	33.3	470	62	36	2	0	1
S.D.	0.313	0.95	2.89	1.30	0.55	0.47	90.6	17.1	16.4	1.2	0.0	0.7
N	10	10	10	10	10	10	10	10	10	10	10	10

DAY 21

ANIMAL NO.	NON-SEGD NEUTRO-PHILS % WBC	NUCLE-ATED RBC'S % WBC	RETICU-LOCYTES % RBC	NON-SEGD LEUKO-CYTES 10*3/CMM
GROUP 3: 5713C-M (10%)				
4612 F	0	0	2.4	9.40
4623 F	0	0	0.9	6.80
4628 F	0	0	0.9	19.40
4629 F	0	0	1.9	20.50
4630 F	0	0	0.6	10.00
4640 F	0	0	0.8	12.90
4646 F	0	0	1.7	13.40
4647 F	0	0	1.2	26.90
4648 F	0	0	0.8	10.10
4650 F	0	0	1.2	12.80
MEAN	0	0	1.2	14.22
S.D.	0.0	0.0	0.58	6.187
N	10	10	10	10

DAY 21

ANIMAL NO.	ERYTHRO-CYTES 10*6/CMM	HEMO-GLOBIN G/DL	HEMA-TOCRIT %	MEAN CORPUS VOLUME FL	MEAN CORPUS HMGLBN PG	MEAN CORPUS HEMO-CON G/DL	PLATE-LETS 10*3/CMM	SEGD NEUTRO-PHILS % WBC	LYMPHO-CYTES % WBC	MONO-CYTES % WBC	BASO-PHILS % WBC	EOSINO-PHILS % WBC
GROUP 4: 5713C-H												
4601 F	5.40	15.2	46.1	85.4	28.1	33.0	600	21	77	1	0	1
4604 F	4.80	13.3	41.1	85.6	27.7	32.4	690	21	78	0	0	1
4614 F	5.10	13.7	41.5	81.3	26.9	33.0	630	39	61	0	0	0
4618 F	5.00	15.1	45.0	90.1	30.2	33.5	540	41	56	0	1	2
4621 F	4.90	13.9	42.5	86.7	28.4	32.7	250	23	74	2	0	1
4622 F	5.10	14.2	42.3	83.0	27.8	33.5	610	41	56	0	0	3
4625 F	4.90	14.2	42.5	86.7	29.0	33.4	530	44	56	0	0	0
4636 F	4.90	13.9	42.1	86.0	28.4	33.0	590	30	68	1	0	1
4638 F	4.90	13.8	41.7	85.1	28.2	33.1	510	21	76	0	0	3
4644 F	5.50	15.2	45.9	83.5	27.6	33.1	610	17	78	1	0	4
MEAN	5.05	14.3	43.1	85.3	28.2	33.1	556	30	68	1	0	2
S.D.	0.232	0.68	1.87	2.41	0.89	0.35	119.7	10.4	9.8	0.7	0.3	1.3
N	10	10	10	10	10	10	10	10	10	10	10	10

DAY 21

ANIMAL NO.	NON-SEGD NEUTRO-PHILS % WBC	NUCLE-ATED RBC'S % WBC	RETICU-LOCYTES % RBC	NON-SEGD LEUKO-CYTES 10*3/CMM
GROUP 4: 5713C-H				
4601 F	0	0	1.1	4.60
4604 F	0	0	1.4	7.10
4614 F	0	0	2.0	6.20
4618 F	0	0	3.2	8.10
4621 F	0	0	2.5	5.90
4622 F	0	0	1.0	7.00
4625 F	0	0	1.9	6.70
4636 F	0	0	1.5	5.30
4638 F	0	0	1.1	6.80
4644 F	0	0	1.9	6.70
MEAN	0	0	1.8	6.44
S.D.	0.0	0.0	0.70	0.989
N	10	10	10	10

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL HEMATOLOGY DATA

DAY 21

ANIMAL NO.	ERYTHRO-CYTES 10*6/CMM	HEMO-GLOBIN G/DL	HEMA-TOCRIT %	MEAN CORPUS VOLUME FL	MEAN CORPUS HMGLBN PG	MEAN CORPUS HEMO-CON G/DL	PLATE-LETS 10*3/CMM	SEGD NEUTRO-PHILS % WBC	LYMPHO-CYTES % WBC	MONO-CYTES % WBC	BASO-PHILS % WBC	EOSINO-PHILS % WBC
STOCK												
4603 F	5.00	14.1	42.5	85.1	28.2	33.1	430	28	70	1	0	1
4605 F	5.10	14.7	43.3	85.0	28.8	33.9	540	29	68	0	0	3
4607 F	4.80	14.1	42.4	88.4	29.4	33.2	390	21	78	1	0	0
4613 F	5.50	15.0	45.5	82.7	27.3	33.0	510	36	62	1	0	1
4615 F	5.40	14.7	44.8	82.9	27.2	32.8	540	31	67	0	0	2
MEAN	5.16	14.5	43.7	84.8	28.2	33.2	482	29	69	1	0	1
S.D.	0.288	0.40	1.39	2.30	0.95	0.42	68.3	5.4	5.8	0.5	0.0	1.1
N	5	5	5	5	5	5	5	5	5	5	5	5

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL HEMATOLOGY DATA

DAY 21

ANIMAL NO.	NON-SEGD NEUTRO-PHILS % WBC	NUCLE-ATED RBC'S % WBC	RETICU-LOCYTES % RBC	NON-SEGD LEUKO-CYTES 10*3/CMM
STOCK				
4603 F	0	0	0.8	5.10
4605 F	0	0	1.2	6.50
4607 F	0	0	0.9	6.10
4613 F	0	0	2.6	5.30
4615 F	0	0	2.5	4.30
MEAN	0	0	1.6	5.46
S.D.	0.0	0.0	0.88	0.865
N	5	5	5	5

APPENDIX I

Individual RBC Morphology Data

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL RBC MORPHOLOGY DATA

DAY 21

ANIMAL NO.	RBC MOR PHOLOGY	MACRO- CYTES	MICRO- CYTES	POIKILO- CYTES	SPHERO- CYTES	OVALO- CYTES	HYPO- CHROMIC	POLY- CHROM- ASIA	MISCELLANEOUS
GROUP 1: 5713C-I (10%)									
4606	F N								
4610	F N								
4619	F N								
4626	F N								
4627	F N								
4633	F N								
4635	F N								
4642	F N								
4643	F N								
4649	F N								

N = NORMAL 1+ = SLIGHT 2+ = MODERATE 3+ = MODERATE TO MARKED 4+ = MARKED

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL RBC MORPHOLOGY DATA

DAY 21

ANIMAL NO.	RBC MOR PHOLOGY	MACRO- CYTES	MICRO- CYTES	POIKILO- CYTES	SPHERO- CYTES	OVALO- CYTES	HYPO- CHROMIC	POLY- CHROM- ASIA	MISCELLANEOUS
GROUP 2: 5713C-K (10%)									
4602	F N								
4608	F N								
4609	F N								
4611	F N								
4617	F N								
4620	F N								
4632	F N								
4639	F N								
4641	F N								
4645	F N								

N = NORMAL 1+ = SLIGHT 2+ = MODERATE 3+ = MODERATE TO MARKED 4+ = MARKED

DAY 21

ANIMAL NO.	RBC MOR PHOLOGY	MACRO- CYTES	MICRO- CYTES	POIKILO- CYTES	SPHERO- CYTES	OVALO- CYTES	HYPO- CHROMIC	POLY- CHROM- ASIA	MISCELLANEOUS
GROUP 3: 5713C-H (10%)									
4612	F	N							
4623	F	N							
4628	F	N							
4629	F	N							
4630	F	N							
4640	F	N							
4646	F	N							
4647	F	N							
4648	F	N							
4650	F	N							

N = NORMAL 1+ = SLIGHT 2+ = MODERATE 3+ = MODERATE TO MARKED 4+ = MARKED

APPENDIX J

Individual Biochemistry Data

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL BIOCHEMISTRY DATA

DAY 21

ANIMAL NO.	ALK PHOS 'TASE IU/L	UREA NITROGEN MG/DL	CALCIUM MG/DL	CHLO-RIDE MMOL/L	CHOLE-STEROL MG/DL	CREA-TININE MG/DL	AST IU/L	POTAS-SIUM MMOL/L	SODIUM MMOL/L	PO4 PHOS-PHORUS MG/DL	TOTAL BILI-RUBIN MG/DL	TOTAL PROTEIN G/DL
GROUP 1: 5713C-I (10%)												
4606 F	203	20	11.22	112	44	0.35	39	4.81	143	5.8	0.50	4.62
4610 F	156	17	10.62	109	43	0.37	70	5.10	141	5.4	0.41	4.70
4619 F	142	18	10.98	114	68	0.39	76	4.45	141	6.5	0.48	4.96
4626 F	185	18	10.84	115	53	0.34	97	5.29	137	6.6	0.67	4.68
4627 F	155	21	11.22	116	58	0.26	54	5.30	140	6.7	0.57	4.92
4633 F	159	20	9.96	111	48	0.36	48	4.78	140	6.6	0.41	4.97
4635 F	259	21	11.16	113	51	0.40	46	5.08	138	6.6	0.43	4.30
4642 F	189	18	11.63	114	46	0.40	194	5.32	142	7.5	0.55	4.86
4643 F	185	21	11.98	115	48	0.49	37	5.94	141	6.8	0.51	4.78
4649 F	174	20	11.27	113	42	0.51	57	5.54	138	7.0	0.50	4.53
MEAN	181	19	11.09	113	50	0.39	72	5.16	140	6.6	0.50	4.73
S.D.	33.4	1.5	0.551	2.2	7.9	0.071	46.7	0.423	1.8	0.59	0.080	0.212
N	10	10	10	10	10	10	10	10	10	10	10	10

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL BIOCHEMISTRY DATA

DAY 21

ANIMAL NO.	A/G RATIO	GLUCOSE MG/DL	GLOBULIN G/DL	ALT IU/L	ALBUMIN G/DL
GROUP 1: 5713C-I (10%)					
4606 F	1.16	126	2.14	28	2.48
4610 F	0.97	122	2.39	27	2.31
4619 F	1.00	135	2.48	36	2.48
4626 F	1.03	172	2.31	39	2.37
4627 F	1.11	168	2.33	34	2.59
4633 F	1.11	147	2.35	31	2.61
4635 F	0.98	202	2.18	32	2.13
4642 F	1.13	138	2.28	58	2.57
4643 F	1.15	142	2.22	28	2.56
4649 F	1.16	137	2.10	28	2.43
MEAN	1.08	149	2.28	34	2.45
S.D.	0.077	24.7	0.119	9.3	0.151
N	10	10	10	10	10

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL BIOCHEMISTRY DATA

DAY 21

ANIMAL NO.	ALK PHOS 'TASE IU/L	UREA NITROGEN MG/DL	CALCIUM MG/DL	CHLO-RIDE MMOL/L	CHOLE-STEROL MG/DL	CREA-TININE MG/DL	AST IU/L	POTAS-SIUM MMOL/L	SODIUM MMOL/L	PO4 PHOS-PHORUS MG/DL	TOTAL BILI-RUBIN MG/DL	TOTAL PROTEIN G/DL
GROUP 2: 5713C-K (10%)												
4602 F	144	21	11.68	109	63	0.41	73	5.37	139	6.9	0.72	4.86
4608 F	84	17	10.63	106	22	0.46	133	5.12	137	4.6	0.46	4.16
4609 F	151	19	11.43	113	36	0.26	67	5.34	143	5.4	0.62	4.26
4611 F	131	21	11.45	111	49	0.40	88	5.59	141	5.6	0.71	4.43
4617 F	113	18	11.72	113	26	0.34	61	4.83	143	5.4	0.50	4.57
4620 F	103	20	11.26	112	28	0.67	100	4.76	142	5.5	0.26	4.79
4632 F	124	23	10.85	115	45	0.41	59	4.75	144	5.0	0.57	4.24
4639 F	142	20	10.69	110	42	0.37	101	4.64	138	6.0	0.48	3.99
4641 F	114	16	10.97	107	37	0.32	90	4.44	140	6.2	0.49	4.63
4645 F	123	19	10.92	107	33	0.39	64	4.75	136	6.1	0.56	5.28
MEAN	123	19	11.16	110	38	0.41	84	4.96	140	5.7	0.54	4.52
S.D.	20.4	2.0	0.401	3.1	12.3	0.110	23.4	0.373	2.8	0.64	0.135	0.385
N	10	10	10	10	10	10	10	10	10	10	10	10

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL BIOCHEMISTRY DATA

DAY 21

ANIMAL NO.	A/G RATIO	GLUCOSE MG/DL	GLOBULIN G/DL	ALT IU/L	ALBUMIN G/DL
GROUP 2: 5713C-K (10%)					
4602 F	0.98	145	2.46	83	2.41
4608 F	1.18	164	1.91	138	2.26
4609 F	1.06	147	2.07	46	2.19
4611 F	1.14	138	2.07	50	2.36
4617 F	1.04	145	2.24	41	2.32
4620 F	1.10	156	2.28	137	2.51
4632 F	1.06	143	2.05	36	2.18
4639 F	1.12	131	1.88	46	2.11
4641 F	0.88	138	2.46	53	2.16
4645 F	0.88	157	2.81	53	2.47
MEAN	1.04	146	2.22	68	2.30
S.D.	0.104	9.9	0.288	38.6	0.138
N	10	10	10	10	10

DAY 21

ANIMAL NO.	ALK PHOS 'TASE IU/L	UREA NITROGEN MG/DL	CALCIUM MG/DL	CHLO-RIDE MMOL/L	CHOLE-STEROL MG/DL	CREA-TININE MG/DL	AST IU/L	POTAS-SIUM MMOL/L	SODIUM MMOL/L	PO4 PHOS-PHORUS MG/DL	TOTAL BILI-RUBIN MG/DL	TOTAL PROTEIN G/DL
GROUP 3: 5713C-M (10%)												
4612 F	123	12	10.91	110	34	0.38	52	3.71	140	5.7	0.64	4.27
4623 F	102	12	10.91	107	29	0.33	55	4.89	140	5.6	0.57	4.06
4628 F	105	11	11.21	105	29	0.42	103	4.60	136	6.0	0.59	4.09
4629 F	136	11	10.24	106	29	0.26	84	4.81	135	5.8	0.64	3.69
4630 F	143	11	10.81	109	26	0.29	88	4.85	138	5.3	0.60	4.12
4640 F	142	8	10.39	109	35	0.44	68	4.64	138	5.2	0.49	4.28
4646 F	112	13	10.66	108	40	0.38	76	4.45	139	5.0	0.53	3.79
4647 F	183	11	10.37	105	29	0.50	114	5.33	139	6.2	0.56	3.65
4648 F	81	18	11.02	111	54	0.39	113	5.32	136	6.0	0.56	4.45
4650 F	114	14	10.67	111	35	0.38	139	4.49	138	4.4	0.44	3.98
MEAN	124	12	10.72	108	34	0.38	89	4.71	138	5.5	0.56	4.04
S.D.	28.4	2.6	0.313	2.2	8.1	0.072	28.1	0.466	1.8	0.55	0.063	0.263
N	10	10	10	10	10	10	10	10	10	10	10	10

DAY 21

ANIMAL NO.	A/G RATIO	GLUCOSE MG/DL	GLOBULIN G/DL	ALT IU/L	ALBUMIN G/DL
GROUP 3: 5713C-M (10%)					
4612 F	1.03	126	2.10	37	2.16
4623 F	1.18	137	1.86	42	2.20
4628 F	1.10	171	1.95	72	2.14
4629 F	1.11	154	1.75	50	1.94
4630 F	1.16	130	1.91	72	2.21
4640 F	0.96	164	2.19	52	2.09
4646 F	1.01	139	1.88	43	1.90
4647 F	1.03	146	1.80	52	1.85
4648 F	1.06	144	2.16	55	2.29
4650 F	1.12	157	1.88	88	2.10
MEAN	1.08	147	1.95	57	2.09
S.D.	0.071	14.7	0.150	16.2	0.145
N	10	10	10	10	10

DAY 21

ANIMAL NO.	ALK PHOS 'TASE IU/L	UREA NITROGEN MG/DL	CALCIUM MG/DL	CHLO-RIDE MMOL/L	CHOLE-STEROL MG/DL	CREA-TININE MG/DL	AST IU/L	POTAS-SIUM MMOL/L	SODIUM MMOL/L	PO4 PHOS-PHORUS MG/DL	TOTAL BILI-RUBIN MG/DL	TOTAL PROTEIN G/DL
GROUP 4: 5713C-H												
4601 F	174	21	11.31	115	59	0.40	32	3.81	142	6.8	0.49	5.18
4604 F	145	20	10.72	115	50	0.38	50	5.25	138	7.5	0.53	4.94
4614 F	157	21	11.27	113	36	0.45	42	4.70	140	6.3	0.37	4.95
4618 F	156	21	11.51	114	54	0.42	51	5.23	142	7.2	0.48	5.34
4621 F	221	22	11.59	120	45	0.38	52	5.37	143	7.9	0.40	4.78
4622 F	228	20	11.18	113	33	0.37	91	5.78	140	6.8	0.45	4.75
4625 F	182	22	11.85	112	47	0.38	41	4.96	141	5.3	0.52	4.73
4636 F	220	20	11.50	112	51	0.32	45	6.06	141	8.0	0.62	4.82
4638 F	159	22	11.23	112	24	0.44	50	4.56	143	7.4	0.54	4.40
4644 F	160	20	11.69	112	55	0.40	86	5.40	142	7.4	0.25	5.07
MEAN	180	21	11.38	114	45	0.39	54	5.11	141	7.1	0.47	4.90
S.D.	31.3	0.9	0.318	2.5	11.1	0.038	19.2	0.643	1.6	0.80	0.105	0.264
N	10	10	10	10	10	10	10	10	10	10	10	10

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL BIOCHEMISTRY DATA

DAY 21

ANIMAL NO.	A/G RATIO	GLUCOSE MG/DL	GLOBULIN G/DL	ALT IU/L	ALBUMIN G/DL
GROUP 4: 5713C-H					
4601 F	1.06	159	2.52	28	2.67
4604 F	0.97	157	2.51	29	2.43
4614 F	1.03	135	2.44	35	2.51
4618 F	0.92	137	2.77	28	2.56
4621 F	1.15	145	2.23	30	2.56
4622 F	1.17	129	2.19	40	2.56
4625 F	1.14	174	2.21	32	2.52
4636 F	0.94	155	2.49	31	2.34
4638 F	0.99	152	2.20	43	2.19
4644 F	1.10	150	2.41	33	2.66
MEAN	1.05	149	2.40	33	2.50
S.D.	0.090	13.2	0.190	5.1	0.146
N	10	10	10	10	10

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL BIOCHEMISTRY DATA

DAY 21

ANIMAL NO.	ALK PHOS 'TASE IU/L	UREA NITROGEN MG/DL	CALCIUM MG/DL	CHLO-RIDE MMOL/L	CHOLE-STEROL MG/DL	CREA-TININE MG/DL	AST IU/L	POTAS-SIUM MMOL/L	SODIUM MMOL/L	PO4 PHOS-PHORUS MG/DL	TOTAL BILI-RUBIN MG/DL	TOTAL PROTEIN G/DL
STOCK												
4603 F	213	18	11.10	104	41	0.43	39	4.80	136	5.8	0.36	4.37
4605 F	173	19	11.67	112	50	0.51	42	5.11	141	6.4	0.48	4.92
4607 F	172	19	11.10	110	70	0.32	46	5.00	137	6.4	0.59	4.55
4613 F	212	22	11.40	115	60	0.30	76	4.44	140	6.0	0.39	4.99
4615 F	143	18	11.39	113	50	0.35	44	5.11	140	7.4	0.60	4.63
MEAN	183	19	11.33	111	54	0.38	49	4.89	139	6.4	0.48	4.69
S.D.	29.8	1.6	0.240	4.2	11.1	0.087	15.1	0.283	2.2	0.62	0.111	0.259
N	5	5	5	5	5	5	5	5	5	5	5	5

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL BIOCHEMISTRY DATA

DAY 21

ANIMAL NO.	A/G RATIO	GLUCOSE MG/DL	GLOBULIN G/DL	ALT IU/L	ALBUMIN G/DL
STOCK					
4603 F	1.22	201	1.97	29	2.40
4605 F	1.07	155	2.38	26	2.54
4607 F	1.13	148	2.14	29	2.41
4613 F	0.91	201	2.61	31	2.38
4615 F	1.08	139	2.23	29	2.40
MEAN	1.08	169	2.27	29	2.43
S.D.	0.112	29.9	0.243	1.8	0.065
N	5	5	5	5	5

APPENDIX K

Individual Gross Necropsy Observations

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL GROSS NECROPSY OBSERVATIONS

				GRADE
ANIMAL NO. 4611	GROUP: 2	FEMALE	FOUND DEAD	
		WHOLE BODY	GROSS: BODY FAT DEPLETION	P
		LUNGS	GROSS: DARK RED	P
			RIGHT APICAL LOBE	
		STOMACH	GROSS: DISTENDED	P
			WITH GAS AND GREEN FLUID	
ANIMAL NO. 4648	GROUP: 3	FEMALE	EUTHANIZED MORIBUND	
		ABDOMINAL CAVITY	GROSS: FLUID CONTENTS	P
			APPROXIMATELY 2.0 ML OF SLIGHTLY CLOUDY CLEAR FLUID	
		TRACHEA	GROSS: CONTENT ABNORMAL	P
			ENTIRE LENGTH, WHITE FOAM	
		LUNGS	GROSS: MOTTLED	P
			ALL LOBES, DARK RED AND RED	
		WHOLE BODY	GROSS: BODY FAT DEPLETION	P
		STOMACH	GROSS: DISTENDED	P
			WITH GAS AND SMALL AMOUNT OF INGESTA	
		SMALL INTESTINE	GROSS: DISTENDED	P
			ENTIRE TRACT, WITH GAS AND WATERY DIGESTA	

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT

APPENDIX L

Added Stock Animals

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL CLINICAL OBSERVATIONS
(POSITIVE FINDINGS)

ANIMAL NO.	CLINICAL OBSERVATIONS	DAY OF STUDY 3 3 3 3 3 4 4 4 4 4 4 4 4 4 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9
4603 F	GROUP 5: 5713C-I (10%) FEW FECES SCHEDULED EUTHANASIA	P P P
4605 F	GROUP 5: 5713C-I (10%) FEW FECES FECES SMALL IN SIZE SCHEDULED EUTHANASIA	P P P P P P P P
4607 F	GROUP 5: 5713C-I (10%) SOFT STOOLS SCHEDULED EUTHANASIA	P P
4615 F	GROUP 5: 5713C-I (10%) FEW FECES SCHEDULED EUTHANASIA	P P P
4616 F	GROUP 6: 5713C-H SCHEDULED EUTHANASIA	 P
4624 F	GROUP 6: 5713C-H SCHEDULED EUTHANASIA	 P
4631 F	GROUP 6: 5713C-H FEW FECES FECES SMALL IN SIZE SCHEDULED EUTHANASIA	P P P P P P
4634 F	GROUP 6: 5713C-H FEW FECES SCHEDULED EUTHANASIA	P P

GRADE CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL BODY WEIGHT DATA (GRAMS)

DAY	0	3	7	9
GROUP 5: 5713C-I (10%)				
4603 F	553	533	515	543
4605 F	497	475	489	507
4607 F	529	515	515	511
4615 F	453	455	442	463
MEAN	508	495	490	506
S.D.	43.3	35.8	34.4	32.9
N	4	4	4	4

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL BODY WEIGHT DATA (GRAMS)

DAY	0	3	7	9	14	21	28	35	42	49	56	60
GROUP 6: 5713C-H												
4616 F	460	473	492	483								
4624 F	604	617	635	642								
4631 F	582	574	586	585								
4634 F	559	579	595	593								
MEAN	551	561	577	576								
S.D.	63.5	61.6	60.5	66.8								
N	4	4	4	4								

SLI STUDY NO.: 3044.697
CLIENT: MONSANTO COMPANY

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL BODY WEIGHT GAIN DATA (GRAMS)

DAY	0-3	3-7	7-9
GROUP 5: 5713C-I (10%)			
4603 F	-20	-18	28
4605 F	-22	14	18
4607 F	-14	0	-4
4615 F	2	-13	21
MEAN	-14	-4	16
S.D.	10.9	14.3	13.8
N	4	4	4

A PASSIVE CUTANEOUS ANAPHYLAXIS ASSAY IN GUINEA PIGS
INDIVIDUAL BODY WEIGHT GAIN DATA (GRAMS)

DAY		0-3	3-7	7-9
GROUP 6: 5713C-H				
4616	F	13	19	-9
4624	F	13	18	7
4631	F	-8	12	-1
4634	F	20	16	-2
MEAN		10	16	-1
S.D.		12.1	3.1	6.6
N		4	4	4

APPENDIX M

SLI Personnel Responsibilities

SLI PERSONNEL RESPONSIBILITIES

Kimberly L. Bonnette, M.S., LATG	Study Director/Manager of Acute Toxicology
George A. Douds, M.S.	Alternate Contact/Assistant Toxicologist
Robert C. Springborn, Ph.D.	Chairman, President and CEO
Malcolm Blair, Ph.D.	Vice President and Managing Director
Joseph C. Siglin, Ph.D., DABT	Director of Toxicology
Deborah A. Douds, M.S.	Assistant Manager of Acute Toxicology
Pamela S. Smith, ALAT	Primary Technician/Supervisor of Acute Toxicology
Delores P. Knippen	Supervisor of Pharmacy
Steven H. Magness, B.S., LATG	Supervisor of Gross and Fetal Pathology
Jan K. Severt, B.S., ALAT	Supervisor of Acute Report Preparation
Anita M. Bosau, RQAP-GLP	Director of Compliance Assurance
Deanna M. Talerico, RQAP-GLP	Supervisor of Nonacute Quality Assurance
Christopher W. Wilson, B.S., RQAP-GLP	Supervisor of Acute Quality Assurance
J. Dale Thurman, D.V.M., M.S., DACVP	Director of Pathology

Appendix 7.3 Cottonseed Meal Analysis

Ralston Analytical Laboratories

5/18/98 REG

Ralston Purina Comp
Checkerboard Sq
Saint Louis, MO

TO R.GOODMAN, CC K. S. PHILLIPS, 2RS
D.G.HAUGHT-2E

LAB NO 604278 ENTERED 05/11/98 REPORTED 05/14/98 0

PO , 'CSA' NBP 6312322 COTTONSEED MEAL
MONSANTO BB5G

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
MOISTURE AT ASSAY MOB	8.36	%	10.00	
PROT.COMB.(N X 6.25) PRCB	23.0	%	20.0	
AMMONIA AMMN	0.140	%		1.00
FAT (ETHER EXT.) FTEE	13.8	%	10.00	20.0
FIBER (CRUDE) FIBR	19.4	%	20.0	
ASH ASHF	4.28	%		5.00
GOSSYPOL (FREE) GOSF	0.480	%	1.00	2.00

THE LETTER CODE LOCATED BELOW EACH ASSAY IS A METHOD REFERENCE CODE.
FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

Study 97-01-00-02

MECH-1 Bt CSM

The term "Less Than" is used to signify the lower limit of quantitation of the procedure under the conditions employed. The use of the term "Less Than" does n traces of analyte were present. Samples submitted to Ralston Analytical Laboratories for routine analysis will be retained for a minimum of thirty (30) days afte analysis is issued. Extended storage requirements must be brought to the attention of Ralston Analytical Laboratories prior to or at the time of sample submis

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

5/18/98

RLA

TO R.GOODMAN,

CC K. S. PHILLIPS, 2RS
D.G.HAUGHT-2E

LAB NO 604281 ENTERED 05/11/98 REPORTED 05/14/98 0

PO , 'CS-D' NB 6312331 COTTONSEED MEAL
MONSANTO BB5G

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
MOISTURE AT ASSAY MOB	8.76	%	10.00	
PROT.COMB.(N X 6.25) PRCB	23.6	%	20.0	
AMMONIA AMMN	0.140	%		1.00
FAT (ETHER EXT.) FTEE	14.3	%	10.00	20.0
FIBER (CRUDE) FIBR	18.0	%	20.0	
ASH ASHF	4.21	%		5.00
GOSSYPOL (FREE) GOSF	0.400	%	1.00	2.00

THE LETTER CODE LOCATED BELOW EACH ASSAY IS A METHOD REFERENCE CODE.
FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

Study 97-01-00-02

MECH-3 non-transgenic CSM

Ralston Analytical Laboratories

Ralston Purina Compar
Checkerboard Square
Saint Louis, MO 63164

5/18/98 KEO

TO R.GOODMAN,

CC K. S. PHILLIPS, 2RS
D.G.HAUGHT-2E

LAB NO 604279 ENTERED 05/11/98 REPORTED 05/14/98 0

PO , 'CS-B' 6312323 COTTONSEED MEAL
MONSANTO BB5G

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
MOISTURE AT ASSAY MOB	7.73	%	10.00	
PROT.COMB.(N X 6.25) PRCB	23.1	%	20.0	
AMMONIA AMMN	0.130	%		1.00
FAT (ETHER EXT.) FTEE	14.5	%	10.00	20.0
FIBER (CRUDE) FIBR	19.5	%	20.0	
ASH ASHF	3.92	%		5.00
GOSSYPOL (FREE) GOSF	0.520	%	1.00	2.00

THE LETTER CODE LOCATED BELOW EACH ASSAY IS A METHOD REFERENCE CODE.
FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

Study 97-01-00-02
MECH-1 non-transgenic CSM

7.4 Feed Analysis Pre-study

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

TO R.E.GOODMAN, CC K. S. PHILLIPS, 2RS

RED 11/14/98

LAB NO 614489 ENTERED 07/15/98 REPORTED 07/20/98

5713 I USD, GUINEA PIG DIET, ROOM TEMP. GROUP 4
MONSANTO BB5G

MECH-1 Bt 10% CS Diet
BT1

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
MOISTURE AT ASSAY MOB	8.00	%		
PROT.COMB.(N X 6.25) PRCB	20.6	%		
FAT (ETHER EXT.) FTEE	5.25	%		
FIBER (CRUDE) FIBR	16.2	%		
ASH ASHF	7.71	%		
IRON FEF	298.	PPM		
TOTAL VITAMIN C VTCA	1200.	PPM		
GOSSYPOL (FREE) GOSF	0.0340	%	0.100	

THE LETTER CODE LOCATED BELOW EACH ASSAY IS A METHOD REFERENCE CODE.
FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

Study 9701-00-02

The term 'Less Than' is used to signify the lower limit of quantitation of the procedure under the conditions employed. The use of the term 'Less Than' does not imply that traces of analyte were present. Samples submitted to Ralston Analytical Laboratories for routine analysis will be retained for a minimum of thirty (30) days after the report of analysis is issued. Extended storage requirements must be brought to the attention of Ralston Analytical Laboratories prior to or at the time of sample submission.

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

TO R.E.GOODMAN, CC K. S. PHILLIPS, 2RS

RED 11/14/98

LAB NO 614488 ENTERED 07/15/98 REPORTED 07/20/98 0

5713H USD, GUINEA PIG DIET, ROOM TEMP. GROUP 10 Control Diet Box 1
MONSANTO BB5G

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
MOISTURE AT ASSAY MOB	10.8	%		
PROT.COMB.(N X 6.25) PRCB	19.9	%		
FAT (ETHER EXT.) FTEE	4.78	%		
FIBER (CRUDE) FIBR	13.6	%		
ASH ASHF	7.12	%		
IRON FEF	281.	PPM		
TOTAL VITAMIN C VTCA	1070.	PPM		
GOSSYPOL (FREE) GOSF	0.0110	%	0.0100	

THE LETTER CODE LOCATED BELOW EACH ASSAY IS A METHOD REFERENCE CODE.
FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

Study 97-01-00-02

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

TO R.E.GOODMAN,   CC K. S. PHILLIPS, 2RS

LAB NO 614493   ENTERED 07/15/98   REPORTED 07/20/98   REO 11/14/98

5713 M USD, GUINEA PIG DIET, ROOM TEMP. GROUP 8
MONSANTO BB5G

MECH-3 non-trang. 10% Diet
Box 1

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
MOISTURE AT ASSAY MOB	13.0	%		
PROT.COMB.(N X 6.25) PRCB	20.1	%		
FAT (ETHER EXT.) FTEE	4.63	%		
FIBER (CRUDE) FIBR	14.5	%		
ASH ASHF	7.40	%		
IRON FEF	276.	PPM		
TOTAL VITAMIN C VTCA	754.	PPM		
GOSSYPOL (FREE) GOSF	0.0360	%	0.100	

THE LETTER CODE LOCATED BELOW EACH ASSAY IS A METHOD REFERENCE CODE.
FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

Study 97-01-00.02

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

TO R.E.GOODMAN, CC K. S. PHILLIPS, 2RS

LAB NO 614495 ENTERED 07/15/98 REPORTED 07/30/98

5713 H REF, GUINEA PIG DIET, REFRIG. GROUP 10
MONSANTO BB5G

REN 11/14/98 Control Diet Box 2
~~MECH~~ RE 11/16/98

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
MOISTURE AT ASSAY MOB	7.72	%		
PROT.COMB.(N X 6.25) PRCB	20.4	%		
FAT (ETHER EXT.) FTEE	4.79	%		
FIBER (CRUDE) FIBR	14.0	%		
ASH ASHF	7.68	%		
IRON FEF	275.	PPM		
TOTAL VITAMIN C VTCA	1320.	PPM		
GOSSYPOL (FREE) GOSF	0.0100	%	0.100	
CARBAMATE SCREEN	CRBP			

CARBAMATE PESTICIDES

OXAMYL	LESS THAN 0.05 PPM
METHOMYL	LESS THAN 0.05 PPM
3-HYDROXYCARBOFURAN	LESS THAN 0.05 PPM
ALDICARB	LESS THAN 0.05 PPM
PROPOXUR	LESS THAN 0.05 PPM
CARBOFURAN	LESS THAN 0.05 PPM
CARBARYL	LESS THAN 0.05 PPM
CARBANOLATE	LESS THAN 0.05 PPM
METHIOCARB	LESS THAN 0.05 PPM

ORGANOPHOSPHATE PEST ORGP

	(PPM)		(PPM)
DIAZINON	LESS THAN 0.02	PARATHION	LESS THAN 0.02
DISULFOTON	LESS THAN 0.02	THIMET	LESS THAN 0.02
ETHION	LESS THAN 0.02	THIODAN	LESS THAN 0.02
MALATHION	LESS THAN 0.02	TRITHION	LESS THAN 0.02
METHYL PARATHION	LESS THAN 0.02		

Study 97-01-00.02

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

TO R.E.GOODMAN, CC K. S. PHILLIPS, 2RS

LAB NO 614491 ENTERED 07/15/98 REPORTED 07/20/98

REY 11/14/98

5713 K USD, GUINEA PIG DIET, ROOM TEMP. GROUP 6
MONSANTO BB5G

MECH-1 non-trans 10% Diet
Box 1

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
MOISTURE AT ASSAY MOB	8.98	%		
PROT.COMB.(N X 6.25) PRCB	20.1	%		
FAT (ETHER EXT.) FTEE	5.46	%		
FIBER (CRUDE) FIBR	15.7	%		
ASH ASHF	7.41	%		
IRON FEF	280.	PPM		
TOTAL VITAMIN C VTCA	1100.	PPM		
GOSSYPOL (FREE) GOSF	0.0370	%	0.100	

THE LETTER CODE LOCATED BELOW EACH ASSAY IS A METHOD REFERENCE CODE.
FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

Study 97-01-00-02

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

TO R.E.GOODMAN, CC K. S. PHILLIPS, 2RS

RSO 11/14/98

LAB NO 614496 ENTERED 07/15/98 REPORTED 07/30/98 0

5713 I REF, GUINEA PIG DIET, REFRIG. GROUP 4
MONSANTO BB5G

Bx 2 mECH-1 Bt 10%

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
MOISTURE AT ASSAY MOB	10.4	%		
PROT.COMB.(N X 6.25) PRCB	19.4	%		
FAT (ETHER EXT.) FTEE	4.56	%		
FIBER (CRUDE) FIBR	13.6	%		
ASH ASHF	7.96	%		
IRON FEF	280.	PPM		
TOTAL VITAMIN C VTCA	1250.	PPM		
GOSSYPOL (FREE) GOSF	0.0110	%	0.100	

Study 97-01-00-02

CARBAMATE SCREEN CRBP

CARBAMATE PESTICIDES

OXAMYL	LESS THAN 0.05 PPM
METHOMYL	LESS THAN 0.05 PPM
3-HYDROXYCARBOFURAN	LESS THAN 0.05 PPM
ALDICARB	LESS THAN 0.05 PPM
PROPOXUR	LESS THAN 0.05 PPM
CARBOFURAN	LESS THAN 0.05 PPM
CARBARYL	LESS THAN 0.05 PPM
CARBANOLATE	LESS THAN 0.05 PPM
METHIOCARB	LESS THAN 0.05 PPM

ORGANOPHOSPHATE PEST ORGP

	(PPM)		(PPM)
DIAZINON	LESS THAN 0.02	PARATHION	LESS THAN 0.02
DISULFOTON	LESS THAN 0.02	THIMET	LESS THAN 0.02
ETHION	LESS THAN 0.02	THIODAN	LESS THAN 0.02
MALATHION	LESS THAN 0.02	TRITHION	LESS THAN 0.02
METHYL PARATHION	LESS THAN 0.02		

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

RT LAB NUMBER 614495

5713 H REF, GUINEA PIG DIET, REFRIG. GROUP 10
MONSANTO BB5G

RE # 11/14/98
CH. Box 2

PESTICIDES & PCB	RSPB (PPM)		(PPM)
ALDRIN	LESS THAN 0.02	ENDRIN	LESS THAN 0.02
ALPHA-BHC	LESS THAN 0.02	HCB	LESS THAN 0.02
BETA-BHC	LESS THAN 0.02	HEPTACHLOR	LESS THAN 0.02
DELTA-BHC	LESS THAN 0.02	HEPTACHLOR EPOXIDE	LESS THAN 0.02
CHLORDANE	LESS THAN 0.02	LINDANE	LESS THAN 0.02
DDE	LESS THAN 0.02	METHOXYCHLOR	LESS THAN 0.02
DDT..(TOTAL)	LESS THAN 0.02	MIREX	LESS THAN 0.02
DIELDRIN	LESS THAN 0.02	PCB	LESS THAN 0.15

THE LETTER CODE LOCATED BELOW EACH ASSAY IS A METHOD REFERENCE CODE.
FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

Study 97-01-00-02

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

TO R.E.GOODMAN,   CC K. S. PHILLIPS, 2RS

RED 11/14/98   97-01-00-

LAB NO 614498   ENTERED 07/15/98   REPORTED 07/30/98   0 Study ~~97-00-01-~~

5713 K REF, GUINEA PIG DIET, REFRIG. GROUP 6   MECH-1 non-trans 10%
MONSANTO BB5G   B rx 2

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
MOISTURE AT ASSAY MOB	11.6	%		
PROT.COMB.(N X 6.25) PRCB	19.6	%		
FAT (ETHER EXT.) FTEE	5.66	%		
FIBER (CRUDE) FIBR	14.5	%		
ASH ASHF	7.77	%		
IRON FEF	259.	PPM		
TOTAL VITAMIN C VTCA	1230.	PPM		
GOSSYPOL (FREE) GOSF	0.0410	%	0.100	
CARBAMATE SCREEN	CRBP			

CARBAMATE PESTICIDES

OXAMYL	LESS THAN 0.05 PPM
METHOMYL	LESS THAN 0.05 PPM
3-HYDROXYCARBOFURAN	LESS THAN 0.05 PPM
ALDICARB	LESS THAN 0.05 PPM
PROPOXUR	LESS THAN 0.05 PPM
CARBOFURAN	LESS THAN 0.05 PPM
CARBARYL	LESS THAN 0.05 PPM
CARBANOLATE	LESS THAN 0.05 PPM
METHIOCARB	LESS THAN 0.05 PPM

ORGANOPHOSPHATE PEST   ORGP

	(PPM)		(PPM)
DIAZINON...........	LESS THAN 0.02	PARATHION..........	LESS THAN 0.02
DISULFOTON.........	LESS THAN 0.02	THIMET.............	LESS THAN 0.02
ETHION.............	LESS THAN 0.02	THIODAN............	LESS THAN 0.02
MALATHION..........	LESS THAN 0.02	TRITHION...........	LESS THAN 0.02
METHYL PARATHION...	LESS THAN 0.02		

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

RT LAB NUMBER 614496

5713 I REF, GUINEA PIG DIET, REFRIG. GROUP 4
MONSANTO BB5G

RSB 11/14/98
Box 2 mech-1 of Study 97-01-00-02

PESTICIDES & PCB	RSPB (PPM)		(PPM)
ALDRIN	LESS THAN 0.02	ENDRIN	LESS THAN 0.02
ALPHA-BHC	LESS THAN 0.02	HCB	LESS THAN 0.02
BETA-BHC	LESS THAN 0.02	HEPTACHLOR	LESS THAN 0.02
DELTA-BHC	LESS THAN 0.02	HEPTACHLOR EPOXIDE	LESS THAN 0.02
CHLORDANE	LESS THAN 0.02	LINDANE	LESS THAN 0.02
DDE	LESS THAN 0.02	METHOXYCHLOR	LESS THAN 0.02
DDT..(TOTAL)	LESS THAN 0.02	MIREX	LESS THAN 0.02
DIELDRIN	LESS THAN 0.02	PCB	LESS THAN 0.15

THE LETTER CODE LOCATED BELOW EACH ASSAY IS A METHOD REFERENCE CODE.
FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 6310

TO R.E.GOODMAN, CC K. S. PHILLIPS, 2RS

11/14/98 REF Study 97-01-0

LAB NO 614501 ENTERED 07/15/98 REPORTED 07/30/98 0

5713 M REF, GUINEA PIG DIET, REFRIG. GROUP 8 MECH 3 - non-heavy. Box 2
MONSANTO BB5G

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
MOISTURE AT ASSAY MOB	12.2	%		
PROT.COMB.(N X 6.25) PRCB	13.8	%		
FAT (ETHER EXT.) FTEE	5.44	%		
FIBER (CRUDE) FIBR	17.8	%		
ASH ASHF	8.08	%		
IRON FEF	280.	PPM		
TOTAL VITAMIN C VTCA	1220.	PPM		
GOSSYPOL (FREE) GOSF	0.0400	%	0.100	

CARBAMATE SCREEN CRBP

CARBAMATE PESTICIDES

OXAMYL	LESS THAN 0.05 PPM
METHOMYL	LESS THAN 0.05 PPM
3-HYDROXYCARBOFURAN	LESS THAN 0.05 PPM
ALDICARB	LESS THAN 0.05 PPM
PROPOXUR	LESS THAN 0.05 PPM
CARBOFURAN	LESS THAN 0.05 PPM
CARBARYL	LESS THAN 0.05 PPM
CARBANOLATE	LESS THAN 0.05 PPM
METHIOCARB	LESS THAN 0.05 PPM

ORGANOPHOSPHATE PEST ORGP

	(PPM)		(PPM)
DIAZINON	LESS THAN 0.02	PARATHION	LESS THAN 0.02
DISULFOTON	LESS THAN 0.02	THIMET	LESS THAN 0.02
ETHION	LESS THAN 0.02	THIODAN	LESS THAN 0.02
MALATHION	0.10	TRITHION	LESS THAN 0.02
METHYL PARATHION	LESS THAN 0.02		

The term "Less Than" is used to signify the lower limit of quantitation of the procedure under the conditions employed. The use of the term "Less Than" does not imply that traces of analyte were present. Samples submitted to Ralston Analytical Laboratories for routine analysis will be retained for a minimum of thirty (30) days after the report of analysis is issued. Extended storage requirements must be brought to the attention of Ralston Analytical Laboratories prior to or at the time of sample submission.

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

RT LAB NUMBER 614498

5713 K REF, GUINEA PIG DIET, REFRIG. GROUP 6
MONSANTO BB5G

REB 11/14/98 Study 97-01-00-0
meth-1 non-trmp 10% Bag 2

PESTICIDES & PCB	RSPB (PPM)		(PPM)
ALDRIN	LESS THAN 0.02	ENDRIN	LESS THAN 0.02
ALPHA-BHC	LESS THAN 0.02	HCB	LESS THAN 0.02
BETA-BHC	LESS THAN 0.02	HEPTACHLOR	LESS THAN 0.02
DELTA-BHC	LESS THAN 0.02	HEPTACHLOR EPOXIDE	LESS THAN 0.02
CHLORDANE	LESS THAN 0.02	LINDANE	LESS THAN 0.02
DDE	LESS THAN 0.02	METHOXYCHLOR	LESS THAN 0.02
DDT..(TOTAL)	LESS THAN 0.02	MIREX	LESS THAN 0.02
DIELDRIN	LESS THAN 0.02	PCB	LESS THAN 0.15

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FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

7.5 Feed Analysis Post-Day 21

Ralston Analytical Laboratories

Ralston Purina Group
Checkerboard Square
Saint Louis, MO 631

RT LAB NUMBER 614501

5713 M REF, GUINEA PIG DIET, REFRIG. GROUP 8
MONSANTO BB5G

RED 11/14/98 Study 97-01-00-0 ←
mech 3 - non trans. Box 2

PESTICIDES & PCB	RSPB (PPM)		(PPM)
ALDRIN	LESS THAN 0.02	ENDRIN	LESS THAN 0.02
ALPHA-BHC	LESS THAN 0.02	HCB	LESS THAN 0.02
BETA-BHC	LESS THAN 0.02	HEPTACHLOR	LESS THAN 0.02
DELTA-BHC	LESS THAN 0.02	HEPTACHLOR EPOXIDE	LESS THAN 0.02
CHLORDANE	LESS THAN 0.02	LINDANE	LESS THAN 0.02
DDE	LESS THAN 0.02	METHOXYCHLOR	LESS THAN 0.02
DDT..(TOTAL)	LESS THAN 0.02	MIREX	LESS THAN 0.02
DIELDRIN	LESS THAN 0.02	PCB	LESS THAN 0.15

THE LETTER CODE LOCATED BELOW EACH ASSAY IS A METHOD REFERENCE CODE.
FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

Ralston Analytical Laboratories

Ralston Purina Compa...
Checkerboard Squa...
Saint Louis, MO 631...

TO R. GOODMAN, CC K. S. PHILLIPS, 2RS

RES 11/20/98

LAB NO 619450 ENTERED 08/18/98 REPORTED 10/22/98

GUINEA PIG CONTROL DIET 5713C-H BOX 1 V98.003.3004 LOT9848-1 Control Diet box #1
MONSANTO

Study #97-01-00-02.

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
TOTAL VITAMIN C VTCA	1160.	PPM		
CONTRACT ANALYSES	OUT			
AFLATOXIN B1	LESS THAN	1.0 PPB		
B2	LESS THAN	1.0 PPB		
G1	LESS THAN	1.0 PPB		
G2	LESS THAN	1.0 PPB		
AFLATOXIN PERFORMED BY HPLC METHOD				
OCHRATOXIN A	LESS THAN	5 PPB		
CITRININ	LESS THAN	0.2 PPM		
TRICHOTHECENES				
T-2 TOXIN	LESS THAN	0.1 PPM		
HT-2 TOXIN	LESS THAN	0.1 PPM		
DIACETOXYSCIRPENOL	LESS THAN	0.3 PPM		
NEOSOLANIOL	LESS THAN	0.5 PPM		
FUSARENON-X	LESS THAN	0.5 PPM		
DEOXYNIVALENOL		0.2 PPM		
NIVALENOL	LESS THAN	0.5 PPM		
ZEARALENONE	LESS THAN	100 PPB		
FUMONISIN B1	LESS THAN	0.1 PPM		
FUMONISIN B2	LESS THAN	0.1 PPM		
FUMONISIN B3	LESS THAN	0.1 PPM		
15 ACETYL-DON	LESS THAN	0.1 PPM		
3 ACETYL-DON	LESS THAN	0.1 PPM		

THE LETTER CODE LOCATED BELOW EACH ASSAY IS A METHOD REFERENCE CODE.
FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

TO R. GOODMAN, CC K. S. PHILLIPS, 2RS

R&A 11/20/98

LAB NO 619453 ENTERED 08/18/98 REPORTED 10/22/98

MOD GUINEA PIG W/10% CS-A 5713C-I BOX 1 S98.019.3044 LOT9848-2
MONSANTO

MeCH-1BT Box 1

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
TOTAL VITAMIN C VTCA	1440.	PPM		
CONTRACT ANALYSES	OUT			
AFLATOXIN B1	LESS THAN 1.0	PPB		
AFLATOXIN B2	LESS THAN 1.0	PPB		
AFLATOXIN G1	LESS THAN 1.0	PPB		
AFLATOXIN G2	LESS THAN 1.0	PPB		
OCHRATOXIN A	LESS THAN 5.0	PPB		
CITRININ	LESS THAN 0.2	PPM		
T-2 TOXIN	LESS THAN 0.1	PPM		
HT-2 TOXIN	LESS THAN 0.1	PPM		
DIACETOXYSCIRPENOL	LESS THAN 0.3	PPM		
NEOSOLANIOL	LESS THAN 0.5	PPM		
FUSARENON X	LESS THAN 0.5	PPM		
DEOXYNIVALENOL	0.2	PPM		
15 ACETYL-DON	LESS THAN 0.1	PPM		
3 ACETYL-DON	LESS THAN 0.1	PPM		
NIVALENOL	LESS THAN 0.5	PPM		
ZEARALENONE	LESS THAN 100	PPB		
FUMONISIN B1	LESS THAN 0.1	PPM		
FUMONISIN B2	LESS THAN 0.1	PPM		
FUMONISIN B3	LESS THAN 0.1	PPM		

Study # 97-01-00-02

THE LETTER CODE LOCATED BELOW EACH ASSAY IS A METHOD REFERENCE CODE.
FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

TO R. GOODMAN, CC K. S. PHILLIPS, ZRS

RGD 11/20/98

LAB NO 619452 ENTERED 08/18/98 REPORTED 10/22/98

Control diet box #3

GUINEA PIG CONTROL DIET 5713C-H BOX 3 V98.003.3004 LOT9848-1
MONSANTO

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
TOTAL VITAMIN C VTCA	1580.	PPM		
CONTRACT ANALYSES	OUT			
AFLATOXIN B1	LESS THAN 1.0	PPB		
B2	LESS THAN 1.0	PPB		
G1	LESS THAN 1.0	PPB		
G2	LESS THAN 1.0	PPB		
AFLATOXIN PERFORMED BY HPLC METHOD				
OCHRATOXIN A	LESS THAN 5	PPB		
CITRININ	LESS THAN 0.2	PPM		
TRICHOTHECENES				
T-2 TOXIN	LESS THAN 0.1	PPM		
HT-2 TOXIN	LESS THAN 0.1	PPM		
DIACETOXYSCIRPENOL	LESS THAN 0.3	PPM		
NEOSOLANIOL	LESS THAN 0.5	PPM		
FUSARENON-X	LESS THAN 0.5	PPM		
DEOXYNIVALENOL	0.2	PPM		
NIVALENOL	LESS THAN 0.5	PPM		
ZEARALENONE	LESS THAN 100	PPB		
FUMONISIN B1	LESS THAN 0.1	PPM		
FUMONISIN B2	LESS THAN 0.1	PPM		
FUMONISIN B3	LESS THAN 0.1	PPM		
15 ACETYL-DON	LESS THAN 0.1	PPM		
3 ACETYL-DON	LESS THAN 0.1	PPM		

Study # 97-01-00-02

THE LETTER CODE LOCATED BELOW EACH ASSAY IS A METHOD REFERENCE CODE.
FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

TO R. GOODMAN, CC K. S. PHILLIPS, 2RS

RES 11/20/98

LAB NO 619454 ENTERED 08/18/98 REPORTED 10/22/98

MOD GUINEA PIG W10% CS-A 5713C-I BOX 2 S98.019.3044 LOT9848-2
MONSANTO

MECH-1 Bt box 2

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
TOTAL VITAMIN C VTCA	1550.	PPM		
CONTRACT ANALYSES	OUT			
AFLATOXIN B1	LESS THAN 1.0	PPB		
AFLATOXIN B2	LESS THAN 1.0	PPB		
AFLATOXIN G1	LESS THAN 1.0	PPB		
AFLATOXIN G2	LESS THAN 1.0	PPB		
OCHRATOXIN A	LESS THAN 5.0	PPB		
CITRININ	LESS THAN 0.2	PPM		
T-2 TOXIN	LESS THAN 0.1	PPM		
HT-2 TOXIN	LESS THAN 0.1	PPM		
DIACETOXYSCIRPENOL	LESS THAN 0.3	PPM		
NEOSOLANIOL	LESS THAN 0.5	PPM		
FUSARENON X	LESS THAN 0.5	PPM		
DEOXYNIVALENOL	0.2	PPM		
15 ACETYL-DON	LESS THAN 0.1	PPM		
3 ACETYL-DON	LESS THAN 0.1	PPM		
NIVALENOL	LESS THAN 0.5	PPM		
ZEARALENONE	LESS THAN 100	PPB		
FUMONISIN B1	LESS THAN 0.1	PPM		
FUMONISIN B2	LESS THAN 0.1	PPM		
FUMONISIN B3	LESS THAN 0.1	PPM		

Study # 97-01-06-02

THE LETTER CODE LOCATED BELOW EACH ASSAY IS A METHOD REFERENCE CODE.
FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

TO R. GOODMAN, CC K. S. PHILLIPS, 2RS

RGD 11/20/98

LAB NO 619456 ENTERED 08/18/98 REPORTED 10/22/98

MOD GUINEA PIG W/10% CS-B 5713C-K BOX 1 S98.021.3044 LOT9848-4
MONSANTO

mech-1 Non-Tr Box 1

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
TOTAL VITAMIN C	1150.	PPM		
VTCA				
CONTRACT ANALYSES	OUT			
AFLATOXIN B1	LESS THAN	1.0 PPB		
AFLATOXIN B2	LESS THAN	1.0 PPB		
AFLATOXIN G1	LESS THAN	1.0 PPB		
AFLATOXIN G2	LESS THAN	1.0 PPB		
OCHRATOXIN A	LESS THAN	5.0 PPB		
CITRININ	LESS THAN	0.2 PPM		
T-2 TOXIN	LESS THAN	0.1 PPM		
HT-2 TOXIN	LESS THAN	0.1 PPM		
DIACETOXYSCIRPENOL	LESS THAN	0.3 PPM		
NEOSOLANIOL	LESS THAN	0.5 PPM		
FUSARENON X	LESS THAN	0.5 PPM		
DEOXYNIVALENOL		0.3 PPM		
15 ACETYL-DON	LESS THAN	0.1 PPM		
3 ACETYL-DON	LESS THAN	0.1 PPM		
NIVALENOL	LESS THAN	0.5 PPM		
ZEARALENONE	LESS THAN	100 PPB		
FUMONISIN B1	LESS THAN	0.1 PPM		
FUMONISIN B2	LESS THAN	0.1 PPM		
FUMONISIN B3	LESS THAN	0.1 PPM		

Study # 97-01-00-02

THE LETTER CODE LOCATED BELOW EACH ASSAY IS A METHOD REFERENCE CODE.
FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

TO R. GOODMAN, CC K. S. PHILLIPS, 2RS

RED 11/20/98
0
MECH-1
Non-Tr
6 of 7

LAB NO 619458 ENTERED 08/18/98 REPORTED 10/22/98

MOD GUINEA PIG W/10%CS-B BOX 3 5713C-K S98.021.3044 LOT9848-4
MONSANTO

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
TOTAL VITAMIN C VTCA	1250.	PPM		
CONTRACT ANALYSES	OUT			
AFLATOXIN B1	LESS THAN	1.0 PPB		
AFLATOXIN B2	LESS THAN	1.0 PPB		
AFLATOXIN G1	LESS THAN	1.0 PPB		
AFLATOXIN G2	LESS THAN	1.0 PPB		
OCHRATOXIN A	LESS THAN	5.0 PPB		
CITRININ	LESS THAN	0.2 PPM		
T-2 TOXIN	LESS THAN	0.1 PPM		
HT-2 TOXIN	LESS THAN	0.1 PPM		
DIACETOXYSCIRPENOL	LESS THAN	0.3 PPM		
NEOSOLANIOL	LESS THAN	0.5 PPM		
FUSARENON X	LESS THAN	0.5 PPM		
DEOXYNIVALENOL		0.3 PPM		
15 ACETYL-DON	LESS THAN	0.1 PPM		
3 ACETYL-DON	LESS THAN	0.1 PPM		
NIVALENOL	LESS THAN	0.5 PPM		
ZEARALENONE	LESS THAN	100 PPB		
FUMONISIN B1	LESS THAN	0.1 PPM		
FUMONISIN B2	LESS THAN	0.1 PPM		
FUMONISIN B3	LESS THAN	0.1 PPM		

Study # 97-01-00-02

THE LETTER CODE LOCATED BELOW EACH ASSAY IS A METHOD REFERENCE CODE.
FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63188

TO R. GOODMAN, CC K. S. PHILLIPS, 2RS

RED 11/20/98
0
MECH-1 Nm-Tr Box 2

LAB NO 619457 ENTERED 08/18/98 REPORTED 10/22/98

MOD GUINEA PIG W/10% CS-B 5713C-K BOX 2 S98.021.3044 LOT 9848-4
MONSANTO

Study # 97-01-00-02

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
TOTAL VITAMIN C VTCA	1160.	PPM		
CONTRACT ANALYSES	OUT			
AFLATOXIN B1	LESS THAN 1.0	PPB		
AFLATOXIN B2	LESS THAN 1.0	PPB		
AFLATOXIN G1	LESS THAN 1.0	PPB		
AFLATOXIN G2	LESS THAN 1.0	PPB		
OCHRATOXIN A	LESS THAN 5.0	PPB		
CITRININ	LESS THAN 0.2	PPM		
T-2 TOXIN	LESS THAN 0.1	PPM		
HT-2 TOXIN	LESS THAN 0.1	PPM		
DIACETOXYSCIRPENOL	LESS THAN 0.3	PPM		
NEOSOLANIOL	LESS THAN 0.5	PPM		
FUSARENON X	LESS THAN 0.5	PPM		
DEOXYNIVALENOL	0.3	PPM		
15 ACETYL-DON	LESS THAN 0.1	PPM		
3 ACETYL-DON	LESS THAN 0.1	PPM		
NIVALENOL	LESS THAN 0.5	PPM		
ZEARALENONE	LESS THAN 100	PPB		
FUMONISIN B1	LESS THAN 0.1	PPM		
FUMONISIN B2	LESS THAN 0.1	PPM		
FUMONISIN B3	LESS THAN 0.1	PPM		

THE LETTER CODE LOCATED BELOW EACH ASSAY IS A METHOD REFERENCE CODE.
FOR ADDITIONAL INFORMATION CONTACT CLIENT SERVICES 1-800-423-6832

Ralston Analytical Laboratories

Ralston-Purina Company
Checkerboard Square
Saint Louis, MO 63164

TO R. GOODMAN, CC K. S. PHILLIPS, 2RS

REA 11/20/97 O

LAB NO 619455 ENTERED 08/18/98 REPORTED 10/22/98

MECH-1 BT box 3

MOD GUINEA PIG W/10%CS-A 5713C-I BOX 3 S98.019.3044 LOT9848-2
MONSANTO

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
TOTAL VITAMIN C VTCA	1460.	PPM		
CONTRACT ANALYSES	OUT			
AFLATOXIN B1	LESS THAN 1.0	PPB		
AFLATOXIN B2	LESS THAN 1.0	PPB		
AFLATOXIN G1	LESS THAN 1.0	PPB		
AFLATOXIN G2	LESS THAN 1.0	PPB		
OCHRATOXIN A	LESS THAN 5.0	PPB		
CITRININ	LESS THAN 0.2	PPM		
T-2 TOXIN	LESS THAN 0.1	PPM		
HT-2 TOXIN	LESS THAN 0.1	PPM		
DIACETOXYSCIRPENOL	LESS THAN 0.3	PPM		
NEOSOLANIOL	LESS THAN 0.5	PPM		
FUSARENON X	LESS THAN 0.5	PPM		
DEOXYNIVALENOL	0.2	PPM		
15 ACETYL-DON	LESS THAN 0.1	PPM		
3 ACETYL-DON	LESS THAN 0.1	PPM		
NIVALENOL	LESS THAN 0.5	PPM		
ZEARALENONE	LESS THAN 100	PPB		
FUMONISIN B1	LESS THAN 0.1	PPM		
FUMONISIN B2	LESS THAN 0.1	PPM		
FUMONISIN B3	LESS THAN 0.1	PPM		

Study # 97-01-00-02

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Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

TO R. GOODMAN, CC K. S. PHILLIPS, 2RS

RES 11/20/98

LAB NO 619460 ENTERED 08/18/98 REPORTED 10/22/98 O

MOD GUINEA PIG W/10% CS-D 5713C-M BOX 2 S98.023.3044 LOT9848-6 MECH-3 Nm-Tr Box 2
MONSANTO

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
TOTAL VITAMIN C VTCA	1110.	PPM		
CONTRACT ANALYSES	OUT			
AFLATOXIN B1	LESS THAN	1.0 PPB		
AFLATOXIN B2	LESS THAN	1.0 PPB		
AFLATOXIN G1	LESS THAN	1.0 PPB		
AFLATOXIN G2	LESS THAN	1.0 PPB		
OCHRATOXIN A	LESS THAN	5.0 PPB		
CITRININ	LESS THAN	0.2 PPM		
T-2 TOXIN	LESS THAN	0.1 PPM		
HT-2 TOXIN	LESS THAN	0.1 PPM		
DIACETOXYSCIRPENOL	LESS THAN	0.3 PPM		
NEOSOLANIOL	LESS THAN	0.5 PPM		
FUSARENON X	LESS THAN	0.5 PPM		
DEOXYNIVALENOL		0.3 PPM		
15 ACETYL-DON	LESS THAN	0.1 PPM		
3 ACETYL-DON	LESS THAN	0.1 PPM		
NIVALENOL	LESS THAN	0.5 PPM		
ZEARALENONE	LESS THAN	100 PPB		
FUMONISIN B1	LESS THAN	0.1 PPM		
FUMONISIN B2	LESS THAN	0.1 PPM		
FUMONISIN B3	LESS THAN	0.1 PPM		

Study # 97-01-00-02

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Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 63164

TO R. GOODMAN, CC K. S. PHILLIPS, 2RS

Rec'd 11/20/98

LAB NO 619459 ENTERED 08/18/98 REPORTED 10/22/98

MECH-3 Non-Tox Box 1

MOD GUINEA PIG W/10% CS-D 5713C-M BOX 1 S98.023.3044 LOT9848-6
MONSANTO

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
TOTAL VITAMIN C VTCA	793.	PPM		
CONTRACT ANALYSES	OUT			
AFLATOXIN B1	LESS THAN 1.0	PPB		
AFLATOXIN B2	LESS THAN 1.0	PPB		
AFLATOXIN G1	LESS THAN 1.0	PPB		
AFLATOXIN G2	LESS THAN 1.0	PPB		
OCHRATOXIN A	LESS THAN 5.0	PPB		
CITRININ	LESS THAN 0.2	PPM		
T-2 TOXIN	LESS THAN 0.1	PPM		
HT-2 TOXIN	LESS THAN 0.1	PPM		
DIACETOXYSCIRPENOL	LESS THAN 0.3	PPM		
NEOSOLANIOL	LESS THAN 0.5	PPM		
FUSARENON X	LESS THAN 0.5	PPM		
DEOXYNIVALENOL	0.3	PPM		
15 ACETYL-DON	LESS THAN 0.1	PPM		
3 ACETYL-DON	LESS THAN 0.1	PPM		
NIVALENOL	LESS THAN 0.5	PPM		
ZEARALENONE	LESS THAN 100	PPB		
FUMONISIN B1	LESS THAN 0.1	PPM		
FUMONISIN B2	LESS THAN 0.1	PPM		
FUMONISIN B3	LESS THAN 0.1	PPM		

Study # 97-01-00-02

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Ralston Analytical Laboratories

Ralston Purina Company
Checkerboard Square
Saint Louis, MO 6315

TO R. GOODMAN, CC K. S. PHILLIPS, 2RS

RED 11/20/98
0
MECH-3 Nm-T
Bx 3

LAB NO 619461 ENTERED 08/18/98 REPORTED 10/22/98

MOD GUINEA PIG W/10%CS-D 5713C-M BOX 3 S98.023.3044 LOT9848-6
MONSANTO

ASSAY	ANALYSIS	UNITS	LOW-LIMIT Z	HIGH-LIMIT
TOTAL VITAMIN C VTCA	1090.	PPM		
CONTRACT ANALYSES	OUT			
AFLATOXIN B1	LESS THAN	1.0 PPB		
AFLATOXIN B2	LESS THAN	1.0 PPB		
AFLATOXIN G1	LESS THAN	1.0 PPB		
AFLATOXIN G2	LESS THAN	1.0 PPB		
OCHRATOXIN A	LESS THAN	5.0 PPB		
CITRININ	LESS THAN	0.2 PPM		
T-2 TOXIN	LESS THAN	0.1 PPM		
HT-2 TOXIN	LESS THAN	0.1 PPM		
DIACETOXYSCIRPENOL	LESS THAN	0.3 PPM		
NEOSOLANIOL	LESS THAN	0.5 PPM		
FUSARENON X	LESS THAN	0.5 PPM		
DEOXYNIVALENOL		0.3 PPM		
15 ACETYL-DON	LESS THAN	0.1 PPM		
3 ACETYL-DON	LESS THAN	0.1 PPM		
NIVALENOL	LESS THAN	0.5 PPM		
ZEARALENONE	LESS THAN	100 PPB		
FUMONISIN B1	LESS THAN	0.1 PPM		
FUMONISIN B2	LESS THAN	0.1 PPM		
FUMONISIN B3	LESS THAN	0.1 PPM		

Study # 97-01-00-0-2.

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R11710-[illegible]