GENOTOXICITY AND ENVIRONMENTAL MUTAGEN SOCIETY

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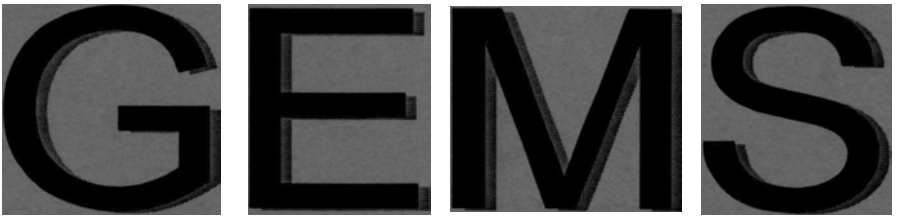

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EIGHTEENTH ANNUAL MEETING
PROGRAM AND ABSTRACTS

WEDNESDAY, OCTOBER 25, 2000

SHERATON IMPERIAL HOTEL
Research Triangle Park, NC

2000 Board of Directors

GEMS FALL MEETING

Genetically Modified Food: Benefits & Risks to Human & Environmental Health

8:00-8:45	Registration & Breakfast
8:45-9:00	Welcome, **Mr. Thomas Hughes,** GEMS President Introduction, **Dr. Michael Cunningham,** GEMS President-Elect
9:00-9:45	**Dr. Fred Gould,** NCSU *Safety of Conventional and Genetically Engineered Crops*
9:45-10:30	**Dr. Scott Uknes,** Paradigm Genetics *Past, Present, and Future of Genetically Enhanced Products*
10:30-12:00	Exhibits, Posters, Coffee
12:00-1:00	Served Luncheon
1:00-1:30	Annual Business Meeting
1:30-2:15	**Dr. Matthew Lorence,** Applied Biosystems *Detection and Quantitation Methods for GMO Regulatory Sequences in Processed Foods*
2:15-3:00	Student talks
3:00-3:15	Break
3:15-4:15	Presentation of Lifetime Achievement Awards to **Dr. Errol Zeiger & Dr. Michael Waters**
4:15-4 :30	Awards for Best Talk and Posters
4 :30-5:30	Reception

Genotoxicity and Environmental Mutagen Society

PO. Box 13475, Researr:h Triangle Park, North Carolina 17709

October 25, 2000

Dear GEMS Members,

Thank you for electing me as your President-Elect and President two years ago. It has been very exciting and interesting to be an officer for the Society, and I have greatly enjoyed my tenure. I also forget how much work it was to be on Board of Directors (BOD)! The GEMS has always been blessed with smart, hard-working scientists who are also great fun to be around. The last two years have been no exception. I encourage you to tell the next President-Elect, Amal Abu-Shakra, that you are interested in being nominated for the next election in the summer of 2001. GEMS will elect three new Councilors, a Treasurer, Secretary and President-Elect at that time.

I am rotating off as President at this meeting on October 25, 2000. Three Councilors will also be leaving: Heinrich Malling, Julian Preston and Jeff Ross. I am very grateful for their service to the Society. The three new Councilors, who will be installed today are: Lois Barnett, Marie Vasquez and Keith Martin. Thank you to all those that ran and did not win. I was blessed with a great BOD this past year. Lance Brooks and Stephen Little both did excellent jobs as Secretary and Treasurer, in addition to sending out the Newsletter every quarter. Mike Cunningham, as President-Elect, organized two exceptional meetings. The 2000 Spring Meeting on gene expression at the Friday Center in Chapel Hill had a record attendance of 200 scientists. I am sure the Fall Meeting today on genetically modified foods will also be highly successful. I thank Jim Fuscoc and Lance Brooks for their assistance with the nominations and ballot counting. Leon King continues to do a great job as Newsletter Editor. Jeff Ross is a wizard as Membership Coordinator. Tasha Smith, a GEMS best talk winner last year and a graduate student at Wake Forest University, was very helpful as a student advisor to the BOD this year. Her professor, Mark Miller, should be very proud of her.

I especially thank Kristine Witt for her help with the awards and taking minutes at the BOD meetings in the absence of Lance Brooks. Beth George organized and published the abstract book. and Lori Phillips single-handedly functioned as Corporate Coordination. Lori and Beth are not even on the BOD, yet they volunteered their time for these very important jobs. Frank Stack, another former BOD member, keeps our web site up-to date with the latest meeting information (http://www.ncncighbors.com/312). Frank also sends this information to EMS, for which I am eternally grateful. Kristine Witt, Carl Blackman and Karen Yeowell-O'Connell were instrumental in several intense discussions that the BOD had this year. These are the people that are running your society. They have worked very hard for no pay. When you see them, thank them. They have all done excellent jobs!

The Society is presently investigating new directions for future meetings. These directions will include broad scientific fields and research areas such as oxidative damage, endrocrinc disruptors and DNA repair. Please voice your ideas to any Board Member. The Board sees these new directions as one of the best ways to inform our membership of new and exciting research areas and a great way to attract new members. Please invite a friend to the next GEMS Spring Meeting in 2001.

In closing, congratulations are in order to Dr. Michael Waters and Dr. Errol Zeiger; both will receive GEMS' Lifetime Scientific Achievement Awards at today's meeting. I enjoyed organizing last year's Spring Meeting on regulatory toxicology, and last year's Fall meeting on new trends in genetic toxicology. Last September, I left the laboratory after thirty years to work as a QA Manager at the U.S. EPA, so this was my last hurrah in genetic toxicology! Thank you again for allowing me to serve the GEMS. Please enjoy this great Fall Meeting organized by Mike Cunningham on genetically modified foods.

Sincerely,

tlrrn...

Thomas J. Hughes
GEMS President

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GEMS and the Board of Directors gratefully acknowledge and appreciate your continued support! You, the corporate members, are the backbone of our Society not only with necessary financial support but with vital technical information and equipment. We, the members, reiterate our thanks to the corporate sponsors for your substantial support of the Society.

Thank you!

ORAL PRESENTATIONS

***T1 AMINO ACID SUBSTITUTION VARIANTS OF DNA REPAIR GENES AND PROSTATE CANCER SUSCEPTIBILITY.** K. Lockett[1], M. C. Hall[1], F. M. Torti[1], D. L. McCullough[1], S. D. Cramer[1], H. W. Mohrenweiser[2], J. Anderson[1,2], T. R. Smith[1], K. Lohman[1], and J. J. Hu[1]. [1]WFUSOM, Winston-Salem, NC 27157 and [2]LLNL, Livermore, CA 94550.

Prostate cancer is the second leading cause of cancer death in men. While human cancer genetics are advancing at a rapid pace, the etiology of prostate cancer is not fully understood. It is well established that mammalian cells are constantly exposed to a wide variety of genotoxic agents from both endogenous and exogenous sources; effective and accurate DNA repair mechanisms are necessary to maintain human genome integrity. Furthermore, the data on mutations of androgen receptor gene and p53 gene and the high frequency of chromosomal aberrations in human prostate tumor tissue suggest that DNA damage/repair plays a critical role in human prostate carcinogenesis. We conducted a molecular epidemiology study (190 prostate cancer cases, 253 high-risk controls, and 80 disease-free controls) to evaluate the association between prostate cancer risk and five amino acid substitution variants of DNA repair genes: *XPD* (Lyn751Gin) for nucleotide excision repair, *XRCC3* (Thr241Met) for double-strand break repair and recombination repair, and *XRCC1* (Arg194Trp and Arg399Gln) and *APE* (Asp148Glu) for base excision repair. Our data suggest that the variant allele of *XRCC3* (241Met) and *XRCC1* (399Gln) may be associated with prostate cancer risk. Subjects with *XRCC3* 241Met/Met or *XRCC1* 399 Gin/Gin genotype have elevated risk for prostate cancer with odds ratio (0R)=1.63 (95% confidence interval [Cl]=0.62-4.36) and OR=1.88 (95%Cl=0.54-7.15), respectively. Inaddition,the variant allele of *APE* (148Glu) may have a protective effect (OR=0.60, 95%Cl=0.25-1.41). Similar association was also observed in high-risk controls. This is the first study to demonstrate potential associations between amino acid substitution variants of DNA repair genes and prostate cancer susceptibility. A larger study is warranted to validate our data and to further evaluate the functional significance of DNA repair genetic polymorphism and human cancer risk.

An asterisk by the abstract title indicates that a presenter is in competition for the Best Talk or Poster Award. The Best Talk recipient will receive up to $1500 to be used to defray costs associated with attendance at a national professional meeting of his or her choice, pending the Board's approval. There are two poster awards. The first place poster winner will be awarded $100 and the second place poster recipient will receive $50.

*T2 HIGH AFFINITY INTERLEUKIN-3 RECEPTOR EXPRESSION ON BLASTS FROM PATIENTS WITH ACUTE MYELOGENOUS LEUKEMIA CORRELATES WITH CYTOTOXICITY OF A DIPHTHERIA TOXIN/IL-3 FUSION PROTEIN. R.L. Alexander[1], G.L. Kucera[2], and A.E. Frankel[2], Departments of [1]Physiology and Pharmacology, [2]Cancer Biology, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, North Carolina 27157

Leukemic blasts from patients with acute myeloid leukemia (AML) frequently show resistance to multiple chemotherapeutic drugs. Novel agents which can overcome multi-drug resistance phenotypes are needed. We prepared a diphtheria fusion protein (DT_{388}IL3) composed of human interleukin-3 (IL3) fused to the catalytic and translocation domain of diphtheria toxin (DT_{388}). Previously, we have demonstrated that DT_{388}IL3 was toxic to a fraction of myeloid leukemia cell lines. Our goal was to assess the activity of this novel agent on patient AML blasts. To this end, we measured IL3 receptor density by using a radiolabeled, high affinity IL3 receptor agonist (SC-65461) and tested the sensitivity of AML-colony forming cells (CFC) to DT_{388}IL3. Ninety-two of the patients' blasts had both high affinity and low affinity IL3 receptors. The blasts had high affinity (Kd = 16 ± 3 pM n = 25, mean ± SEM) IL3 receptor densities that ranged from 0 to 1220 receptors per cell and low affinity (= 7060 ± 1388 pM n = 25, mean ± SEM) receptor densities that ranged from 263 to 18250 receptors per cell. We then tested the sensitivity of patient leukemic blasts to DT_{388}IL3 on the 25 patients' blasts. DT_{388}IL3 was cytotoxic (greater than 1 log cell kill) in 9 of 25 (36%) AML patients' blasts. There was a statistically significant correlation between DT_{388}IL3 log cell kill and blast high affinity IL3 receptor density ($p = 0.0044$) and no correlation between low affinity IL3 receptor density and log cell kill. These results show that specific high affinity IL3 binding is one factor important in the sensitivity of patients' leukemic blasts to DT_{388}IL3 and lend further support for the continued preclinical development of DT_{388}IL3 in AML. During clinical testing, selection of patients for treatment with DT_{388}IL3 should include assessment of the density of high affinity IL3 receptors.

GEMS would like to thank Corning Science Products for their contribution to the Best Talk Travel Award. We appreciate your support.

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POSTERS

P1 SAFETY ASSESSMENT OF BIOTECHNOLOGY-ENHANCED CROP PLANTS. L.Privalle, L.Artim-Moore and J.Stein, Novartis Seeds, 3054 Cornwallis Dr,RTP, NC 27709

Prior to commercialization , crop plants ---€nhanced through biotechnology undergo extensive safety assessments conducted by government regulatory agencies in countries where these products will be grown or consumed . In the United States, three federal agencies, the Food and Drug Administration (FDA), Environmental Protection Agency (EPA) and U.S. Department of Agriculture (USDA),work together in a coordinated fashion to assess the environmental impact and food and feed safety of these products . This safety assessment includes an extensive molecular characterization of the transgene(s) introduced into the crop plant, as well as a rigorous biochemical examination of the novel protein(s) that are expressed. Issues such as gene source, protein function, specificity, and mode of action are considered . Plant growth developmental studies (from seed to harvest) are conducted to determine both temporal and spatial expression levels of the novel protein(s). Mouse toxicity studies are conducted as one component of the mammalian safety assessment. Allergenicity potential of the novel protein(s) is evaluated by conducting digestibility studies and homology comparisons to known food allergens. The nutrient composition of plant parts destined for food or feed use is determined by measuring components such as protein, fat, fiber , carbohydrates , and vitamins as compared to non-transgenic versions of the crop plant. Nutritional equivalence is further established through livestock feeding trials . Environmenta.1 safety is assessed by measuring the impact of the novel proteins on beneficial organisms such as honeybees and ladybeetles , non-target organisms such as fish,aquatic invertebrates, birds,and soil organisms such as earthworms and springtails.

P2 ANIMAL FEEDING STUDIES CONFIRM NUTRITIONAL EQUIVALENCE BETWEEN GENETICALLY-ENHANCED AND CONVENTIONAL CROP PLANTS. L. Artim-Moore , L.Privalle, S.Chartton, and J.Stein, Novartis Seeds, 3054 Cornwallis Drive, RTP, NC 27709

Biotechnology-enhanced crcip plants undergo a comprehensive and rigorous safety assessment prior to commercialization. This process includes extensive biochemical analysis of the expressed trait , toxicology testing , allergenicity evaluation, and environmental and non-target organism impact assessment. An integral part of the analysis includes an extensive nutrient composition analysis of plant parts destined for food and feed use. Nutrient analysis typically includes proximates (fat, fiber, protein, moisture, ash), starch, amino acid content, fatty acid profile, minerals and P-carotene, xanthophylls and vitamins . To further establish nutritional equivalency of biotechnology-enhanced crop plants with their non-transgenic counterparts, numerous animal performance studies including poultry (layers and broilers),swine, beef cattle, dairy cows and sheep have been conducted. These studies further demonstrate nutritional equivalence and indicate no unintended health effects . All of the studies completed to date have shown that animals perform in a comparable manner when fed biotech crops as compared to conventional counterparts .

P3 POTENTIAL FOR REDUCTION OF MYCOTOXINS IN MAIZE THROUGH TRANSGENIC INSECT CONTROL. Gary P. Munkvold[1], Richard L. Hellmich[2], Cassandra M. Biggerstaff[1], P. Frank Ross[3], and Larry G. Rice[3]. [1] Dept. of Plant Pathology, Iowa State University, Ames, IA 50011, [2] USDA-ARS Corn Insects & Crop Genetics Research Unit, Ames, IA 50011 [3]USDA-APHIS NVSL, Ames, IA 50010

Infection of maize kernels by fumonisin-producing *Fusarium* species often is associated with insect damage. Infestation of conventional maize hybrids with European corn borer (ECB) larvae enhances kernel infection by *F. moniliforme* and fumonisin levels in the kernels. Control of ECB using transgenic maize hybrids (Bt hybrids) may provide an opportunity to reduce *Fusarium* infection and fumonisin concentrations in maize kernels. During four years of field studies, we evaluated the effects of transgenic insect control on Fusarium ear rot symptoms and fumonisin concentrations. Representatives of the five commercially available Bt transformation events were included: MON810, 176, BT11, CBH351, and DBT418. With either natural or manual ECB infestation, Bt hybrids that express CrylA(b) in all plant tissues (events MON810 and BT11) consistently experienced significantly less ear rot and lower fumonisin concentrations compared to near-isogenic, non-Bt hybrids. Differences between Bt and non-Bt hybrids were more evident in treatments manually infested with ECB. Fumonisin concentrations in non-Bt hybrids were sometimes 10X higher (up to 32.5 µg/g) than near-isogenic MON810 or BT11 hybrids (<1.0 to 6.0 µg/g). Bt hybrids that express CrylA(b) only in green tissue and pollen (event 176) occasionally demonstrated similar results but did not consistently differ from non-Bt hybrids. Ear rot symptoms and fumonisin concentrations were consistently low in hybrids expressing Cry9C but these hybrids did not always differ from their near-isogenic, non-Bt counterparts. ECB damage to kernels was significantly correlated with fumonisin concentrations. These results indicate that genetic engineering for insect resistance can suppress fumonisin concentrations and enhance the safety of maize for animal and human consumption.

*P4 ALLELE FREQUENCIES INASTHMA CANDIDATE GENES AND DRUG TARGETS VARY AMONG ETHNICALLY DIVERSE GROUPS. K. Jordan, C.S. Sprankle, Z. Xue, S. Sharma, C.G. Binnie, W.H. Anderson, M.E. Fling and P.A. Sherman. Glaxo Wellcome, Research Triangle Park, NC

Asthma is a common disease, affecting 17 million Americans. A large body of evidence indicates that asthma has an important genetic component, but the gene or genes involved in the inheritance of a predisposition to asthma remain to be determined. There is also a substantial interindividual variability in the response to asthma medications, suggesting the presence of genetic variation in the genes coding for drug target proteins or proteins interacting with the drug target. The Allele Discovery group at Glaxo Wellcome has developed a number of assays for the genotyping of SNPs (Single Nucleotide Polymorphisms) in asthma candidate genes and genes coding for proteins involved in the leukotriene pathway, which contains several important asthma drug targets. We performed 19 assays, representing 11 genes, on DNAs from a group of healthy individuals from various ethnic groups to determine the frequency of these SNPs in the general population. The 5' nuclease assays were run on DNAs from 88 Caucasians, 86 African-Americans, 50 Hispanics, 30 Asians and 8 Southwest American Indians. Overall frequencies of the variant alleles ranged from <1% to 49%. Frequencies of variant alleles of eight SNPs were fairly consistent among ethnic groups. Eight SNPs exhibited an increase in variant allele frequency in one or two ethnic groups compared to the majority, while three SNPs exhibited a decrease in variant allele frequency. This information indicates the range of variation in frequency of variant alleles of these SNPs and demonstrates the value of knowing allele frequencies in ethnically diverse groups when designing and analyzing association and pharmacogenetics studies.

***PS CAN APOPTOTIC AND NECROTIC CELLS BE DISTINGUISHED USING THE NEUTRAL DIFFUSION COMET ASSAY?** R. Stoner, R.R. Tice. ILS, P.O. Box 13501, RTP, NC 27711.

The neutral diffusion Comet assay allows for the detection of apoptotic/necrotic cells based on the extent of DNA diffusion in a 0.5% agarose gel matrix under neutral, non-electrophoretic conditions (Vasquez and Tice, Environ. Molec. Mutagenesis 29(S28): 53, 1997). However, under these conditions, it is not possible to distinguish between apoptosis and necrosis-induced DNA degradation. Here, we evaluate if the neutral diffusion assay can be modified to distinguish between these two mechanisms of DNA damage (double-strand breaks) by embedding cells in a range of agarose concentrations and comparing the resulting extent of DNA diffusion. Our expectation is that the DNA in terminal apoptotic cells will have a lower molecular weight than DNA in necrotic cells. A preliminary range finding test was conducted using Chinese hamster ovary (CHO) cells killed by exposure to hydrogen peroxide to select the optimum range of agarose concentrations. Subsequently, using agarose concentrations ranging from 0.5 to 3%, neutral DNA diffusion associated with apoptosis versus necrosis was compared using two cells lines derived from Syrian hamster embryo cells; under low serum (0.2%) conditions, sup•^{5} cells undergo apoptosis while sup^{3} cells undergo necrosis (Preston et al., Cancer Res. 54: 4214, 1994). Each cell culture was assessed for viability using ethidium bromide: 5-6 carboxyfluorescein diacetate, for the incidence of cells with low molecular weight DNA based on the extent of diffusion observed visually, and for the extent of diffusion determined using the Komet Version 4.0 Image Analysis System. The presence of apoptosis in sup•^{5} cells was verified by detecting the presence of a DNA ladder in a DNA agarose gel.

*P6 DIFFERENT MUTANT Ki-ras ALLELES DETERMINE SUBSEQUENT DAMAGE AT THE *Ink4a* LOCUS IN TRANSPLACENTALLY INDUCED MURINE LUNG TUMORS. M C Mizesko, M S Miller, C Grewe, and A Grabner. Department of Cancer Biology, Wake Forest University School of Medicine, Winston-Salem, NC.

Activation of the Ki-ras gene has been implicated as an early event in the pathogenesis of lung tumors, particularly in adenocarcinomas in smokers, ranging in incidence from 30-80% of the tumors examined. Several groups have shown a correlation between the presence of a mutated Ki-ras gene and patient prognosis, which appears to depend on the actual base substitution present. Our previous studies demonstrated that, following treatment of pregnant D2 x (B6D2F1)F2 or Balb/c mice with 3-methylcholanthrene, lung tumors induced in the transplacentally exposed offspring exhibited a high incidence of mutations in the Ki-ras gene. The type of mutation present in the lesions appeared to influence tumor development. The presence of the VAL^{12}, ARG^{12}, and ARG^{13} mutant alleles correlated with a more progressive tumor stage (adenomas and adenocarcinomas) compared to the CYS^{12} mutation, which appeared predominantly in hyperplastic lesions. In order to examine the role of different mutant Ki-ras alleles in lung tumor progression, we determined the methylation status of the *Ink4a* tumor suppressor gene in transplacentally induced lung tumors by methylation-specific PCR and screened for the presence of single base pair mutations by single strand conformation polymorphism analysis. Only 8% of the murine tumors exhibited methylation of the *Ink4a* promoter region, while an additional 6% of the tumors showed single base pair mutations at this gene locus. Three of the 5 tumors exhibiting promoter hypermethylation were adenocarcinomas, and 4 of these 5 tumors contained mutant *ras* alleles that were associated with the more oncogenic phenotype. In contrast, 3 of the 4 tumors harboring mutations in the *Ink4a* gene occurred in tumors containing the least oncogenic Ki-ras mutations. Tissue specific effects were also noted. Liver tumors, which all contained the ARG^{13} mutant *ras* allele, showed a higher incidence of point mutations (5/19) than promoter methylation (1 tumor). It thus appears that the type of damage seen at the *Ink4a* locus correlates with the type of mutation occurring in the Ki-ras gene, suggesting that early damage to Ki-ras may determine subsequent events occurring during tumor progression. Supported by NIEHS grants ES06501 and ES08252.

*P7 TRANSMISSION OF MUTATIONS IN TRANSGENES TO THE OFFSPRING OF ENU-TREATED BIG BLUE™ TRANSGENIC MALE MICE.L.B. Barnett', R.W. Tyl', B.S. Shane[2], M.D. Shelby[3], and S.E. Lewis'. 'RTI, P.O. Box 12194, RTP, NC 27709-2194; [2]Louisiana State University, Institute for Environmental Studies, Baton Rouge, LA 70803; [3]NIEHS, RTP, N.C. 27709, and •903 Lexington Ct., Cary, NC 27516

Male mice hemizygous for the *lambda/lac/* transgene were treated with the mammalian germ cell mutagen Ethylnitrosourea (ENU) in three weekly-fractionated doses of 100 mg/kg. Ten weeks later they were mated to T-stock females to produce progeny that were screened for both transgene mutations and specific locus mutations. The study was designed to determine if mutations in the transgene were transmitted to progeny. Among the 597 offspring screened, five carried specific locus mutations giving a mutant frequency of 0.0014 per locus which is consistent with previous results using the same treatment regimen. Mutant *lac/* genes were carried by four of the 280 progeny screened. Each of the *lac/* mutant F1 mice carried a mutation at a different site in the transgene as determined by DNA sequence analysis. Each F1 transgene mutant had the same mutation in all somatic tissues sampled, as well as in their germ cells. These results demonstrate that *lac/* mutations induced in male germ cells are effectively transmitted to their progeny. Therefore, transgenic mutation assays can be legitimately used to study induction of mutations in mammalian germ cells and thus can contribute to genetic risk assessment. (This project was supported by NIH R01 ES-06339 and Research Triangle Institute R6599-002).

PS WINDOWS® 32-BIT SOFTWARE FOR THE EPA/IARC GENETIC ACTIVITY PROFILE DATABASE. HF Stack', MA Jackson', WJA Lohman[2], PHM Lohman[2], D McGregor3 and MD Waters•; 'Alpha-Gamma Technologies, Inc., Raleigh, NC 27609; [2]Leiden University Medical Center, Leiden, The Netherlands; [3]International Agency for Research on Cancer, Lyon, France; •usEPA, RTP, NC 27711.

Genetic and related effects data are available in the EPA/IARC Genetic Activity Profile (GAP) database from volumes 1-73 of the IARC Monographs and from selected EPA priority chemical projects. The GAP2000 software for Windows® is used to display histogram plots (profiles), tabular listings, and bibliographies of the toxicological studies on approximately 700 chemicals. The software and database are freely available for downloading via the Internet at www.epa.gov/gapdb. Profiles provide a visual overview of each chemical's test results. The lowest effective dose or highest ineffective dose is recorded from the published primary literature, and a logarithm of the dose is plotted on the histogram for each study. Tests are identified by three-letter codes that are graphically arranged according to the phylogeny of the organisms and the genotoxicity endpoints. GAP2000 uses unique mouse functions to examine the underlying profile data. Icon-activated tool bars, clipboard copying, and windowing features enable the viewing of multiple profiles and data listings. Additional features include Internet hyperlinks to access the IARC carcinogenicity evaluations, a bibliography of the source references for each chemical, and searchable bibliographies and help files. GAP's graphic display is useful for comparative assessments of qualitative and quantitative results across several dimensions (e.g., chemical concordance across species and endpoints, identifying data gaps, and evaluating relative potencies of chemicals). By examining the profiles of chemical analogs, it is possible to make better-informed decisions regarding the selection of tests to evaluate chemicals and their possible modes-of-action. Also, GAP data profiles may be useful in assessing the weight--of-evidence for hazard ranking schemes. *This is an abstract for a proposed scientific presentation and may not necessarily reflect EPA policy.*

A special thanks to GREINER for their contribution to the Coffee Break refreshments

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Pamphlet prepared by Beth George