EXHIBIT 38

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

IN RE: ROUNDUP PRODUCTS LIABILITY LITIGATION	Case No. 16-md-02741-VC MDL No. 2741
This document relates to: ALL ACTIONS	

Glyphosate: Review and Interpretation of Key Aspects of the Scientific Literature Concerning Genotoxicity and Oxidative Stress Data

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Background

I am a Professor in the Department of Pharmacology and Toxicology at Michigan State University. I hold a B.S. degree from Long Island University's College of Pharmacy in Brooklyn, New York. I obtained my Ph.D. in Pharmacology in 1969 from the University of Michigan, Ann Arbor, Michigan. I then completed a post-doctoral fellowship in 1971 at the University of Wisconsin's McArdle Laboratory for Cancer Research. I am board certified by the American Board of Toxicology and Academy of Toxicological Sciences.

After my fellowship, I joined the faculty of Michigan State University's Department of Pharmacology (renamed the Department of Pharmacology and Toxicology in 1978), where I have continued to teach and conduct research on toxicology, with a focus on the mechanisms involved in carcinogenesis, for over four decades. I teach mutagenesis, carcinogenesis, toxicology in drug development, and risk/safety

assessment of carcinogens to undergraduate, and, primarily, graduate students. Additionally, I have taught courses in antibiotics, antiviral drugs and cancer chemotherapy to medical students, and I coordinate a pharmacology course for veterinary students, where I teach the antibiotics section. From 1979-1997, I chaired MSU's Department of Pharmacology and Toxicology's Graduate Committee, playing a key role in recruiting, admission, course development/requirements, comprehensive examination and monitoring student progress.

I have served on a number of advisory committees and boards, including the Boards of Scientific Counselors of the National Toxicology Program and the National Institute of Health's National Institutes of Environmental Health Sciences, Chair of the Carcinogenesis Subcommittee, Committee for the Review of Functions and Purposes of the National Toxicology Program, Department of Health and Human Services, the Advisory Committee to the Director of the Centers for Disease Control and Prevention, the Pharmaceutical Sciences Advisory Committee to the U.S. Food and Drug Administration, the Board of Directors of the American Board of Toxicology, as well as a member of the Expert Review Group, U.S. Environmental Protection Agency Workshop on Cancer Risk Assessment Guideline Issues, Review of the draft revisions to the Guidelines for Carcinogen Risk Assessment. I am currently a member of the Committee on Inorganic Arsenic, National Academies of Science, National Research Council, and Board on Environmental Studies and Toxicology.

I have authored over 130 publications and currently serve as an Associate Editor for the journal *Regulatory Toxicology and Pharmacology* and I am a member of the Editorial Board for the journal *Toxicology*. I previously served as President of the Society of Toxicology (1999-2000) and was recently elected to membership on the Society's Nominating Committee (2017-2019), and I am currently the first American to serve as a member of the Education Subcommittee of the Federation of European Toxicologists & European Societies of Toxicology (EUROTOX). I am also a member of several professional societies, including the American Society for Pharmacology and Experimental Therapeutics, Society of Toxicology, American Association for the

Advancement of Science, American Chemical Society, International Society of Regulatory Pharmacology and Toxicology (I am currently a member of the Society's Council) and the Toxicology Forum (I am currently a member of the Forum's Board of Directors). I have received several awards for my work in Toxicology, including International Society of Regulatory Toxicology and Pharmacology's International Achievement Award (2014), Society of Toxicology's Merit Award (2014), the Toxicology Forum's George H. Scott Memorial Award (2007), John Barnes Prize Lecture, awarded by the British Toxicology Society (2005), among others.

My research interests involve a long-standing focus on discerning epigenetic mechanisms underlying carcinogenesis, with an emphasis on enhancing our understanding of mechanisms by which non-genotoxic compounds can cause cancer. My curriculum vitae, which more fully sets forth my qualifications, is attached as Attachment A.

My opinion is based on my review of the related scientific literature and my professional education, training, research, and experience. Unless otherwise stated, all of my opinions are offered to a reasonable degree of scientific certainty. I reserve the right to supplement or amend this report as new information comes to my attention or becomes available. A list of materials I have considered in forming my opinions is attached as Attachment B.

I am being compensated for my work in this matter at a rate of $450/hour. Over the past four years I have not provided any expert testimony.

Conclusion

My review of the scientific literature dealing with the potential genotoxicity of glyphosate-based formulations (GBFs), glyphosate and aminomethylphosphonic acid (AMPA) leads me to conclude that these should be regarded as non-genotoxic materials. Furthermore, while GBFs and/or glyphosate might be capable of causing oxidative stress under certain experimental conditions, my review of the scientific

literature leads me to conclude that it is not appropriate to use this observation to support a contention that these materials are capable of causing cancer.

My disagreements with the conclusions drawn by Plaintiffs' experts (Drs. Jameson, Nabhan, Neugut, Portier, Ritz and Weisenburger) stem from a difference in perspective. Plaintiffs' experts tend to cite the scientific literature in a fashion that emphasizes the authors' bottom line conclusions without further analysis, while also ignoring large portions of the available science. My approach involves consideration of a larger number of scientific articles and is more focused on taking a constructive, scholarly, critical look at the underlying experimental design and methodology employed to produce the data in order to place the author's results and conclusions into proper perspective.

An example of how this difference in perspective between Plaintiffs' experts and myself leads to different conclusions can be seen in the section of this Report entitled "Genetic Effects (DNA damage or Chromosomal damage) of Glyphosate-Based Formulations (GBFs) in Allegedly Exposed Humans," which appears on p. 12-17. There I present a comparison of my evaluation of two key papers (Paz-y-Mino *et al*. 2007 and Bolognesi *et al*. 2009) which report that genotoxicity is caused in humans exposed to a glyphosate-based formulation (GBF) with views expressed by Plaintiffs' experts.

A Basic Introduction to Toxicity Testing

In a fundamental sense, biology is very complex chemistry. When biological systems, e.g., whole animals, cells in culture, or subcellular organelles (e.g., mitochondria) are exposed to a chemical it is to be expected that effects might occur and not all of these are necessarily indicative of toxicity. Just what these effects are will be dependent on multiple factors, e.g., the particular chemical, test system (e.g., species), dose/concentration used, dosing frequency and route of administration. For example, dosing by the oral route does not necessarily yield the same result as dosing by intravenous administration. When evaluating data obtained from experiments aimed

at identifying the potential of a chemical to cause toxicity these factors need to be taken in to account. In particular, there are three key points that must be kept in mind:

1. The basic maxim in toxicology is that "the dose makes the poison." Thus, what happens at high doses is not necessarily going to occur at lower doses. For example, swallowing a whole bottle of aspirin tablets can be lethal; however, this fact certainly should not dissuade someone from taking a couple of aspirin tablets to alleviate a headache. Additionally, any chemical can cause harm if the dose is pushed high enough, e.g., drinking a very large amount of potable water can be lethal.
2. When looking at various aspects of potential toxicity (e.g., genotoxicity) it is not appropriate to include data obtained when doses/concentrations of the chemical in question are so high that they cause a generalized toxicity to the cell (referred to as cytotoxicity) or cell death. This is because effects observed can occur secondary to cytotoxicity rather than because of the chemical *per se*. For example, when cells are moribund (approaching death), the release of certain enzymes (protein catalysts) from subcellular compartments can damage the cells' genetic material (DNA). Thus, it would be wrong to attribute this damage to a direct effect of the chemical in question.
3. Results obtained from treating cells in culture (*in vitro*, in a plastic dish) with the chemical in question are not directly translatable to what might occur if a whole animal were treated. In the whole animal, a chemical must reach its site of action (the location where the potential toxicity might be triggered) to be able to cause toxicity. This involves absorption and distribution within the body, possibly metabolism (being chemically changed), and excretion from the body (e.g., in urine). All of these factors influence the possibility of toxicity occurring (e.g., a chemical that is excreted rapidly is generally less likely to cause toxicity) and, importantly all are absent when a test chemical is added to cells (or a subcellular organelle, e.g., mitochondria) in a culture dish.

Proper evaluation of the potential for a chemical to cause toxicity includes avoiding biases that could compromise the ability to reach appropriate conclusions. Three of the biases to shun are:

1. Excessive focus on hazard identification. Hazard identification refers to treatment with higher and higher doses/concentrations of the chemical of interest in order to see an adverse effect. An excessive focus on hazard identification represents a bias to be avoided because it ignores the fact that what happens at high doses does not necessarily occur at lower, real world doses. In this context, consider the key points regarding aspirin and water noted above.
2. Ignoring studies which are performed pursuant to internationally accepted regulatory agency guidelines (or well performed studies that were precursors to guideline studies) but not published in the peer reviewed literature. This bias should be avoided because (as will be discussed below) these studies provide a substantial amount of valuable, reliable information for chemicals that are on the market pursuant to approval by regulatory agencies in the US, Europe, and elsewhere.
3. Accepting the results of a study without due consideration of the methodology employed and potential confounding factors. This bias should be avoided because a constructive, critical evaluation of the methodology and potential for confounding factors is necessary in order to have confidence in the results of a study.

Definition of Genotoxicity

Genotoxic chemicals are chemicals capable of damaging DNA. Testing for this needs to be performed under conditions where the use of excessive, cytotoxicity-causing doses/concentrations are avoided in order to not confuse damage secondary to cytotoxicity as being the result of a direct effect of the chemical in question. Genotoxic chemicals can act by either interacting directly with DNA (adduct formation, for example) or following formation of a DNA-reactive metabolite (the chemical of interest is

metabolized, changed in the body to a different form of the original chemical), to a form that is capable of firmly binding (the technical term is “covalent binding”) to DNA (Weisburger and Williams, 1981). Chemicals that test positive for genotoxicity are viewed with some concern regarding their potential to act as carcinogens.

However, not all genotoxic chemicals are carcinogens and not all carcinogens are genotoxic. It is also important to note that genotoxicity (damage to DNA) does not equate with mutagenicity. The term “mutation” refers to a heritable change in DNA. A number of additional steps are involved before genetic damage leads to a mutation. This is because cells have the capacity to repair DNA damage. A very large amount of DNA damage (genotoxicity) occurs in mammalian cells, e.g., in humans, on a daily basis with much of this being endogenous DNA Damage attributed to normal metabolism (Marnett and Plasters 2001). While some of this can result in mutations which are occurring normally (Marnett and Plasters 2001), mammalian cells have developed a capacity to repair DNA damage in order to deal with the DNA damage that is occurring constantly (De Roos *et al.* 2016; Jeggo *et al.* 2016). DNA repair is a key factor which contributes to the observations of no observed effects (e.g., no mutations) following treatment with low doses of genotoxic compounds (Adams *et al.* 2013). Thus, damage to DNA does not necessarily result in a mutation or carcinogenicity.

Genotoxicity and Carcinogenicity

At the outset, it is crucial to place genotoxicity into perspective regarding its relationship to carcinogenicity. When current testing methodologies are employed, all carcinogens are not genotoxic, all genotoxic chemicals are not carcinogens, and many non-carcinogens test positive for genotoxicity. For example, when using a combination of three very commonly used *in vitro* (meaning in a laboratory culture dish, not in a living whole animal or human) genotoxicity tests to evaluate 177 chemicals that were deemed to be non-carcinogenic after testing in a standard, life-time bioassay in male and female rats and mice, 75+% of them gave positive results for genotoxicity in at least one of the genotoxicity assays (Kirkland *et al.* 2005). More weight should be placed on genotoxicity

evaluations when they are conducted properly *in vivo* (meaning in whole animals and/or humans). An important take home message here is the fact that a chemical testing positive for genotoxicity does not equate with it being a carcinogen.

Assessing the Reliability of Genotoxicity Tests

There are considerable advantages to the use of genotoxicity tests performed according to established guidelines (accepted in the US, Europe and many other countries) in order to produce reliable, reproducible results. A key factor that should be considered when evaluating the reliability of genotoxicity tests is an understanding that use of excessive doses/concentrations of a test chemical can cause cytotoxicity (damage to a cell to an extent that it becomes moribund) which can lead to a false positive result in that it occurs secondary to use of an inappropriate high amount of test chemical and therefore is not helpful in evaluating genotoxicity. Furthermore, while we are interested in tests that are reproducible, repeating tests over and over and over again runs the risk of obtaining sporadic false positive results by chance alone.

Test Guidelines: Advantages

The evaluation of the ability of chemicals to cause adverse effects is facilitated by having a series of internationally accepted, periodically updated, standardized methods, e.g., for assessing the potential to cause cancer in rodents and/or genotoxicity. This does not preclude giving consideration to individual research laboratory approaches. However, widely agreed upon standardized procedures are a very important component of safety evaluation because they have been evaluated for reproducibility and readily permit comparisons of the capabilities of multiple chemicals to affect a particular parameter (e.g., a particular aspect of genotoxicity). For example, we know that using excessive concentrations of test chemicals can lead to results that are not relevant to real world situations. Thus, it is very helpful to have agreed upon criteria for the upper level of doses/concentrations of chemicals evaluated in particular tests.

The Organization for Economic Cooperation and Development (OECD) assists countries in harmonizing test methods for chemical safety in order to ensure high quality and reliable data. Membership in this international organization includes most industrialized nations (including the United States) which maintain comprehensive testing requirements for chemicals. The OECD Guidelines for the testing of chemicals are a collection of relevant and internationally agreed testing methods used by governments, industry and independent laboratories to assess the safety of chemicals (http://www.oecd.org/chemicalsafety/testing/oecdguidelinesforthetestingofchemicals.htm) (OECD 2015).

The US Environmental Protection Agency (EPA) (https://www.epa.gov/test-guidelines-pesticides-and-toxic-substances/about-test-guidelines-pesticides-and-toxic) and Food and Drug Administration (FDA) (https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/IngredientsAdditivesGRASPackaging/ucm078311.htm) typically make their data requirements compatible with the OECD's guidelines.

There are 100+ different tests available that purport to assess the genotoxic potential of chemicals. At the outset, these can be narrowed down to four tests which, taken together, focus on covering a spectrum of potential genotoxic events: mutation in bacteria, mutation in mammalian cells in culture, chromosome damage in mammalian cells in culture, and chromosome damage in mammalian cells in vivo. This forms the basic battery of tests employed internationally for registration/approval of chemicals (including medicines) intended to be marketed.

Importantly, a genotoxicity evaluation is one screening tool that can be employed when considering the potential of a chemical to cause toxicity (e.g., cancer) and the results of this should be viewed within a context that can include rodent cancer bioassay and epidemiology data.

The four basic tests employed internationally for registration/approval of chemicals (including medicines and pesticides) intended to be marketed include:

1) **Ames test**: This is a bacterial reverse mutation test. The genetic material (DNA) of the bacteria used contains specific mutations in a gene which carries the information for the synthesis of an essential nutrient. Thus, the bacteria cannot grow without this nutrient being added to the culture media. The test evaluates the ability of the chemical in question to produce a reverse mutation which permits the bacteria to synthesize the essential nutrient and, therefore, allows the bacteria to grow without a requirement for the nutrient to be added to the culture media.
   Many of the chemicals of interest are not capable of causing mutations unless they are metabolized to a form that can react with DNA, i.e., a DNA-reactive metabolite. Bacteria are not capable of carrying out this metabolism. Therefore, a mammalian metabolizing system prepared from rat liver (referred to as the S9 fraction) is routinely employed to simulate metabolic activation which might occur *in vivo*. Thus, the Ames test is typically performed in the presence and absence of an S9 fraction.

2) **Evaluation of mutagenic potential in mammalian cells *in vitro* (the Mouse Lymphoma Assay at the tk locus or use of CHO cells at the HPRT locus).** The tests involve treating cells with a chemical (the "selective agent," which is different from the chemical in question) that requires metabolism (a chemical change) to a form that inhibits growth. These tests evaluate the ability of the chemical in question to cause a mutation that results in blocking the metabolism of the selective agent and, thus, the cells can now grow in its presence.

3) **Evaluation of the potential to cause chromosome aberrations in mammalian cells *in vitro* (chromosome aberration assay) or a micronucleus assay.**

4) **An *in vivo* assay using mice and/or rats (micronucleus test or testing for chromosome aberrations in bone marrow cells).**

Genotoxicity Testing on Glyphosate and Glyphosate-Based Formulations

There have been well over 100 laboratory studies reporting on genotoxicity tests on glyphosate, glyphosate-based formulations, and the metabolites and surfactants related to those formulations. Many of these studies use non-traditional test systems, including fish, oysters, insects, plants, frogs, snails, clams, mussels and worms. Genotoxicity studies using these non-traditional, non-mammalian test systems are dubious, at best, regarding relevance and reliability due to limited/infrequent use and lack of validation. There are also studies in mammalian test systems that are not as informative as the four categories of testing described above, e.g., the Sister Chromatid Exchange assay. Thus, results from these mammalian tests along with the non-mammalian tests mentioned are accorded less weight when considering the potential of a chemical to cause genotoxicity. Accordingly, in evaluating the genotoxic potential of glyphosate-based formulations (GBFs), glyphosate and Aminomethylphosphonic Acid (AMPA), I have emphasized the tests outlined in the four categories noted above. In addition to my view that this is appropriate from a scientific perspective, it is consistent with the fact that they form the backbone of genotoxicity testing employed when evaluating a chemical that is intended to be marketed as a drug or crop protection chemical (e.g., glyphosate).

Genotoxicity Tests Performed on Glyphosate-Based Formulations (GBFs)

Numerous tests have been performed to evaluate the genotoxic potential of glyphosate-based formulations. These include tests involving bacteria (the Ames test),

rodents, mammalian cells in culture (including rodent cells and human cells), and cells obtained from humans who were allegedly exposed to GBFs. There is considerable interest in data obtained from studies involving humans.

I. Genetic Effects (DNA damage or Chromosomal damage) of Glyphosate-Based Formulations (GBFs) in Allegedly Exposed Humans

I have reviewed three publications that report on genetic and related effects (DNA damage and chromosomal damage) in humans reported to be exposed to GFBs.

The first publication (Paz-y-Mino *et al*. 2007) reported that DNA strand breaks (Comet assay) were observed in individuals in Ecuador in areas sprayed with a GBF. The author concludes (as stated in the Abstract) that "These results suggest that the formulation used during aerial spraying glyphosate had a genotoxic effect on the exposed individuals." My review of this paper reveals four major concerns which cast serious doubt on the validity of the conclusion reached:

1) On p. 457 of the paper, the author states "A clinical history was completed for each of the exposed individuals and a wide-range of reactions were noted, including intestinal pain and vomiting, diarrhea, fever, heart palpitations, headaches, dizziness, numbness, insomnia, sadness, burning of eyes or skin, blurred vision, difficulty in breathing and blisters or rash." These people appear to be seriously ill. A thorough investigation would have been necessary in order to ascertain the cause(s) of their illness, including what other chemicals they were exposed to, and how that might have contributed to the DNA strand breaks reported. Under these circumstances, it is not appropriate to simply conclude that DNA damage is related directly to GBF exposure.
2) Furthermore, blood samples were taken from people between two weeks and two months after exposure to aerial spraying. During this excessive lag time the people might have been exposed to numerous chemicals, other than GBFs, which could have influenced the results. Therefore, because of the excessive lag

time one cannot state with any degree of certainty that any effects observed were due to GBFs. The type of DNA damage detected by the Comet Assay can be repaired by the cell or, if it is severe, lead to cell death. Thus, DNA damage detected weeks to months after spraying of a GBF is highly unlikely to be due to a GBF.

3) When describing the methodology employed, Paz-y-Mino *et al.* 2007 state (p. 458 of the paper) that "Cells were visually allocated to classified one of five predefined categories (A-E) according to the amount of DNA in the comet's tail, tail and a rank-number of from 0 (A) to 400 (E) was assigned to quantify the damage in each cell and calculate a mean of the amount of DNA damage (Anderson *et al*., 1994)." However, the way this "rank number" was used to arrive at the data presented in Table 1 of the Paz-y-Mino *et al.* 2007 paper is not stated clearly. Furthermore, the reference cited for the methodology (Anderson *et al*., 1994) does not mention anything about using "a rank-number of from 0 (A) to 400 (E) was assigned to quantify the damage in each cell and calculate a mean of the amount of DNA damage." Additionally, the Anderson *et al*., 1994 paper (p. 264 of the paper) states that their analysis was performed by one slide reader in order to minimize variability due to subjective scoring and the particular author who performed the analysis is identified. The Paz-y-Mino *et al.* 2007 paper does not indicate that a particular author performed the analysis. This suggests that multiple individuals might have participated and raises the possibility that subjectivity entered into the data analysis.
4) The author used a Comet assay described by Singh *et al*. 1988 to test for the presence of DNA strand breaks. Singh *et al*. 1988 indicate (bottom of p. 190) that they observe cellular heterogeneity (e.g., there was not uniformity, there were differences between cells) in response to DNA damage. Thus, it becomes important for Paz-y-Mino *et al*. 2007 to discuss the degree to which they encountered heterogeneity and how this was taken into account when their data were analyzed. This was not done.

Furthermore, the EPA's Office of Pesticide Programs places the Paz-Mino 2007 study in a list of studies "assigned a low quality ranking and not evaluated in detail" (EPA 2016 – Appendix D, p. 196).

Conclusion regarding the Paz-y-Mino *et al*. 2007 paper: The Paz-y-Mino *et al*. 2007 paper is flawed to the point that it represents an inadequate study to evaluate the potential of GBFs to cause genotoxicity in humans.

Differences Between My Perspective on the Paz-y-Mino *et al*. 2007 paper and the Perspectives presented by the Plaintiff's Experts

My review of the Paz-y-Mino *et al*. 2007 publication reveals major concerns which cast serious doubt on the validity of the conclusion reached. The author indicates that the people were seriously ill and there is a problem with the methodology used. However, the two Plaintiff's experts (Drs. Neugut and Portier) who refer to this paper in their reports simply accept the conclusion reached by the author. Dr. Neugut (on p. 37 of his report) reproduces a portion of the IARC 2015 Report's Table 3A which very briefly summarizes Paz-y-Mino *et al*. 2007 without any of his own analysis of it. Dr. Portier (on pp. 53-54 of his report) summarizes Paz-y-Mino *et al*. 2007 and concludes "In essence, some of the DNA had been fragmented by the exposure." However, he neither identifies nor addresses the serious methodological concerns described in my report.

The second publication (Paz-y-Mino *et al*. 2011) reported that no damage (chromosomal aberrations) was detected in blood cells (cell type not specified) obtained from 92 individuals from the Northeastern Ecuadorian border which had undergone aerial spraying with GBFs up until 2 years prior to when the blood samples were taken. This result provides further support of the lack of genotoxicity of GBFs, especially lack of persistent genotoxicity.

The third publication (Bolognesi *et al*. 2009) reported chromosomal damage (micronucleus formation) in blood cells (lymphocytes) in five regions of Colombia. Blood was obtained from human subjects from five regions of Colombia and lymphocytes were evaluated. An increased frequency of binucleated cells with micronuclei (BNMN) was used as a measure of genotoxicity. The authors report (Abstract) that compared with Sana Marta where organic coffee is grown without pesticides (presumably glyphosate was lumped into the term pesticide) the frequency of BNMN was higher in subjects from the other four regions. However, the highest reported frequency of BNMN was in Boyaca where *no* aerial spraying of glyphosate was conducted. As stated in the Abstract, "The increase in frequency of BNMN observed immediately after the glyphosate spraying was **not** [emphasis added] consistent with the rates of application used in the regions and there was no association between self-reported direct contact with eradication sprays and frequency of BNMN." Furthermore, the authors' conclusion (last sentence of the Abstract) is very tentative in stating that "Evidence indicates that the genotoxic risk potentially associated with exposure to glyphosate in the areas where the herbicide is applied for coca and poppy eradication is low." The paper's Discussion states:

> …one of the major drawbacks of environmental epidemiology studies is the characterization of exposures to the agents being investigated … Although temporality was satisfied in the increase in frequency of BNMN after spraying, this response did not show strength as it was not consistently correlated with the rate of application. Recovery was also inconsistent with decreases in frequency of BNMN in the areas of eradication spraying but not in the area where lower rates were applied on sugar cane. Further studies are needed to better characterize the potential genotoxic risk associated with the application of glyphosate for sugar cane maturation. The smaller number of subjects recruited in this study and small amount of information about exposure precluded any conclusions … there is not sufficient information to correlate the frequency of MN to the pesticide exposure.

The IARC Monograph on Glyphosate (Table 4.1) indicates that the study provides positive results for genotoxicity in three of the regions of Colombia (Nariño, Putumayo and Valle del Cauca) (IARC 2015). However, IARC fails to note that the highest frequency of BNMN was reported to occur in Boyaca, an area where there was

no aerial spraying of glyphosate (Bolognesi *et al*. 2009). Furthermore, the EPA's Office of Pesticide Programs places the Bolognesi 2009 study in a list of studies "assigned a low quality ranking and not evaluated in detail" based on several valid concerns (EPA 2016 – Appendix D, p. 196).

Conclusion Regarding the Findings Reported by Bolognesi *et al*. 2009

Based on the limitations of the Bolognesi *et al*. 2009 study reviewed above, which are reflected in the EPA's view that the study is of "low quality," I conclude that the paper is flawed to the point that it represents an inadequate study to evaluate the potential of GBFs to cause genotoxicity in humans.

Differences Between My Perspective on the Bolognesi *et al*. 2009 paper and the Perspectives presented by the Plaintiff's Experts

My review of the Bolognesi *et al*. 2009 publication reveals major concerns which cast serious doubt on the validity of even the weak conclusion reached (the authors' conclusion, stated in the last sentence of the Abstract is that "Evidence indicates that the genotoxic risk potentially associated with exposure to glyphosate in the areas … is low."). I point out that the authors raise serious doubts concerning their own conclusion when they state in the paper that:

> this response [the genotoxic response] did not show strength as it was not consistently correlated with the rate of application… Further studies are needed to better characterize the potential genotoxic risk associated with the application of glyphosate [actually a GBF was involved] ... The smaller number of subjects recruited in this study and small amount of information about exposure **precluded any conclusions** [emphasis added] … there is **not sufficient information** [emphasis added] **to correlate the frequency of MN** [the genotoxic effect being evaluated, emphasis added] **to the pesticide exposure** [emphasis added]."

I also note that the US EPA considers the study to be of "low quality" (EPA 2015).

However, the Plaintiffs' experts fail to mention the serious concerns about the validity of the weak conclusion reached by Bolognesi *et al*. 2009. Dr. Neugut mentions Bolognesi *et al*. 2009 on p. 18 of his report stating that "the observed increases in micronuclei formation was reported to be inconsistent with the rates of application used;" however, he does not talk about how this calls into question the validity of the study. Drs. Nabhan, Weisenburger, and Jameson talk about Bolognesi *et al*. 2009 (on p. 9, 8, and 30 of their reports, respectively); however, they do not address the concerns I have raised. Dr. Portier talks about the data presented Bolognesi *et al*. 2009 on pp. 54-55 of his report. However, he, too, says nothing about the concerns I have raised. It is noteworthy that none of the Plaintiffs' experts mention the concerns regarding the severe limitations of the Bolognesi *et al*. 2009 study that are presented by the study's authors themselves.

Conclusion regarding genetic effects (DNA damage or chromosomal damage) of glyphosate-based formulations (GBFs) in exposed humans

The publications reviewed above do not support a contention that GBFs cause genotoxicity in humans.

II. Genetic Effects of Glyphosate-Based Formulations (GBFs) in bacteria, mammalian cells *in vitro*, and non-human mammals *in vivo*

The EPA has done a very good job compiling many of the genotoxicity tests performed on GBFs (EPA 2016). These data are presented in the Appendix (Appendices 1-5). I have made comments regarding each category of test (Ames, *in vitro* chromosome damage, *in vivo* chromosome aberrations, *in vivo* micronuclei, and other assays for detecting DNA damage) below.

A. Ames Tests[1]

I have reviewed the underlying study reports for 38 Ames tests, as well as relevant study summaries for at least 12 additional Ames tests, conducted with GBFs. Each was performed in the presence and absence of a metabolic activation system and all of them involved the use of multiple tester strains of bacteria and multiple doses of the test chemical. This is a very rich data set. All of the studies were negative (no indication of genotoxic potential).

For example, Kier 1992 evaluated the mutagenic potential of a GBF (MON 14445) in four tester strains of *S. typhimurium* in both the presence and absence of added mammalian drug metabolizing enzymes (to compensate for the fact that bacteria lack the ability mammalian cells have to metabolize some chemicals to a form that is capable of causing mutations). Multiple, appropriate concentrations of the test chemical were used. Toxicity was observed consistently at the high dose, for all four strains and with or without added drug metabolizing enzymes. Positive controls were used to confirm that the test systems were indeed functioning as they should. The positive controls consistently produced positive responses while the GBF consistently produced negative results.

In another example, not considered by EPA, Wagner 2013 evaluated the mutagenic potential of a GBF (MON 76855) in four tester strains of *S. typhimurium* and in one tester strain of E. coli, in both the presence and absence of added mammalian drug metabolizing enzymes (to compensate for the fact that bacteria lack the ability mammalian cells have to metabolize some chemicals to a form that is capable of causing mutations). Very high doses of the GBF were employed and some toxicity was observed at the higher doses of 1,500 and 5,000 µg/plate. This is an indication that the test was pushed to its limits in an attempt to discern a positive result. Positive controls were used to confirm that the test systems were indeed functioning as they should. The

[1] Appendix-1: EPA's Table F.1. *In Vitro* tests for gene mutations in bacteria [Ames Test]: GBFs

positive controls consistently produced positive responses while the GBF consistently produced negative results.

All of these studies indicate that GBFs do not cause mutations in bacterial-based test systems.

B. *In Vitro* tests for chromosomal damage in mammalian cells[2]

I have reviewed two studies which evaluated the ability of GBFs to cause chromosomal damage in mammalian cells *in vitro*. The first study (Holeckova 2006) was negative with regard to chromosomal damage when concentrations of 28, 56, 140, 280, 560, and 1120 µmolar were evaluated. The author indicated that the GBF used contained "glyphosate [at] approximately 62% by weight with 38% inert ingredients." Therefore, it appears that the molar concentrations used were based on the amount of glyphosate present. The author reported a slight but statistically significant increase in polyploidy (a condition that occurs when a cell contains more than the expected two paired sets of chromosomes) at only one of the concentrations tested, the 56 µmolar concentration. There was no statistically significant increase at any of the other concentrations tested. The lack of a dose-response relationship indicates there is not a basis for considering that the GBF caused an increase in polyploidy under the reported test conditions.

The second study, study by Koller *et al*. 2012, the author reported that all concentrations of the GBF evaluated showed a statistically significant increase in cytotoxicity (damage to cell membranes), including the lowest concentration tested (10 mg/L). This indicates that the experimental conditions were not appropriate for evaluating genotoxicity. It is likely that the chromosome damage reported is secondary to cytotoxicity and not because the GBF is genotoxic.

[2] Appendix 2: EPA's Table F.2. *In Vitro* tests for chromosomal damage in mammalian cells: GBFs

I conclude that the studies captioned above do not indicate that GBFs are capable of causing chromosomal damage in mammalian cells.

C. *In Vivo* tests for chromosomal aberrations in mammals[3]

I have reviewed the results of three *in vivo* studies for chromosomal aberrations. One study reported negative results (Dimitrov *et al.* 2006), while two reported positive results (Prasad *et al*. 2009; Helal and Moussa 2005).

Prasad *et al*. 2009 evaluated the ability of a GBF (Roundup) to cause chromosome aberrations or micronuclei in bone marrow cells of mice following intraperitoneal (i.p.) administration, and reported a statistically significant increase in chromosome aberrations and micronuclei. However, two factors need to be kept in mind: 1) the doses of GBF used were cytotoxic to bone marrow cells (as evidenced by a decrease in mitotic index; and 2) the GBF was administered by the i.p. route, the peritoneal cavity has a very rich blood supply and i.p. injection of a test chemical results in extremely rapid absorption, similar to an intravenous injection. This is highly non-physiological, meaning that it is very dissimilar from the relatively slower expected rates of absorption which occurs from typical routes (e.g., oral, inhalation, dermal) of human exposure. The much higher rate of absorption following i.p. administration might result in toxicity that would not be observed following dosing under the more physiological routes of administration.

I conclude, based on the discussion above, that the Prasad *et al.* 2009 study should not be used as a basis for considering whether or not GBFs might cause chromosomal aberrations in mammals. Thus, of the three studies reported in Table F.3, I consider that only one (Helal and Moussa 2005) of them might be positive, though the dose used and 2-month continuous dosing period appear to be quite high and an evaluation of toxicity was not performed for this dosing scenario. Additionally, and

[3] Appendix 3: EPA's Table F.3. *In Vivo* tests for chromosomal aberrations in mammals: GBFs

importantly, the study is compromised by the fact that chromosomes from only 50 bone marrow cells were evaluated for each animal as compared to the OECD Guidelines (OECD 2016) which call for evaluating chromosomes from at least 200 cells/animal. Furthermore, OECD Guidelines (OECD 2016) call for an evaluation of cytotoxicity to be performed for all animals. These issues cause me to question whether the effects observed by Helal and Moussa 2005, who performed a less rigorous evaluation than that called for by OECD, are pertinent to the human experience.

D. *In vivo* tests for micronuclei induction in mammals[4]

I reviewed the results of 20 studies of *in vivo* tests for micronuclei induction in mammals. All 20 studies reported negative results. My review included studies beyond those reviewed by EPA. For example Kier 1992 evaluated the ability of a GBF (RODEO Herbicide Formulation) to cause formation of micronuclei in male and female mice using three doses (850, 1,700 and 3,400 mg/kg), a positive control was included, and results from this indicated the test system was working. The highest dose used (3,400 mg/kg) is very close to (80% of) the lethal dose. It is important to note that the highly non-physiological i.p. route of administration (discussed in detail above) was used. Even under these extreme conditions, no statistically significant increases in micronuclei were observed in either male or female mice.

E. Other assays for detecting DNA damage[5]

I reviewed the results of 8 studies that EPA classifies as "other assays for detecting DNA damage" and all of them are considered by their authors to be positive. None of these tests fall into the category of the four types of genotoxicity guideline tests, described above, which are most relied on by regulatory agencies in the US and Europe.

[4] Appendix 4: EPAs Table F.4. *In vivo* tests for micronuclei induction in mammals: GBFs
[5] Appendix 5: EPAs Table F.5. Other assays for detecting DNA damage: GBFs

Three of the tests reported as positive involve the Sister Chromatid Exchange (SCE) assay. The SCE assay was deleted from the Organization for Economic Cooperation and Development's approved Test Guidelines in 2014 because "of a lack of understanding of the mechanism(s) of action of the effect detected by the test" (OECD 2016). Therefore, the results obtained from this assay should not be used in an evaluation of the genotoxic potential of GBFs.

One of the tests reported to be positive is a Bacterial SOS Chromotest (Raipulis *et al.* 2009). This test is very infrequently used. The paper does not provide an indication as to how many replicates were performed for each dose of GBF evaluated. The results of the assay are depicted in Figure 3 of the paper and what we see are single points for each concentration. Importantly, we do not have an indication of the degree of variability, as no statistical analysis is presented. This omission precludes the reader's ability to determine whether or not there is a real difference between treatment and control or if there is a true dose-response relationship. Therefore, it is not appropriate to use the results presented by Raipulis *et al*. 2009 in an evaluation of the genotoxic potential of GBFs. Furthermore, the Bacterial SOS Chromotest has been eclipsed by the Ames bacterial test and, as noted above, GBFs have been shown to be negative in all 38 studies and 12 study summaries I reviewed based on the Ames test. Therefore, the results of testing in bacteria show quite clearly that GBFs overwhelmingly test negative.

One of the tests reported to be positive involved evaluating DNA adducts in mice using the ^{32}-P-postlabeling technique (Peluso *et al*. 1998). However, the highly non-physiological i.p. route of administration was used. As discussed above, the much higher rate of absorption following i.p. administration might result in toxicity that would not be observed following dosing under the more physiological routes of administration. Therefore, I conclude that the Peluso *et al*. 1998 study should not be used as a basis for considering whether or not GBFs might cause pertinent DNA damage in mice.

Another test reported to be positive involved evaluating DNA oxidative damage in mice, again using the non-physiological i.p. route of administration (Bolognesi *et al.* 1997). As discussed above, the much higher rate of absorption following i.p. administration might result in toxicity that would not be observed following dosing under the more physiological routes of administration. Additionally, Bolognesi *et al*. 1997 did not include an evaluation of cytotoxicity at the doses tested in their study. This raises the very real possibility that the oxidative stress reported might have been secondary to cytotoxicity. Therefore, in light of the use of the i.p. route of administration and lack of an evaluation of cytotoxicity, I conclude that it is not appropriate to use results reported by Bolognesi *et al.* 1997 in an overall evaluation of the potential of GBFs to cause DNA damage.

An additional test reported to be positive involved use of mice and an Alkaline Elution Assay-DNA Single Strand Breaks [what we would now refer to as a Comet Assay] (Bolognesi *et al*. 1997). However, the highly non-physiological i.p. route of administration was used. As discussed above, the much higher rate of absorption following i.p. administration might result in toxicity that would not be observed following dosing under the more physiological routes of administration. Additionally, as mentioned above, Bolognesi *et al*. 1997 did not include an evaluation of cytotoxicity at the doses tested in their study. This raises the very real possibility that that the DNA damage reported might have been secondary to cytotoxicity. Therefore, in light of the use of the i.p. route of administration and lack of an evaluation of cytotoxicity, I conclude that it is not appropriate to use results reported by Bolognesi *et al*. 1997 in an overall evaluation of the potential of GBFs to cause DNA damage.

One of the tests reported to be positive (Koller *et al*. 2012) used a Single Cell Gel Electrophoresis (SCGE) assay (a Comet assay) to evaluate the ability of a GBF (Roundup Ultra Max) to cause DNA damage. However, the paper also reports that there is a statistically significant increase in cell membrane damage at concentrations of 10 mg/ml and higher. Therefore, it appears likely that the DNA damage observed was

not due to the GBF but, rather, secondarily to the use of excessive concentrations of glyphosate which resulted in cytotoxicity.

Conclusion Regarding the Genotoxic Potential of GBFs

I conclude that GBFs are not genotoxic. It is important to note that the results of the reliable, reproducible guideline studies indicate that GBFs are not genotoxic. The few non-guideline studies which report that GBFs are genotoxic have methodological faults.

Genotoxicity Tests Performed on Glyphosate

The EPA has done a very good job compiling the genotoxicity tests performed on glyphosate (EPA 2016). These studies indicate that glyphosate is a non-genotoxic compound. These data are presented in the Appendix (Appendices 1-7). I have made comments regarding each category of studies, below.

A. Ames Tests[6]

I have reviewed underlying study reports or relevant study summaries for 27 Ames studies conducted with glyphosate. Each was performed in the presence and absence of a metabolic activation system and all of them involved the use of multiple tester strains of bacteria and multiple doses of the test chemical. As with GBFs, this is a very rich data set. All of the studies were negative (no indication of genotoxic potential).

For example, Callander 1999 evaluated the mutagenic potential of a potassium salt of glyphosate in four tester strains of *S. typhimurium* and two tester strains of *E. coli* in both the presence and absence of added mammalian drug metabolizing enzymes (to

[6] Appendix-6: EPA's Table 5.1. *In Vitro* tests for gene mutations in bacteria [Ames Test]: Glyphosate technical

compensate for the fact that bacteria lack the ability mammalian cells have to metabolize some chemicals to a form that is capable of causing mutations). Multiple, appropriate concentrations of the test chemical were used. A positive control, a known mutagen, was use to confirm that the test systems were indeed functioning as they should. The positive control consistently produced positive responses while glyphosate consistently produced negative responses.

B. *In Vitro* mammalian gene mutation assays[7]

I have reviewed underlying study reports or relevant study summaries for 4 *in vitro* mammalian gene mutation assay studies on glyphosate. Each was performed in the presence and absence of a metabolic activation system. All of the studies were negative (no indication of genotoxic potential).

For example, a CHO/HGPRT Gene Mutation Assay was conducted with glyphosate by A.P. Li in 1983 (Li 1983). This study included a preliminary toxicity test which showed that a glyphosate concentration of 30 mg/ml caused an extreme level of cytotoxicity and, therefore 25 mg/ml was selected as the highest concentration for testing. The tests were performed in the presence and absence of added mammalian drug metabolizing enzymes. Furthermore, two positive controls were used, one that requires metabolism in order to act as a mutagen and one that does not. The positive controls behaved as expected, thus validating the fact that the test system was functioning properly. Glyphosate did not cause evidence of mutation in this test system.

C. *In Vitro* tests for chromosomal aberrations in mammalian cells[8]

I have reviewed relevant study summaries or published articles for 8 *in vitro* tests for chromosomal aberrations in mammal cells conducted with glyphosate. The results

[7] Appendix-7: EPA's Table 5.2. *In Vitro* mammalian gene mutation assays: Glyphosate technical

[8] Appendix 8: EPA's Table 5.3. *In Vitro* tests for chromosomal aberrations in mammalian cells: Glyphosate technical

of 6 were negative (no indication of genotoxic potential) while 2 were positive (possibly suggestive of genotoxic potential). The positive results might have occurred, for example, due to the use of excessive concentrations of the test chemical or, possibly, by chance alone. There is a need to look at the body of data, including the methodology employed to produce it, in order to place results into proper perspective.

As an example, one of the studies which reported negative results (Matsumoto 1995) is based on the use of multiple time points and experiments in which cells were treated both in the absence and presence of mammalian drug metabolizing enzymes. In addition, a positive control was employed. It yielded the anticipated chromosomal aberrations and, thus demonstrated that the experimental system was working.

In contrast to this methodology, one of the studies reported that glyphosate produced chromosome aberrations in cultured human lymphocytes following treatment for 72 hours (Lioi *et al*. 1998). The authors evaluated cell viability (an indication of cytotoxicity) at 6 hours after exposure to glyphosate and reported "an increasing trend of cell death" which was not statistically significant. In light of this finding, the author should have repeated the cytotoxicity evaluation at the 72-hour time point at which chromosome aberrations were observed. One can reasonably anticipate that more cytotoxicity would be observed at the longer treatment period. Failure to perform the appropriate cytotoxicity evaluation raises very serious doubts concerning the validity of the author's conclusion. It appears likely that the chromosome aberrations observed were not due to glyphosate but, rather, secondarily to the use of excessive concentrations of glyphosate which resulted in cytotoxicity.

D. *In vitro* tests for micronuclei induction in mammalian cells[9]

I have reviewed 6 *in vitro* studies for micronuclei induction in mammalian cells with glyphosate. Four were positive (possibly suggestive of genotoxic potential) and

[9] Appendix-9: EPA's Table 5.4. *In vitro* tests for micronuclei induction in mammalian cells: Glyphosate technical

two were deemed to be equivocal. As outlined below, several factors may have affected the validity of the results/conclusions reported in these six studies.

Koller *et al*. 2012 reported that frequencies of micronuclei were elevated following treatment of glyphosate at concentrations on 10-20 mg/ml. However, the paper also reports that there is a statistically significant increase in cell membrane damage at concentrations of 10 mg/ml and higher. Therefore, it appears likely that the micronuclei induction observed was not due to glyphosate but, rather, secondarily to the use of excessive concentrations of glyphosate which resulted in cytotoxicity.

Roustan *et al*. 2014 failed to demonstrate the dose-response relationship which is anticipated if induction of micronuclei were due to treatment with glyphosate.

Piesova *et al*. 2004 and 2005 failed to demonstrate the dose-response relationships anticipated if induction of micronuclei were due to treatment with glyphosate and, importantly, did not evaluate cytotoxicity.

Mladinic *et al*. 2009a and 2009b did not evaluate cytotoxicity and it is important to note that Mladinic *et al*. 2009a state (in the Abstract) that "Since for any of the assays applied, no clear dose-dependent effect was observed, it indicates that glyphosate in concentrations relevant to human exposure do not pose significant health risk."

E. *In vivo* tests for chromosomal aberrations in mammals[10]

I have reviewed underlying study reports or relevant study summaries for 3 chromosomal aberration tests and 2 rodent dominant lethal tests and all were negative (no indication of genotoxic potential).

[10] Appendix-10: EPA's Table 5.5. *In vivo* tests for chromosomal aberrations in mammals: Glyphosate technical

The *in vivo* chromosomal aberration test involves administration of the chemical of interest to whole animals (male and female rats were used in the test summarized here) and evaluating its ability to cause aberrations (damage) to chromosomes of bone marrow cells. There is a very large amount of cell proliferation that normally occurs in bone marrow and this provides an environment where chromosome aberrations can be relatively easily detected, if they occur. The study by Li 1983 involved the use of one very high dose of glyphosate (1,000 mg/kg) or a solvent control and evaluation of bone marrow at three time points (6, 12 and 24 hours after treatment). Importantly a positive control, a chemical expected to produce chromosomal aberrations, was included and caused its expected effect, indicating the test system was working. Treatment with glyphosate did not result in an increase in chromosomal aberrations above control levels.

The rodent Dominant Lethal test involves treatment of males (rats or mice) with the test substance prior to mating them with untreated, virgin females. The endpoint is lethality to embryos/fetuses after implantation and prior to delivery. The underlying premise is that an increase in lethality over control indicates the chemical in question caused a mutation in sperm. The study by Wrenn 1980 represents a robust experiment involving 10 male mice per treatment group. The groups consisted of: a positive control (a chemical that is known to give a positive result in the assay and is used to verify that the assay is working); a vehicle control (which is just the solvent that the chemical of interest is dissolved in, which is used to see if the solvent by itself can affect the assay's results), and three very high doses of glyphosate (200, 800 and 2,000 mg/kg). Each male was mated with 16 mature virgin females who were examined 13-days after mating. The positive control produced the expected increase in fetal deaths, indicating the test system was working properly, while the glyphosate-treated groups showed no increases over the vehicle control.

F. *In vivo* tests for micronuclei induction in mammals[11]

I have reviewed relevant study summaries or published articles for 19 *in vivo* tests for micronuclei induction in mammals. Three were positive (possibly suggestive of genotoxic potential) while 16 were negative (no evidence of genotoxic potential).

Positive responses were reported by Bolognesi *et al*. 1997 and Mañas *et al*. 2009 following administration of glyphosate to mice using doses of 300 mg/kg and 200 mg/kg, respectfully. Regarding Bolognesi *et al*. 1997, a highly non-physiological i.p. route of administration was used. As discussed above, the much higher rate of absorption following i.p. administration might result in toxicity that would not be observed following dosing under the more physiological routes of administration. Additionally, Bolognesi *et al*. 1997 did not include an evaluation of cytotoxicity in their study. This is a fundamental error. Without this the possibility that the finding reported might have been secondary to cytotoxicity cannot be ruled out. Therefore, in light of the use of the i.p. route of administration and lack of an evaluation of cytotoxicity, I conclude that it is not appropriate to use results reported by Bolognesi *et al*. 1997 in an overall evaluation of the potential of glyphosate to cause DNA damage.

There are 9 studies which employed doses of 300 mg/kg or higher (6 of these involved doses of 1,000 to 5,000 mg/kg) and reported that there was no induction of micronuclei. In one study, a significant increase was reported to occur in female mice following treatment with a dose of 5,000 mg/kg (Suresh 1993a). This is in contrast to two studies (Jensen 1991; Fox and Mackay 1996) which reported negative results when glyphosate doses of 5,000 mg/kg were used. To place this extremely high dose into perspective, it should be noted that the US EPA estimates that the exposure of the US population to glyphosate by food and water is 0.088 mg/kg/day (Solomon 2016) and US EPA considers children 1-2 years old the most highly exposed subpopulation with an estimated combined exposure of 0.47 mg/kg/day (EPA 2016) making a 5,000 mg/kg

[11] Appendix 11: EPAs Table 5.6. *In vivo* tests for micronuclei induction in mammals: Glyphosate technical

dose to the mice equivalent to 56,818 and 10, 638 times higher than the human daily dose, respectively. Thus, the body of evidence indicates that glyphosate is not genotoxic based on the *in vivo* tests for induction of micronuclei.

G. Assays for detecting primary DNA damage[12]

I have reviewed relevant study summaries or published articles for 15 studies with glyphosate detecting primary DNA damage. None of these tests fall into the four types of genotoxicity guideline tests, described above, which are most relied on by regulatory agencies in the US and Europe in assessing genotoxicity. Ten were positive (possibly suggestive of genotoxic potential) and 5 were negative (no evidence of genotoxic potential). It is important to understand that these assays do not measure mutation or damage to chromosomes. The endpoints evaluated might cause cell death. However, it is very possible that the damage in question could be repaired. Furthermore, for some of these tests, e.g., the Comet assay, a positive result can occur secondary to excessive dose (concentration)-induced cytotoxicity.

The Sister Chromatid Exchange (SCE) assay accounted for four of the ten positive tests. As noted above, there are significant concerns regarding this test. Therefore, the results obtained from this assay should not be used in an evaluation of the genotoxic potential of glyphosate.

Positive results using the Comet assay were reported by Mañas *et al*. 2009b and Alvarez-Moya *et al.* 2014. However, neither of these studies included an evaluation of glyphosate-induced cytotoxicity. Since a positive in the Comet assay can be secondary to cytotoxicity and given the omission of this analysis, it would be inappropriate to view the results of these studies as indicating that glyphosate is a genotoxic compound. Additionally, the data reported in both studies do not show a clear dose-response

[12] Appendix- 12: EPAs Table 5.7. Assays for detecting primary DNA damage: Glyphosate technical

relationship. This adds to the concern over the validity of the conclusions reached and thus they cannot be relied on to conclude glyphosate is genotoxic.

Conclusion Regarding the Genotoxic Potential of Glyphosate

Based on the data and discussion presented above, I conclude that glyphosate should be viewed as a non-genotoxic compound. While there were occasional positives, some of which might have occurred by chance, among the very numerous tests for genotoxicity, these are far outweighed by the overwhelmingly negative results.

This conclusion is consistent with:

1. US Environmental Protection Agency (EPA)

The EPA recently released a "Glyphosate Issue Paper: Evaluation of Carcinogenic Potential" (EPA 2016) which includes a thorough evaluation of the genotoxic potential of glyphosate. The Agency stated (Section 6.3, p. 131) "Over 80 genotoxicity studies with the active ingredient glyphosate were analyzed for the current evaluation. The overall weight-of-evidence indicates that there is no convincing evidence that glyphosate is genotoxic *in vivo* via the oral route. When administered via i.p. injection the studies were predominantly negative. In the two cases where an increase in micronuclei were reported via this route, the effects were not observed in other i.p. injection studies at similar or higher doses. Technical glyphosate was negative in all gene mutation studies. There was limited evidence of positive findings in studies evaluating primary DNA damage; however, as discussed in Section 5.6, the endpoints measured in these assays are less specific in regards to detecting permanent DNA changes (mutations) and can be attributed to other factors, such as cytotoxicity or cell culture conditions. Although some positive findings were reported for chromosomal alterations *in vitro*, these findings were limited to a few studies and are not supported by the *in vivo* studies that are the most relevant for human risk assessment."

2. European Food Safety Authority (EFSA)

EFSA published its "conclusion on the peer review of the pesticide risk assessment of the active substance glyphosate" (EFSA 2015). The report states (p. 10) that "Glyphosate did not present genotoxic potential…."

3. Joint FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization) Meeting on Pesticide Residues (JMPR 2016)

The JMPR stated that "Glyphosate has been extensively tested for genotoxic effects using a variety of tests in a wide range of organisms. The overall weight of evidence indicates that administration of glyphosate and its formulation products at doses as high as 2000 mg/kg body weight by the oral route, the route most relevant to human dietary exposure, was not associated with genotoxic effects in an overwhelming majority of studies conducted in mammals, a model considered to be appropriate for assessing genotoxic risks to humans." (JMPR 2016).

4. European Chemicals Agency (ECHA) (ECHA 2017)

On 15 March 2017 ECHA issues a statement entitled "Glyphosate not classified as a carcinogen by ECHA" (ECHA 2017) which stated "ECHA's Committee for Risk Assessment (RAC) … concluded that the available scientific evidence did not meet the criteria to classify glyphosate as a carcinogen, as a mutagen or as toxic for reproduction."

5. Williams *et al*. (2000). Safety evaluation and risk assessment of the herbicide roundup and its active ingredient, glyphosate, for humans. Regulatory Toxicology and Pharmacology 31: 117-165.

Williams *et al*. (2000) stated that "In view of the clear negative responses in relevant, well-validated assays conducted under accepted conditions, it is concluded

that glyphosate is neither mutagenic or clastogenic. On the basis of this evaluation, glyphosate does not pose a risk for production of heritable or somatic mutations in humans." Furthermore, the Abstract states "There was no convincing evidence for direct DNA damage *in vitro* or *in vivo*, and it was concluded that Roundup and its components do not pose a risk for the production of heritable/somatic mutations in humans."

6. Kier, L.D. and Kirkland, D.J. (2013). Review of genotoxicity studies of glyphosate and glyphosate-based formulations. Critical Reviews in Toxicology 43: 283-315.

Kier and Kirkland (2013) concluded that "Glyphosate and typical GBFs (glyphosate-based formulations) do not appear to present significant genotoxic risk under normal conditions of human or environmental exposure."

7. Brusick *et al*. (2016). Genotoxicity Expert Panel review: weight of evidence evaluation of the genotoxicity of glyphosate, glyphosate-based formulations and aminomethylphosphonic acid. Critical Reviews in Toxicology 46 (S1): 56-74.

Brusick *et al*. 2016 concluded "… glyphosate, glyphosate formulations, and AMP (aminomethylphosphonic acid) do not pose a genotoxic hazard…."

Genotoxicity Tests Performed on Aminomethylphosphonic Acid (AMPA)

Aminomethylphosphonic acid (AMPA) is a biodegradation product of glyphosate sometimes found in soil. I have reviewed the four genotoxicity studies on AMPA in mammalian cells *in vitro* or *in vivo* which were presented in IARC's Monograph on Glyphosate (IARC Monograph 112, Tables 4.2, 4.3 and 4.4, 2015) plus two additional studies (Shirasu 1980; Kier and Stegeman 1993).

Four studies presented in IARC's Monograph on Glyphosate (IARC Monograph 112, Tables 4.2, 4.3 and 4.4, 2015

Three of these studies (Comet assay using the liver Hep-2 cells *in vitro*, Chromosomal Aberrations using human lymphocytes *in vitro* and Bone Marrow Micronucleus formation using Balb C mice *in vivo*) are reported in one publication (Mañas *et al.* 2009).

The Comet assay was reported to be positive using an AMPA concentration of 4.5 mM (500 µg/ml). The results of the assay are presented in Figure 1 where Tail Moment, percent DNA in the Tail and Tail length are depicted for controls (no AMPA). Positive controls (a chemical known to be positive in the assay and Tail Length (Mañas *et al.* 2009). This is a bar-graph in which the x-axis is missing, thus making it difficult to interpret. The data presented are puzzling. The Tail Moment is calculated as the product of the percent DNA in the Tail and Tail Length. An examination of Figure 1 indicates that both percent DNA in the Tail and Tail length are higher for the positive control as compared to the corresponding values when 2.5mM and 4.5mM AMPA are evaluated. However, the figure depicts the Tail Moment for the positive control as being lower than the Tail Moments for 2.5mM and 4.5 mM. This cannot be, and it calls into question the data presented in Figure 1. Furthermore, Zouaoui *et al*. 2013 reported that the average blood concentration of AMPA in people who have ingested glyphosate in suicidal or accidental cases was 0.3 µg/ml for those who exhibited mild to moderate clinical signs of toxicity and 10.3 µg/ml for those who died. The 500 µg/ml AMP concentration in the culture medium reported to give a positive result in the Comet assay is 1,666 and 49 times higher than the blood levels in people who exhibited mild-moderate clinical signs of toxicity or died, respectively. Under these circumstances, it is not appropriate to conclude that data from Mañas *et al.* 2009 indicate that AMPA can cause genotoxicity based on the Comet assay.

A Chromosomal Aberration assay was reported to be positive using at only the highest AMPA concentration, 1.8 mM (200 µg/ml). Based on the clinical study reported

by Zouaoui *et al*. 2013, discussed in the paragraph above, the 200 µg/ml concentration in the culture medium reported to give a positive result in the Chromosomal Aberration assay is 667 and 19 times higher than the blood levels in people who exhibited mild-moderate clinical signs of toxicity or died, respectively. Under these circumstances, it is not appropriate to conclude that data from Mañas *et al.* 2009 indicate that AMPA can AMPA can cause genotoxicity based on the Chromosomal assay.

Regarding the *in vivo* Bone Marrow Micronucleous test using Balb C mice, Mañas *et al.* 2009 report statistically significant increases in micronuclei following treatment with doses of 200 and 400 mg/kg using the intraperitoneal (i.p.) route of administration. These positive findings should be discounted because of a combination of the following: 1) there is no dose-response relationship; 2) the i.p. route of administration is very non-physiological; and 3) the doses used are extremely high. Since AMPA is a biodegradation product of glyphosate which is sometimes found in soil it is reasonable to assume that exposure to it is much less than exposure to glyphosate. The average human exposure to glyphosate from food and water is estimated to be 0.088 mg/kg/day (Solomon 2016). Thus, rodent doses of 200 and 400 mg/kg are 2,273 and 4,545 higher than the human dose. It is reasonable to say that the margins of exposure to AMPA are much higher.

The fourth study (Roustan *et al.* 2014) reported that AMPA caused chromosomal damage in an *in vitro* assay using Chinese Hamster cells. The validity of this study is, at best, dubious because the highest increase in damage was observed at an extremely low concentration (0.0005 µg/mL) in the presence of light irradiation which, by itself, can damage DNA.

In summary, I conclude that the results of the four mammalian-based AMPA genotoxicity assays, discussed above, are inadequate for use in making a decision regarding whether or not AMPA is a genotoxic compound.

In addition to the studies cited by IARC, I have reviewed underlying study reports for other studies on AMPA including:

Microbial Mutagenicity study (Shirasu 1980)

This study evaluated the ability of AMPA to cause mutations in two types of bacteria-based mutagenicity assays: 1) a recombination assay (rec-assay), which evaluates the ability of a compound to cause mutations in a strain of bacteria that lacks the ability to carry out a particular type of DNA repair as compared to a strain which has this capability. After addition of the chemical in question the impact (if any) is evaluated indirectly by assessing the extent of growth inhibition. If both strains grow equally well, that is taken as an indication the chemical in question is not mutagenic. If the strain lacking the ability to carry out DNA repair exhibits growth inhibition relative to the strain which has repair capability, this is taken as an indication the chemical in question is capable of causing mutations; and 2) the Ames test, as described above. The procedures followed are described thoroughly and positive controls were used to confirm that the systems were working. The results indicated that AMPA does not act as a mutagen.

Bone marrow micronucleus assay (Kier and Stegeman 1993)

This study evaluated the ability of AMPA to cause chromosomal damage in a bone marrow micronucleus assay, *in vivo*, in male and female mice. Three doses of AMPA were used (100, 500 and a very large high dose of 1,000 mg/kg), sampling was performed at three time points (24, 48 and 72 hours after dosing) and a positive control was used to confirm that the system was working. A statistically significant increase in micronuclei was observed only in the low does (100 mg/kg) female group at the 72 hour time point (in males all of the results were negative). However, this was still within the laboratory's range of historical controls. This coupled with the fact that no increases in micronuclei were observed in female mice at the two higher doses, at any time point, indicates that the effect seen at the low dose, 72 hour time point was not related to

treatment with AMPA. The data indicate that AMPA did not exhibit genotoxicity when evaluated in this in vivo bone marrow micronucleus assay.

Additionally, a recent review of genotoxicity data concluded that "glyphosate, glyphosate formulations and AMPA do not pose a genotoxic hazard" (Brusick *et al.* 2016).

Conclusion Regarding the Genotoxic Potential of AMPA

Based on the data and discussion presented above, I conclude that AMPA should be viewed as a non-genotoxic compound.

Oxidative Stress

Oxygen can be metabolized within cells to reactive oxidants that are capable of binding to cellular components (e.g., DNA, proteins and lipids) and affecting their functions. The reactive oxidants are referred to as free radicals which are oxygen-containing molecules that have an unpaired electron, and this is what makes it chemically reactive, e.g., reactive oxygen species (ROS). Production of free radicals is a normal phenomenon and cells have an ability to defend against damage that might be produced. The cell can counteract (detoxify) free radicals by producing antioxidants which are molecules that can donate an electron to the free radical without becoming destabilized. The production of free radicals and the production of antioxidants are processes which occur normally. Situations can arise where there is an over production of free radicals relative to the body's (cell's) ability to counteract (detoxify) them. When this imbalance occurs, it is referred to as oxidative stress. There are multiple mechanisms (pathways) that can lead to oxidative stress (Klaunig *et al.* 2011) and, thus, there are numerous approaches that can be taken to evaluate the phenomenon and these involve challenges and limitations (Kalyanaraman *et al.* 2012).

ROS might lead to mutations and play a role in toxicity and development of diseases including, but not limited to, cancer. However, the role of ROS in tumor development and progression is controversial (Klaunig *et al*. 2011). Furthermore, a recent publication using liver carcinogenesis as a model has shown that oxidative stress mechanisms do not discriminate between genotoxic and non-genotoxic carcinogens (Deferme *et al*. 2015).

In cases where a chemical is shown to be capable of causing genotoxicity there might be an inclination to evaluate its potential to induce ROS as a possible mechanism underlying the DNA damage observed. However, this would not be the case when dealing with glyphosate-based formulations, glyphosate or AMPA because the most reliable results described above indicate that these are non-genotoxic materials.

In this context, it should be noted that there are beneficial effects of ROS, too (Kawagishi and Finkel 2014). In a review of oxidative stress and oxidative damage, Klaunig *et al.* 2011 conclude that "ROS has been well recognized for playing a dual role as both beneficial and deleterious species … overproduction of ROS via various sources can cause damage to both nuclear and mitochondrial DNA, which have been associated with a number of human cancers. ROS act as secondary messengers in multiple intracellular pathways that confer carcinogenic effects, while ROS can also induce apoptosis and promote cellular senescence, therefore functioning as anticarcinogenic species … ROS involve in cellular defense against infectious agents and ROS-mediated … expression of antioxidant enzymes protect cells against ROS-induced oxidative stress…." Chemicals that are capable of causing oxidative stress do not necessarily do this at all doses, i.e., there might be thresholds below which an effect is not observed.

Furthermore, the way oxidative damage might contribute to carcinogenesis remains to be discerned. The US EPA's Guidelines for Carcinogen Risk Assessment 2005 state (in Section 2.3.5.2, p. 2-33): "At certain doses an agent may also generate reactive oxygen species that produce oxidative damage to DNA and other

macromolecules … The role of cellular alterations that are attributable to oxidative damage in tumorigenesis (e.g., 8-hydroxyguanine) is currently unclear" (EPA 2005).

The fact that a chemical is capable of causing oxidative stress does not necessarily mean that it can act as a carcinogen. When considering a possible relationship between a chemical's ability to cause oxidative stress and its ability to cause cancer two important questions (in addition to key considerations like dose-response relationships) need to be considered. The first question is how many (what percent) of the chemicals reported to cause oxidative stress in laboratory experiments are also able to act as rodent carcinogens? I am not aware of a robust data base that would permit us to make a reasonable prediction. The second question is how many (what percent) of the chemicals which test negative in the rodent bioassay (i.e., what percent of the non-carcinogens) are reported to cause oxidative stress in laboratory experiments. I am not aware of a robust data base that would permit us to make a reasonable prediction. Therefore, at the present time: 1) we do not know if oxidative stress is a sensitive indicator of a chemical's carcinogenic potential (e.g., we do not know what percent of chemicals that cause oxidative stress are capable of causing cancer), and 2) we do not know if oxidative stress is a specific indicator of a chemical's carcinogenic potential (e.g., we do not know what percent of non-carcinogens cause oxidative stress). Additionally, we do not have a robust data base that includes aspects of the possible role that chemically-induced oxidative stress might play in causing cancer with regard to key questions such as the temporal relationship between increased oxidative stress and cancer - how much of an increase in oxidative stress is necessary to cause cancer and how prolonged must this be? Furthermore, oxidative stress might occur as a consequence of the carcinogenic process rather than a direct result of chemical-treatment. Therefore, in my opinion, the ability of a chemical to cause oxidative stress under some laboratory conditions should not be construed as a reliable biomarker of its ability to cause cancer.

A lengthy listing of studies claiming that glyphosate or GBFs can cause oxidative stress in human cell lines *in vitro* or in rodents *in vivo* is presented in the report provided

by one of the Plaintiffs' experts (Dr. Portier, pp. 69-73 of his report). Typically, in these studies, very high doses/concentrations of glyphosate or GBFs are used and/or the test compounds are administered to rodents by the i.p. route of administration which is highly non-physiological for the reasons described above. The much higher rate of absorption following i.p. administration might result in toxicity that would not be observed following dosing under the more physiological routes of administration. My concerns regarding the use of high concentrations of test material and the non-physiological i.p. route of administration are not discussed by Dr. Portier. For example, let us consider three of the studies he relies on:

1. Mladinic *et al.* 2009 (claimed to show oxidative stress in human cells *in vitro*):

   Dr. Portier (p. 69 of his Expert Report) refers to this study by saying "Mladinic *et al.* (2009) examined the induction of oxidative stress from exposure to glyphosate … in lymphocytes from three healthy human donors … at concentrations of 0.5, 2.91, 3.5, 92.8 and 580 µg/ml. Cells with and without S9 activation [S9 = drug metabolizing enzymes were added] saw increases in total antioxidant capacity [indication of oxidative stress] at only the highest dose for cells without S9 activation although a clear concentration response pattern was seen with S9 activation." However, this does not accurately reflect the data presented. There are no instances where there is a "clear concentration response pattern." In the last paragraph of the Discussion Section (p. 806 of the paper), Mladinic *et al.* 2009 state "In conclusion, only the highest concentration tested (580 µg/ml) of glyphosate showed statistical significance with various methods." Furthermore, in the paper's Abstract the authors state "Since for any of the assays applied, no clear dose-dependent effect was observed, it indicates that glyphosate in concentrations relevant to human exposure does not pose significant health risk." Additionally, and importantly, it is instructive to note that Zouaoui *et al.* 2013 evaluated glyphosate-poisoning in people who ingested a GBF as a result of an accident or attempted suicide. Individuals who exhibited clinical signs of mild-

moderate intoxication had an average blood glyphosate concentration of 61 mg/L (corresponding to 61 µg/ml) with a range of 0.6-150 mg/L (corresponding to 0.6 -150 µg/ml). In light of the fact that lymphocytes are found in blood, it reasonable to compare the concentrations of glyphosate the cultures of lymphocytes used by Mladinic *et al.* 2009 with glyphosate concentrations in the blood of the GBF-poisoning patients evaluated by Zouaoui *et al.* 2013. However, these acute toxicities are not cancer.

The only concentration of glyphosate which Mladinic *et al.* 2009 indicated to be capable of causing oxidative stress was the highest concentration used (580 µg/ml) and this is far above the range of concentrations (0.6 – 150 µg/ml) which is associated with mild-moderate clinical signs of intoxication in people who ingested a GBF as a result of an accident or attempted suicide. Additionally, and importantly, the three lower concentrations of glyphosate (2.91, 3.5 and 92.8 µg/ml) which Mladinic *et al.* 2009 showed to not cause any statistical increase in oxidative stress are all within the range of blood glyphosate concentrations which are associated with mild to moderate clinical intoxication in people who ingested a GBF as a result of an accident or attempted suicide. In my opinion the high concentrations of glyphosate used in the *in vitro* experiments reported by Mladinic *et al.* 2009 make their paper an inadequate study to use for an evaluation of the potential for glyphosate to cause oxidative stress in humans.

2. Kwiatkowska *et al.* 2014 (claimed to show oxidative stress in human cells *in vitro*): Human erythrocytes (red blood cells) in primary cell culture were treated with glyphosate at concentrations of 0.01 mM, 0.05 mM, 0.1 mM, 0.25 mM and 5 mM (equivalent to 1.7, 8.4, 17, 42.3, 85 and 845 µg/ml, respectively) and (as noted in Dr. Portier's Expert Report, p. 69) the authors reported a statistically significant increase in oxidative stress when the three higher concentrations (42.3, 85 and 845 µg/ml) were used. However, Dr. Portier did not indicate that Kwiatkowska *et al.* 2014 reached the conclusion

(last sentence of their Abstract) that "The results clearly show that the changes induced in the erythrocytes can occur only as a result of poisoning with these compounds." This statement is based on the reference Kwiatkowska *et al.* 2014 make to a paper by Zouaoui *et al.* 2013 who evaluated glyphosate-poisoning in people who ingested a GBF as a result of an accident or attempted suicide. Individuals who exhibited clinical signs of mild-moderate intoxication had an average blood glyphosate concentration of 61 mg/L (corresponding to 61 µg/ml) with a range of 0.6-150 mg/L (corresponding to 0.6 -150 µg/ml). An individual who exhibited clinical signs of severe intoxication had a blood glyphosate concentration of 838mg/L (corresponding to 838 µg/ml. Individuals who died had an average blood glyphosate concentration of 4,146 mg/L (corresponding to 4,146 µg/ml) with a range of 690-7,480 mg/L (corresponding to 690 -7,480 µg/ml). In light of the fact that red blood cells are found in blood, it reasonable to compare the concentrations of glyphosate in the cultures of red blood cells used by Kwiatkowska *et al.* 2014 with glyphosate concentrations in the blood of the GBF-poisoning patients evaluated by Zouaoui *et al.* 2013. The two lower concentrations of glyphosate (42.3 and 85 µg/ml, respectively) reported to cause an increase in oxidative stress are in the range of blood glyphosate concentrations that caused mild to moderate clinical signs of toxicity in humans. The higher concentration of glyphosate (845 µg/ml) reported to cause an increase in oxidative stress is slightly above the blood glyphosate concentration (838 µg/ml) that cause severe signs of toxicity in a human and, importantly, clearly within the range of blood glyphosate concentrations (to 690 -7,480 µg/ml) found in the people who died. Additionally, and importantly, the three lower concentrations of glyphosate (1.7, 8.4 and 17 µg/ml) which Kwiatkowska *et al.* 2014 showed to not cause oxidative stress are all within the range of blood glyphosate concentrations which are associated with mild to moderate clinical intoxication in people who ingested a GBF as a result of an accident or attempted suicide. In my opinion the high concentrations of glyphosate used in the experiments reported by

Kwiatkowska *et al.* 2014 make their paper an inadequate study to use for an evaluation of the potential for glyphosate to cause oxidative stress in humans.

3. Bolognesi *et al.* 1997 (claimed to show oxidative stress *in vivo*, in mice): The mice were dosed with glyphosate (300 mg/kg) or Roundup (900 mg/kg, equivalent to 270 mg/kg of glyphosate) by i.p. injection. Dr. Portier's Expert Report states (bottom of p. 70 – top of p. 71) "Samples of liver and kidneys from these mice were evaluated for levels of 8-hydroxy-2'-deoxyguanosine (8-0HdG) which is a biomarker of oxidative stress. There was a significant increase in the liver of 8-0HdG at 24 hours following glyphosate exposure…At both eight hours and 24 hours, Roundup increased 8-0HdG in the kidneys…." However, he does not discuss the non-physiological aspect of i.p. administration nor does he indicate that the doses of glyphosate used are 638 and 574 times higher, respectively, than the 0.47 mg/kg daily dose of glyphosate that children are estimated to receive (EPA 2016), and 3,409 and 3,068 times higher, respectively, than the 0.088 mg/kg daily dose of glyphosate that the US population is estimated to receive (Solomon 2016). In my opinion the use of high doses in combination with the non-physiological route of administration make Bolognesi *et al.*1997 an inadequate study to use for an evaluation of the potential for glyphosate or Roundup to cause oxidative stress in humans.

As described above, the doses at issue in Bolognesi *et al*. 1997 are hundreds or thousands of times higher than the human daily dose reported by EPA for the US population or children, respectively. Further, the *in vitro* concentrations used in Mladinic *et al.* 2009 and Kwiatkowska *et al.* 2014 render these studies inadequate to use for an evaluation of the potential for glyphosate to cause oxidative stress in humans. Therefore, in my opinion, the results of such studies are inappropriate to use for human risk assessment, especially regarding both genotoxicity and oxidative stress. The concerns I have expressed are not discussed by Dr. Portier. Also, importantly, the

oxidative stress phenomenon in the list of studies presented in Dr. Portier's Expert Report (pp. 69-73) is not linked convincingly in a cause-effect relationship to an apical toxic endpoint (e.g., not linked convincingly to genotoxicity and not linked convincingly to induction of cancer).

Conclusion Regarding the Possibility that Glyphosate or GBFs Can Cause ROS and Implications of this for Predicting that Glyphosate or GBFs Might Act as a Mutagen or Carcinogen

In light of the discussion presented above, it is clear that detection of ROS in a test system following chemical-treatment is not a diagnostic criterion indicating that the chemical in question is capable of acting as a mutagen or a carcinogen. This conclusion is supported by the fact that both in the United States and in Europe, evaluation of the ability of a chemical to induce ROS is not on the list of tests for toxic potential that are required in order to place a chemical on the market as, for example, a medicine or crop protection chemical.

Conclusion

Based upon my review of the scientific literature dealing with the potential genotoxicity of GBFs, glyphosate, and AMPA, I conclude that these should be regarded as non-genotoxic materials. Furthermore, while GBFs and/or glyphosate might be capable of causing oxidative stress under certain experimental conditions, my review of the scientific literature leads me to conclude that it is not appropriate to use this observation to support a contention that these materials are capable of causing cancer.

Jay Goodman

APPENDICIES

The following 12 appendices consist of 12 tables summarizing genotoxicity data presented in the Glyphosate Issue Paper: Evaluation of Carcinogenic Potential, Office of Pesticide Programs US Environmental Protection Agency, September 12, 2016. Tables 1-5 contain data pertaining to GBFs and Tables 6-12 contain data pertaining to glyphosate.

Appendix-1 - EPA's Table F.1. *In Vitro* tests for gene mutations in bacteria – GBFs

Table F.1. *In vitro* Test for Gene Mutations in Bacteria: Glyphosate Formulations.

Test/Endpoint	Test System	Concentrations	Test Material/ Concentration	Results	Reference	Comments
Bacterial Reverse Mutation	*S. typhimurium* TA1535, TA1537, TA1538, TA98 and TA100; *E. coli* WP2 *uvrA* pKM101 ± S9	1.6-5000 µg/plate ± S9 (plate incorporation)	ICIA 0224 57.6% in water	Negative ± S9	Callander (1988)	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537; *E. coli* WP2P and *uvrA* ± S9	100-5000 µg/plate ±S9 plate incorporation & pre-incubation protocols	TMSC (tri-methyl-sulfonium chloride) 95% purity	Negative ± S9	Callander (1993)	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA102, TA1535, and TA1537 ± S9	26, 43, 72, 120, 200 µg/plate	Glyphosate liquid formulation (480 g/L isopropylamine salt)	Negative ± S9	Camolesi (2009)[1]	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA102, TA1535, and TA1537 ± S9	26, 43, 72, 120, 200 µg/plate	MON 77280 equivalent of glyphosate acid: 495 g/L	Negative ± S9	Camolesi (2010)	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA102, TA1535, and TA1537 ± S9	0.2-2000 µg/plate	MON 76190 53.2% glyphosate	Negative ± S9	Catoyra (2009)[1]	
Bacterial Reverse Mutation	*S. typhimurium* TA97a, TA98, TA100 and TA102± S9	2 µg/plate (toxic)	Perzocyd 10 SL formulation	Negative ± S9	Chruscielska *et al.* (2000)	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA102, TA1535, and TA1537 ± S9	0.03-3.0 µL/plate	MON 8080 (87.6%)	Negative ± S9	Flowers (1981)	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA102, TA1535, and TA1537 ± S9	3.16-1000 µg/plate	TROP M (Glyphosate 480); 35.84% purity based on acid, 48.46% pure based on IPA salt	Negative ± S9	Flügge (2010a)[1]	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA102, TA1535, and TA1537 ± S9	0.316-100	Glyphosate 757 g/kg granular formulation (76.1%	Negative ± S9	Flügge (2010d)[1]	

Appendix-1 - EPA's Table F.1. *In Vitro* tests for gene mutations in bacteria – GBFs (continued)

Table F.1. *In vitro* Test for Gene Mutations in Bacteria: Glyphosate Formulations.

Test/Endpoint	Test System	Concentrations	Test Material/ Concentration	Results	Reference	Comments
			monoammonium glyphosate salt)			
Bacterial Reverse Mutation	*S. typhimurium* TA97a, TA98, TA100, and TA1535 ± S9	1-5000 µg/plate	Roundup WG 784 g/kg ammonium salt equivalent	Negative ± S9	Gava (1998)	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537± S9	50-5000 µg/plate	Rodeo® (containing IPA salt and water only); 40% glyphosate (acid equivalent)	Negative ± S9	Kier *et al.*, (1992)	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537 ± S9	5-500 µg/plate (-S9)/ 15-1500 µg/plate (+S9)	MON 2139 (Roundup®) 31% Glyphosate (acid equivalent)	Negative ± S9	Kier *et al.*, (1992)	Cytotoxic at top concentrations
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537 ± S9	5-500 µg/plate (-S9)/ 15-1500 µg/plate (+S9)	MON 14445 (Direct®); 75% Glyphosate (acid equivalent)	Negative ± S9	Kier *et al.*, (1992)	Cytotoxic at the top concentrations, occasionally at lower concentrations
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537 ± S9	0.2-2000 µg/plate	MON 79672 (Roundup Ultramax); 74.7% monoammonium glyphosate salt; 68.2% glyphosate	Negative ± S9	Lope (2008)[1]	
Bacterial Reverse Mutation	*S. typhimurium* TA1535, TA1537, TA1538, TA98 and TA100 ± S9	0.617-50 µL/plate ± S9	SC-0224, 19.2% purity	Negative ± S9	Majeska (1982)	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537 and *E. coli* WP2 *uvrA* ± S9	TA strains: 10 - 5000 µg/plate (+S9); 3.33-3330 µg/plate (-S9); E. coli: 33.3-5000 µg/plate (+/- S9)	MON 78239 36.6% glyphosate (44.9% potassium salt of glyphosate)	Negative	Mecchi (2003a)	Increase in revertants seen in TA98 and TA1535 -S9 on first trial, not conc-dep; however no increase in revertants seen in repeat in those strains; overall negative.

Appendix-1 - EPA's Table F.1. *In Vitro* tests for gene mutations in bacteria – GBFs (continued)

Table F.1. *In vitro* Test for Gene Mutations in Bacteria: Glyphosate Formulations.

Test/Endpoint	Test System	Concentrations	Test Material/ Concentration	Results	Reference	Comments
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537 and *E. coli* WP2 *uvrA* ± S9	TA strains: 3.33-3330 µg/plate (+S9); 1.0-1000 µg/plate (-S9); E. coli: 33.3-5000 µg/plate (+/- S9)	MON 78634 65.2% w/w glyphosate (71.8% w/w as monoammonium salt of glyphosate)	Negative	Mecchi (2003b)	
Bacterial Reverse Mutation	*S. typhimurium* TA 98, TA100, TA1535, TA1537 and *E. coli* WP2 *uvrA* ± S9	10 - 5000 µg/plate (+/-S9)	MON 79864 38.7% glyphosate acid (wt %)	Negative	Mecchi (2008a)	Inhibited growth seen at ≥2000 -S9
Bacterial Reverse Mutation	*S. typhimurium* TA 98, TA100, TA1535, TA1537 and *E. coli* WP2 *uvrA* ± S9	33.3-5000 µg/plate	MON 76313 30.9% glyphosate acid	Negative	Mecchi (2008b)	
Bacterial Reverse Mutation	*S. typhimurium* TA 98, TA100, TA1535, TA1537 and *E. coli* WP2 *uvrA* ± S9	10-5000 µg/plate (+/-S9)	MON 76171 31.1% glyphosate	Negative	Mecchi (2008c)[1]	
Bacterial Reverse Mutation	*S. typhimurium* TA 98, TA100, TA1535, TA1537 and *E. coli* WP2 *uvrA* ± S9	10-5000 µg/plate (+/-S9)	MON 79991 71.6% glyphosate acid	Negative	Mecchi (2009a)	
Bacterial Reverse Mutation	*S. typhimurium* TA 98, TA100, TA1535, TA1537 and *E. coli* WP2 *uvrA* ± S9	10-5000 µg/plate (+/-S9)	MON 76138 38.5% glyphosate	Negative	Mecchi (2009b)[1]	
Bacterial Reverse Mutation	*S. typhimurium* TA97a, TA98, TA100, and TA1535 ± S9	1-5000 µg/plate	MON 77280 646.4 g/L salt equivalent	Negative	Perina (1998)	

Appendix-1 - EPA's Table F.1. *In Vitro* tests for gene mutations in bacteria – GBFs (continued)

Table F.1. *In vitro* Test for Gene Mutations in Bacteria: Glyphosate Formulations.

Test/Endpoint	Test System	Concentrations	Test Material/ Concentration	Results	Reference	Comments
Bacterial Reverse Mutation	*S. typhimurium* TA98 and TA100 ± S9	0-1440 µg/plate (calculated as glyphosate IPA salt)	Roundup, 480 g/L glyphosate isopropylamine salt	Negative – S9, Equivocal +S9	Rank *et al.* (1993)	Stat significant increase at 360 µg/plate for TA98 (-S9) and 720 µg/plate for TA100 (+S9). Not significant at higher concentrations and were not replicated. Effects occurred at close to toxic levels.
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA102, TA1535, and TA1537 ± S9	500-5000 µg/plate;	495 g/L glyphosate isopropylamine salt; 371.0 g/L (equivalent of glyphosate acid)	Negative ± S9	Silvino (2011)	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA102, TA1535, and TA1537 ± S9	1.5-5000 µg/plate	MON 8709 495 g/L glyphosate isopropylamine salt; 371.0 g/L (equivalent of glyphosate acid)	Negative ± S9	Silvino (2011)	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA102, TA1535, and TA1537 ± S9	15-5000 µg/plate	MON 76313 468 g/L glyphosate isopropylamine salt (351 g/L glyphosate acid equivalent)	Negative ± S9	Silvino (2012)	Cytotoxic at 5000 µg/plate for some strains
Bacterial Reverse Mutation	*S. typhimurium* TA97a, TA98, TA100 and TA1535 ± S9	1-5000 µg/plate	Glifos formulation (glyphosate isopropylammonium salt , Berol 907 and water)	Negative ± S9	Vargas (1996)	Cytotoxic at the two upper concentrations

Table F.1. *In vitro* Test for Gene Mutations in Bacteria: Glyphosate Formulations.

Test/Endpoint	Test System	Concentrations	Test Material/ Concentration	Results	Reference	Comments
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA102, TA1535, TA1537± S9	3.16-316 µg/plate	FSG 3090-H1 360 g/L	Negative ± S9	Uhde (2004)[1]	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100 ± S9	0.01-100 µg/plate	64% (glyphosate Isopropylammonium salt)	Negative ± S9	Wang *et al.* (1993)	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537 and *E. coli* WP2 *uvrA* ± S9	All strains: 33.3-5000 µg/plate (+S9); 10-3330 µg/plate (-S9)	MON 78910 30.3% glyphosate acid	Negative ± S9	Xu (2006)	Cytotoxic ≥1000 µg/plate (-S9)

[1] Study was cited in Kier and Kirkland (2013). Supplementary information about the study was provided online including test guideline, test material purity, control chemicals and summary data tables.

Appendix-2 - EPA's Table F.2. *In Vitro* tests for chromosome damage in mammalian cells – GBFs

Table F.2. *In Vitro* Tests for Chromosome Damage in Mammalian Cells- Glyphosate Formulations

Test/Endpoint	Test System	Concentrations	Test Material/ Concentration	Results	Reference	Comments
***In vitro* Chromosomal Aberration using fluorescent in situ hybridization (FISH)**	Bovine lymphocytes (from two 6-8 month old calves) -whole chromosome (1) painting probe	28-1120 µM 24 h exposure	62% Isopropylamine salt of glyphosate (38% inert ingredients)	Negative.	Holeckova (2006)	Small but significant increase in polyploidy seen at 56µM No positive control reported.
***In vitro* Cytokinesis Block Micronucleus Assay (with FISH analysis)**	TR146 cells (human-derived buccal epithelial cell line)	0, 10, 15 and 20 mg/L; 20 minute exposure.	Roundup Ultra Max (450 g/l glyphosate acid)	Positive Increase in MN at all test concentrations	Koller *et al.* (2012)	No apoptosis observed at any conc. Necrosis reported at 20 mg/L. Increase in NB and NPB seen at all concentrations

MI= mitotic index. FISH= fluorescent in situ hybridization, MN= micronuclei; NB= nuclear buds; NPB= nucleoplasmic bridges.

Appendix-3 - EPA's Table F.3. *In Vivo* tests for chromosome aberrations in mammals – GBFs

Table F.3. *In Vivo* Tests for Chromosomal Aberrations in Mammals- Glyphosate Formulations.

Test/Endpoint	Test System	Route of Administration	Doses	Test Material Purity	Results	Reference	Comments
Bone Marrow Chromosomal Aberration	Swiss albino mice (males only) Vehicle: DMSO	Intraperitoneal injection; sampling 24, 48 and 72 h	0, 25 and 50 mg/kg (5/dose)	Roundup (>41% isopropylamine glyphosate)	Positive Increase in MN at all time points at both doses	Prasad *et al.* (2009)	Significant decrease in mitotic index seen at all doses and time points
Bone Marrow Chromosomal Aberration	C57BL mice (males only) Vehicle: water	Oral administration; sampling 6, 24, 48, 72, 96 and 120 h	0.05, 0.01, 0.5 and 1.0% (8/dose)	Roundup	Negative	Dimitrov *et al.* (2006)	
Bone Marrow Chromosomal Aberration	New Zealand white rabbits (males only) Vehicle:	Drinking water for 60 days	0, 750 ppm (5/dose)	Roundup	Positive	Helal and Moussa (2005)	

BM= bone marrow, SC= spermatocyte.

Appendix- 4 - EPA's Table F.4. *In Vivo* tests for micronuclei induction in mammals – GBFs

Table F.4. *In Vivo* Tests for Micronuclei Induction in Mammals- Glyphosate Formulations.

Test/Endpoint	Test System	Route of Administration	Doses	Test Material Purity	Results	Reference	Comments
Bone Marrow Micronucleus Test	Swiss CD1 mice (males only)	Intraperitoneal injection; 2 injections of half the dosage of 135 mg/kg 24 h apart; sampling at 6 and 24 h	0, 450 mg/kg roundup, equiv. to 135 kg glyphosate (3/dose)	Roundup, 30.4% glyphosate	Positive	Bolognesi *et al.* (1997)	Stat significant increase in MN at 6 and 24 h
Bone Marrow Micronucleus Test	C3H mice (males only) Vehicle: water	Intraperitoneal Injection (single treatment); sampling after 24, 48 and 72 h	0, 90 mg/kg	Not reported	Negative	Chruscielska *et al.* (2000)	
Bone Marrow Micronucleus Test	Swiss mice (males and females) Vehicle: water	Intraperitoneal Injection (2 treatments, 24 h apart); sampling after 24 h (last treatment)	0, 50, 100 and 200 mg/kg	480g/L Isopropylamine salt of glyphosate	Negative	Grisolia (2002)	
Bone Marrow Micronucleus Test	CD-1 mice (males and females)	Intraperitoneal injection; sampling 24, 48 and 72 h	0, 140, 280, and 555 mg/kg	Roundup (31% glyphosate salt)	Negative	Kier (1992)	Some deaths observed at high dose (HD), ↓PCE/NCE ratio at HD at 48 h in males.
Bone Marrow Micronucleus Test	Swiss albino mice (males and females)	Intraperitoneal Injection (2 treatments, 24 h apart); sampling after 24 h (last treatment)	0, 212.5, 425 and 637.5 mg/kg	MON 77280 646.4 g/L glyphosate salt equivalent	Negative	Monma (1998)	Doses tested corresponded to 25%, 50% and 75% LD50

Appendix- 4 - EPA's Table F.4. *In Vivo* tests for micronuclei induction in mammals – GBFs (continued)

Table F.4. *In Vivo* Tests for Micronuclei Induction in Mammals- Glyphosate Formulations.

Test/Endpoint	Test System	Route of Administration	Doses	Test Material Purity	Results	Reference	Comments
Bone Marrow Micronucleus Test	NMRI-Bom mice	Intraperitoneal Injection (single treatment); sampling after 24 h	0, 133 and 200 mg/kg (4/sex/dose)	Roundup, 480 g glyphosate isopropylamine salt per liter	Negative	Rank *et al.* (1993)	BM toxicity indicated by %PCE decreased at 200 mg/kg
Bone Marrow Micronucleus Test	Swiss albino mice (males only[2]) Vehicle: water	Oral gavage (two treatments, 24 h apart); sampled at 18 and 24 h after last dose	0, 2000 mg/kg	MON 8709494.7 g/L salt of isopropylamine (371.0 glyphosate acid)	Negative	Claro (2011)	OECD 474 Guideline No significant signs of toxicity observed in main study.
Bone Marrow Micronucleus Test	C57BL mice (males only) Vehicle: water	Oral administration; sampling 6, 24, 48, 72, 96 and 120 h	0.05, 0.01, 0.5 and 1.0% (1%=1080 mg/kg) (8/dose)	Roundup	Negative	Dimitrov *et al.* (2006)	Toxicity seen in 1.0% dose group
Bone Marrow Micronucleus Test	Crl:CD-1(ICR) BR mice (males only[2]) Vehicle: water	Oral gavage (single treatment); sampling after 24 and 48 h (high dose only)	0, 500, 1000, and 2000 (mg/kg) (5/dose)	MON 78239 (36.6% glyphosate)	Negative	Erexson (2003a)	EPA Guideline (84-2) No significant signs of toxicity observed in main study.
Bone Marrow Micronucleus Test	Crl:CD-1(ICR) BR mice (males only[2]) Vehicle: water	Oral gavage (single treatment); sampling after 24 and 48 h (high dose only)	0, 500, 1000, and 2000 (mg/kg) (5/dose)	MON 78634 (65.2% glyphosate)	Negative	Erexson (2003b)	EPA Guideline (84-2) No significant signs of toxicity observed in main study.
Bone Marrow Micronucleus Test	Crl:CD-1(ICR) BR mice (males only[2]) Vehicle: water	Oral gavage (single treatment); sampling after 24 and 48 h (high dose only)	0, 500, 1000, and 2000 (mg/kg) (5/dose)	MON 78910 (30.3% glyphosate)	Negative	Erexson (2006)	EPA Guideline (84-2) No significant signs of toxicity observed in main study.

Table F.4. *In Vivo* Tests for Micronuclei Induction in Mammals- Glyphosate Formulations.

Test/Endpoint	Test System	Route of Administration	Doses	Test Material Purity	Results	Reference	Comments
Bone Marrow Micronucleus Test	CD-1(ICR)BR mice (males only[2]) Vehicle: water	Oral gavage (single treatment); sampling after 24 and 48 h (high dose only)	0, 500, 1000, and 2000 (mg/kg) (5/dose)	MON 76138 (38.5% glyphosate)	Negative	Xu (2009b)[1]	EPA Guideline (84-2) /OECD 474 No significant signs of toxicity observed in main study.
Bone Marrow Micronucleus Test	Hsd:CD-1(ICR)BR mice (males only[2]) Vehicle: water	Oral gavage (single treatment); sampling after 24 and 48 h (high dose only)	0, 500, 1000, and 2000 (mg/kg) (5/dose)	MON 76313 (30.9% glyphosate)	Negative	Xu (2009c)[1]	EPA Guideline (84-2) /OECD 474 No significant signs of toxicity observed in main study.
Bone Marrow Micronucleus Test	CD rats (males and females) Vehicle: 0.8% hydroxypropylmethyl cellulose	Oral gavage (single treatment); sampling after 24 and 48 h (high dose only)	0, 500, 1000, and 2000 mg/kg (5/sex/dose)	757 g/kg granular formulation (69.1% glyphosate acid)	Negative	Flügge (2010e)[1]	OECD Guideline 474 No significant signs of toxicity observed in main study

[1] Study was cited in Kier and Kirkland (2013). Supplementary information about the study was provided online including test guideline, test material purity, control chemicals and summary data tables.

[2] Only males tested; report indicated that there were no difference between sexes seen in range finding study.

BM= bone marrow, CA= chromosomal aberrations, MN= micronucleated erythrocytes, NCE= normochromatic erythrocytes, PCE=polychromatic erythrocytes.

Appendix- 4 - EPA's Table F.4. *In Vivo* tests for micronuclei induction in mammals – GBFs (continued)

Table F.4. *In Vivo* Tests for Micronuclei Induction in Mammals- Glyphosate Formulations.

Test/Endpoint	Test System	Route of Administration	Doses	Test Material Purity	Results	Reference	Comments
Bone Marrow Micronucleus Test	NMRI mice (males and females) Vehicle: 0.8% hydroxypropylmethyl cellulose	Oral gavage (single treatment); sampling after 24 and 48 h (high dose only)	0, 500, 1000, and 2000 mg/kg (5/sex/dose)	TROP M (Glyphosate 480); 358.4 g/L glyphosate acid; 483.6 g/L IPA salt	Negative	Flügge (2010c)[1]	OECD Guideline 474 No significant signs of toxicity observed in main study.
Bone Marrow Micronucleus Test	Swiss mice (males only[2]) Vehicle: water	Oral gavage (2 treatments, 24 h apart); sampling after 24 h (last treatment)	0, 2000 mg/kg (6/dose)	A17035A 289.7 g/L glyphosate	Negative	Negro Silva (2009)[1]	OECD Guideline 474 No significant signs of toxicity observed in main study.
Bone Marrow Micronucleus Test	Swiss mice (males only[2]) Vehicle: water	Oral gavage (2 treatments, 24 h apart); sampling after 24 h (last treatment)	0, 2000 mg/kg (6/dose)	Glyphosate SL (499.35 g/L glyphosate)	Negative	Negro Silva (2011)[1]	OECD Guideline 474 No significant signs of toxicity observed in main study
Bone Marrow Micronucleus Test	Hsd:CD-1(ICR) mice (males only[2]) Vehicle: water	Oral gavage (single treatment); sampling after 24 and 48 h (high dose only)	0, 500, 1000, and 2000 (mg/kg) (5/dose)	MON 79864 (38.7% glyphosate)	Negative #	Xu (2008a)	EPA Guideline (84-2) /OECD 474 No significant signs of toxicity observed in main study.
Bone Marrow Micronucleus Test	CD-1(ICR)BR mice (males only[2]) Vehicle: water	Oral gavage (single treatment); sampling after 24 and 48 h (high dose only)	0, 500, 1000, and 2000 (mg/kg) (5/dose)	MON 76171 (31.1% glyphosate)	Negative	Xu (2008b)	EPA Guideline (84-2) /OECD 474 No significant signs of toxicity observed in main study.
Bone Marrow Micronucleus Test	CD-1(ICR)BR mice (males only[2]) Vehicle: water	Oral gavage (single treatment); sampling after 24 and 48 h (high dose only)	0, 500, 1000, and 2000 (mg/kg) (5/dose)	MON 79991 (71.6% glyphosate)	Negative	Xu (2009a)	EPA Guideline (84-2) /OECD 474 No significant signs of toxicity observed in main study.

Appendix-5 - EPA's Table F.5. *Other assays for detecting DNA damage* – GBFs

Table F.5. Other Assays for Detecting DNA Damage- Glyphosate Formulations.

Test/Endpoint	Test System	Route of Administration	Doses/ Concentrations	Test Material/ Concentration	Results	Reference	Comments
Bacterial SOS Chromotest	*Escherichia coli* PQ37 strain	NA (*in vitro*)	0.25µg/sample	Roundup BIO formulation;	Positive	Raipulis *et al.* (2009)	
DNA Adducts ^{32}P-postlabeling	Swiss CD1 mice (males and females) Liver and kidney evaluated	Intraperitoneal injection	0, 400, 500 and 600 mg/kg, corresponding to 122, 152 and 182 mg/kg glyphosate salt	Roundup (30.4% isopropylammonium salt of glyphosate)	Positive (liver and kidney)	Peluso *et al.* (1998)	
DNA oxidative damage: 8-OHdG formation	Swiss CD-1 mice (males) liver and kidney evaluated	Intraperitoneal injection (single dose); sampling 4 and 24 h after injection	900 mg/kg corresponding to 270 mg/kg glyphosate (3/dose)	900 mg/kg corresponding to 270 mg/kg glyphosate	Kidney: positive at 8 and 24 h Liver: negative	Bolognesi *et al.* (1997)	
Single-cell gel electrophoresis (SCGE) assays-COMET assay	TR146 cells (human-derived buccal epithelial cell line). Alkaline conditions	NA (*in vitro*)		Roundup Ultra Max (450 g/l glyphosate acid)	Induced DNA migration at >20 mg/L	Koller *et al.* (2012)	Also measured multiple cellular integrity parameters to assess cytotoxicity. Formulation was more toxic than technical. Significant increase in LDHe at all concentrations tested. Cytotoxic ≥ 60 mg/L
Sister Chromatid Exchange (SCE)	Bovine lymphocytes	NA (*in vitro*)	28 - 1112 µM;; ±S9; sampling at 24 and 48 h	62% Isopropylamine salt of glyphosate	Positive	Sivikova & Dianovsky (2006)	

Table F.5. Other Assays for Detecting DNA Damage- Glyphosate Formulations.

Test/Endpoint	Test System	Route of Administration	Doses/ Concentrations	Test Material/ Concentration	Results	Reference	Comments
Sister Chromatid Exchange (SCE)	Human lymphocytes (2 donors)	NA (*in vitro*)	250, 2500 and 25000 µg/mL	Roundup; Isopropylamine salt of glyphosate (purity not stated)	Stat. significant increase ($p<0.001$) at 250 µg/mL in both donors, and in one donor at 2500 µg/mL	Vigfusson and Vyse (1980)	No growth seen at highest concentration (25 mg/mL)
Sister Chromatid Exchange (SCE)	Human lymphocytes	NA (*in vitro*)	-S9: 0, 0.1 and 0.33 mg/mL; 72 h exposure	Roundup, 30.4% glyphosate	Positive	Bolognesi *et al.* (1997)	Stat significant increase in SCE/cell at ≥ 0.1 mg/mL
Alkaline elution assay-DNA single strand breaks	Swiss CD-1 mice (males) liver and kidney evaluated	Intraperitoneal injection (single dose); sampling 4 and 24 h after injection	900 mg/kg corresponding to 270 mg/kg glyphosate (3/dose)	900 mg/kg corresponding to 270 mg/kg glyphosate	Positive (Increased elution rate) at 4 hours in liver and kidney At 24 h, returned to control levels	Bolognesi *et al.* (1997)	Return to control values at 24 h may indicate DNA repair or reflect rapid elimination of compound

h= hour, NA= not applicable, SCE= sister chromatid exchange, LDHe= extracellular lactate dehydrogenase

Appendix-6 - Glyphosate: EPA's Table 5.1. *In Vitro* tests for gene mutations in bacteria

Table 5.1. *In vitro* Test for Gene Mutations in Bacteria: Glyphosate Technical.

Test/Endpoint	Test System	Concentrations	Purity	Results	Reference	Comments
Bacterial Reverse Mutation	*S. typhimurium* TA1535, TA1537, TA98 and TA100 and WP *uvrA* ± S9	156-5000 µg/plate	95.68%	Negative ± S9	Akanuma (1995) [MRID 50017102]	
Bacterial Reverse Mutation	*S. typhimurium* TA535, TA1537, TA98 and TA100 and *E. coli* WP2P and WP2P *uvrA* ± S9	100-5000 µg/plate in DMSO	95.6% glyphosate acid	Negative ± S9	Callander (1996) [MRID 44320617]	
Bacterial Reverse Mutation	*S. typhimurium* TA 1535, TA1537, TA98 and TA100 and *E. coli* WP2P and WP2P *uvrA* ± S9	100-5000 µg/plate in water	60% potassium glyphosate salt	Negative ± S9	Callander (1999)[1]	
Bacterial Reverse Mutation	*S. typhimurium* TA97a, TA98, TA100 and TA102, ± S9	25-2000 µg in aqueous solution	Not provided	Negative ± S9	Chruscielska *et al.* (2000)	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537 ± S9	10-1000 µg/plate	98.4%	Negative ± S9	Flowers and Kier (1978) [MRID 00078620]	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA102, TA1535, TA1537 ± S9	31.6-3160 µg/plate	98.8%	Negative ± S9	Flügge (2009a)[1]	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA102, TA1535, TA1537 ± S9	31.6-3160 µg/plate	96.4% technical	Negative ± S9	Flügge (2010b)[1]	
Bacterial Reverse Mutation	*S. typhimurium* TA1535, TA1537, TA98 and TA100	310-5000 µg/plate (+S9); 160-2500 µg/plate (–S9)	98.6%	Negative ± S9	Jensen (1991a) [MRID 49961502]	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA102, TA1535, TA1537 ± S9	1-1000 µg/plate	98.05%	Negative ± S9	Miyaji (2008)[1]	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537, TA1538 ± S9	5000 µg/plate	Not reported	Negative ± S9	Moriya et al. (1983)	
Bacterial Reverse Mutation	*S. typhimurium* TA1535, TA97, TA98 and TA100 ± S9	33-10,000 µg/plate	99%	Negative ± S9	NTP (1992)	Hamster and rat S9

Appendix-6 – Glyphosate: EPA's Table 5.1. *In Vitro* tests for gene mutations in bacteria (continued)

Table 5.1. *In vitro* Test for Gene Mutations in Bacteria: Glyphosate Technical.

Test/Endpoint	Test System	Concentrations	Purity	Results	Reference	Comments
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535 and TA97a ± S9	1-5000 µg/plate	61.27 % Glyphosate isopropyl-amine salt	Negative ± S9	Ranzani (2000)[1]	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA102, TA1535, TA1537 ± S9	648-5000 µg/plate	98.01%	Negative ± S9	Ribeiro do Val (2007) [MRID 50000903]	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537 and *E. Coli* WP2 *uvrA* ± S9	31.6-5000 µg/plate	96.0% technical	Negative ± S9	Schreib (2010)[1]	
Bacterial Reverse Mutation	*S. typhimurium* TA1535, TA1537, TA1538, TA98, TA100 and *E. coli* WP2 *hcr* ± S9	10-5000 µg/plate	98.4%	Negative ± S9	Shirasu *et al*. (1978) [MRID 00078619]	Published in Li & Long, 1988
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537 and *E. coli* WP *uvrA* ± S9	3-5000 µg/plate (plate-incorporation), 33-5000 µg/plate (pre-incubation test)	95.1%	Negative ± S9	Sokolowski (2007a) [MRID 49957406]	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537 and *E. coli* WP *uvrA* ± S9	3-5000 µg/plate (plate–incorporation) 33 – 5000 µg/plate (pre-incubation test)	97.7%	Negative ± S9	Sokolowski (2007b) [MRID 49957407]	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537 and *E. coli* WP *uvrA* ± S9	3-5000 µg/plate (plate–incorporation) 33-5000 µg/plate (pre-incubation test)	95.0%	Negative ± S9	Sokolowski (2007c) [MRID 49957408]	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537 and *E. coli* WP *uvrA* ± S9	3-5000 µg/plate	96.66% technical	Negative ± S9	Sokolowski (2009a)[1]	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537 and *E. coli* WP2 *uvrA* pKM 101 and WP2 pKM 101 ± S9	3-5000 µg/plate	96.3% glyphosate acid	Negative ± S9	Sokolowski (2009b) [MRID 49961801]	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537 and *E. coli* WP *uvrA* ± S9	3-5000 µg/plate	97.16 %	Negative ± S9	Sokolowski (2010) [MRID 50000902]	

Appendix-6 - Glyphosate: EPA's Table 5.1. *In Vitro* tests for gene mutations in bacteria (continued)

Table 5.1. *In vitro* Test for Gene Mutations in Bacteria: Glyphosate Technical.

Test/Endpoint	Test System	Concentrations	Purity	Results	Reference	Comments
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537, TA1538 ± S9	1-1000 µg/plate	96.0%	Negative ± S9	Suresh (1993a)[1]	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537 and *E. coli* WP *uvrA* ± S9	0-5000 µg/plate	95.3%	Negative ± S9	Thompson (1996) [MRID 49957409]	
Bacterial Reverse Mutation	*S. typhimurium* TA98, TA100, TA102, TA1535, TA1537 ± S9	31.6-5000 µg/plate	98.2%	Negative ± S9	Wallner (2010)[1]	
Bacterial Reverse Mutation	*S. typhimurium* TA98 and TA100 ± S9	25 µg/plate	Not reported	Negative ± S9	Wilderman and Nazar (1982)	Rat S9 and plant cell-free homogenates were used for metabolic activation
Bacterial Reverse Mutation	*S. typhimurium* TA1535, TA1537, TA1538, TA98 and TA100 ± S9	0.12-10 mg/plate –S9 0.56-15 mg/plate +S9	90% glyphosate trimesium salt	Negative ± S9	Majeska et al. (1982a) [MRID 00126612]	
Bacterial Reverse Mutation	*S. typhimurium* TA1535, TA1537, TA98 and TA100 ± S9	0.005-50 µL/mL	55.6% glyphosate trimesium salt	Negative ± S9	Majeska (1985a) [MRID 00155527]	

[1] Study was cited in Kier and Kirkland (2013). Supplementary information about the study was provided online including test guideline, test material purity, control chemicals and summary data tables.

Appendix-7 - Glyphosate: EPA's Table 5.2. *In Vitro* mammalian gene mutation assays: Glyphosate technical

Table 5.2. *In vitro* Mammalian Gene Mutation Assays: Glyphosate Technical.

Test/Endpoint	Test System	Concentrations/ Conditions	Test Material Purity	Results	Reference	Comments
Gene Mutations in Mammalian Cells	Mouse lymphoma L5178Y TK$^{+/-}$ cells ± S9	296-1000 µg/mL	95.6%	Negative	Clay (1996)[1]	Relative survival was 90% (-S9) and 57% (+S9) at top concentration
Gene Mutations in Mammalian Cells	Mouse lymphoma L5178Y TK$^{+/-}$ cells ± S9	520–4200 µg/mL (+S9); 610–5000 µg/mL (-S9)	98.6%	Negative	Jensen (1991b) [MRID 49961504]	Reported no significant reduction in cloning efficiency at any concentration.
Gene Mutations in Mammalian Cells	Chinese hamster ovary (CHO) cells, HPRT locus ± S9	500–25000 µg/mL (+S9); 500-22500 µg/mL (-S9)	98.7%	Negative	Li (1983a); [MRID 00132681]	Tested S9 from 1-10% Cytotoxic at 22.5 mg/mL (-S9, and with 1,2 and 10% S9) and at 17.5 mg/ml (10% S9)
Gene Mutations in Mammalian Cells	Mouse lymphoma L5178Y TK$^{+/-}$ cells ± S9	1-5 µl/mL	55.6% *Glyphosate trimesium salt*	Negative	Majeska (1985b) [MRID 00155530]	Negative with pH adjusted

[1] Study was cited in Kier and Kirkland (2013). Supplementary information about the study was provided online including test guideline, test material purity, control chemicals and summary data tables.

Appendix 8 - Glyphosate: EPA's Table 5.3. *In Vitro* tests for chromosomal aberrations in mammalian cells: Glyphosate technical

Table 5.3. *In vitro* Tests for Chromosome Aberrations in Mammalian Cells- Glyphosate Technical

Test/Endpoint	Test System	Concentrations/ Conditions	Test Material Purity	Results	Reference	Comments
In vitro Chromosomal Aberration	Chinese hamster ovary (CHO) cells	4-10 µl/mL, ± S9	55.6% *Glyphosate trimesium salt*	Negative	Majeska (1985c) [MRID 00155530]	pH adjusted (7.4-7.6)
In vitro Chromosomal Aberration	Chinese Hamster lung (CHL) cells	±S9: 0, 250, 500, 1000 and 2000 µg/mL; 24 and 48 h treatment - S9; 6 h treatment ±S9 harvest 24 h	95.68%	Negative	Matsumoto (1995) [MRID 50017106]	Decline in pH noted at 500 and 1000 µg/mL.
In vitro Chromosomal Aberration	Chinese hamster lung (CHL) cells	-S9: 24 & 48-hr exposure: 0-1250 µg/mL; +S9: 0-1250 µg/mL	95.3%	Negative	Wright (1996) [MRID 49957410]	Excessive decrease in pH >1250 µg/mL
In vitro Chromosomal Aberration	Bovine lymphocytes	-S9 only: 0, 7, 85 and 170 µM; 72 h exposure	≥98%	Positive (all concs.)	Lioi *et al*. (1998b)	
In vitro Chromosomal Aberration	Bovine lymphocytes	±S9: 0, 28, 56, 140, 280, 560 and 1120 µM; 24 h exposure	62.0%	Negative	Sivikova and Dianovsky (2006)	Decreased MI and PI at ≥ 560 µM
In vitro Chromosomal Aberration	Human lymphocytes	±S9: 100-1250 µg/mL cultures analyzed; 68 & 92 h	95.6%	Negative	Fox (1998) [MRID 49961803]	Excessive decrease in pH >1250 µg/mL
In vitro Chromosomal Aberration	Human lymphocytes	-S9 only: 0, 5.0, 8.5, 17.0 and 51.1 µM; 72 h exposure	≥98%	Positive ≥ 8.5 µM	Lioi *et al*. (1998a)	No significant ↓ in MI observed.
In vitro Chromosomal Aberration	Human lymphocytes	-S9: 0, 200, 1200 and 6000 µM; 48 h exposure	96.0%	Negative	Manas *et al*. (2009)	No toxicity observed up to 6000 µM

[1] Study was cited in Kier and Kirkland (2013). Supplementary information about the study was provided online including test guideline, test material purity, control chemicals and summary data tables.
CA= chromosomal aberrations, MI= mitotic index, PI= proliferation index.

Appendix 9 - Glyphosate: EPA's Table 5.4. *In vitro* tests for micronuclei induction in mammalian cells: Glyphosate technical

Table 5.4. *In vitro* Tests for Micronuclei Induction in Mammalian Cells- Glyphosate Technical

Test/Endpoint	Test System	Concentrations/ Conditions	Test Material Purity	Results	Reference	Comments
In vitro Cytokinesis Block Micronucleus Assay (with FISH analysis)	TR146 cells (human-derived buccal carcinoma cell line)	10, 15 and 20 mg/L; 20 minute exposure.	95%	Positive Statistically significant ($p<0.05$) increase in MN at 15 and 20 mg/L.	Koller *et al.* (2012)	Apoptosis and necrosis reported at 20 mg/L Also reported ↑ in NB and NPB
In vitro Cytokinesis Block Micronucleus Test	CHO-K1 cells	5 - 100 µg/mL, ±S9	Not stated	Negative –S9 Positive +S9 at 10-100 µg/mL	Roustan et al., (2014)	No clear dose response
In vitro Cytokinesis Block Micronucleus Test	Bovine lymphocytes (2 donors)	0, 28, 56, 140, 280 and 560 µM 24 & 48 h exposure	62%	24 h: Negative 48 h: Equivocal ↑ MN at 280 µM only (donor A) ↑ MN at 560 µM only (donor B)	Piesova, 2004	No dose-response No significant decrease in CBPI observed.
In vitro Cytokinesis Block Micronucleus Test	Bovine lymphocytes (2 donors)	0, 28, 56, 140, 280 and 560 µM; 2 h (±S9) and 48 h (-S9) exposure	62%	2 h: Negative 48 h: Equivocal ↑ MN at 280 µM only (donor A) and at 560 µM only (donor B)	Piesova, 2005	No dose-response; No significant decrease in CBPI observed. Metabolic activation had no effect on MN formation after 2 h exposure.

Table 5.4. *In vitro* Tests for Micronuclei Induction in Mammalian Cells- Glyphosate Technical

Test/Endpoint	Test System	Concentrations/ Conditions	Test Material Purity	Results	Reference	Comments
In vitro Cytokinesis Block Micronucleus Assay (with FISH analysis)	Human lymphocytes (treated with cytochalasin B)	4h treatment ±S9; 0.5, 2.91, 3.50, 92.8 and 580 µg/mL; harvested 72 h	98.0%	Negative –S9 Positive +S9, ↑ MN at 580 µg/mL, but not at 0.5-92.8 µg/mL Also observed ↑ in NB at 580 µg/mL (±S9); ↑ NPB at 580 µg/mL (+S9)	Mladinic *et al.* (2009a)	Cells were exposed to glyphosate and washed prior to treatment with PHA. Authors did not report being blind to treatment.
In vitro Cytokinesis Block Micronucleus Assay (with FISH analysis)	Human lymphocytes (treated with cytochalasin B)	4h treatment ±S9; 0.5, 2.91, 3.50, 92.8 and 580 µg/mL	98%	Negative –S9 Positive +S9 ↑ MN at 580 µg/mL, but not at 0.5 -92.8 µg/mL ↑ apoptosis and necrosis at 580 µg/mL (-S9); ↑ apoptosis at ≥ 2.91 µg/mL and necrosis at 580 µg/mL (+S9) ↑ in NB at 580 µg/mL (±S9) and NPB at 580 µg/mL (+S9)	Mladinic *et al.* (2009b)	Cells were exposed to glyphosate and washed prior to treatment with PHA. Authors did not report being blind to treatment. .

CBPI= cytokinesis block proliferation index, FISH= fluorescent in situ hybridization; MN= micronuclei; NB= nuclear buds; NPB= nucleoplasmic bridges.

Appendix 10 - Glyphosate: EPA's Table 5.5. *In vivo* tests for chromosomal aberrations in mammals: Glyphosate technical

Table 5.5. *In Vivo* Tests for Chromosomal Aberrations in Mammals- Glyphosate Technical.

Test/Endpoint	Test System	Route of Administration	Doses	Test Material Purity	Results	Reference	Comments
Bone Marrow Chromosomal Aberration Test	Sprague Dawley rats (males and females)	Intraperitoneal injection; sampled at 6, 12 and 24 h after treatment	0, 1000 mg/kg (6/sex/dose/sampling time)	98%	Negative	Li (1983b) [MRID 00132683]	No toxicity observed. A separate study using ^{14}C-glyphosate showed that glyphosate reaches BM 0.5 h after dosing with ½ life elimination at 7.6 h. Peak BM value was 400 ppm, corresponding to 2000 ppm plasma value.
Bone Marrow Chromosomal Aberration Test	Sprague Dawley rats (males and females) Vehicle: distilled water	Oral gavage, sampling after 6, 12, 24, 48 h and 5 d	0, 21, 63 and 188 mg/kg	58.5% *Glyphosate trimesium salt*	Negative	Majeska (1982c) [MRID 00132176]	
Bone Marrow Chromosomal Aberration Test	Swiss Albino mice (males and females) Vehicle: peanut oil	Oral gavage (2 treatments, 24 h apart); sampling after 24 h (last treatment)	0, 5000 mg/kg (5/sex/dose)	96.8%	Negative	Suresh (1994) [MRID 49987408]	Significant ($p<0.05$) decrease in bw of females at high dose.
Rodent Dominant Lethal Test	CD-1 mice Each dosed male mated with 2 females/week for 8 weeks	Oral gavage	0, 200, 800, and 2000 mg/kg	98.7%	Negative	Rodwell (1980) [MRID 00046364]	
Rodent Dominant Lethal Test	Wistar rat Each dosed male mated with 1 female/week for 10 weeks	Oral gavage	0, 200, 100 and 5000 mg/kg	96.8%	Negative	Suresh (1992) [MRID 49987404]	

Appendix 11 - Glyphosate: EPAs Table 5.6. In vivo tests for micronuclei induction in mammals: Glyphosate technical

Table 5.6. In Vivo Tests for Micronuclei Induction in Mammals- Glyphosate Technical.

Test/Endpoint	Test System	Route of Administration	Doses	Test Material Purity	Results	Reference	Comments
Bone Marrow Micronucleus Test	Swiss CD1 mice (males only)	Intraperitoneal injection; 2 injections of half the dosage of 300 mg/kg 24 h apart; sampling at 6 and 24 h	0, 300 mg/kg (3/dose)	99.9%	Positive Stat significant increase in MN at 24 h	Bolognesi *et al*. (1997)	Material and methods indicate 3 animals/dose; however, Table 1 of article indicates 4 animals were evaluated.
Bone Marrow Micronucleus Test	Balb C mice (males and females) Vehicle: Saline	Intraperitoneal Injection (two injections, 24 h apart); sampling after 24 h (last treatment)	0, 50, 100, and 200 mg/kg (5/sex/dose)	96%	Positive ↑MN at 200 mg/kg, but not at 50 or 100 mg/kg	Manas *et al*. (2009)	No significant signs of toxicity observed.
Bone Marrow Micronucleus Test	C3H mice (males only) Vehicle: water	Intraperitoneal Injection (single treatment); sampling after 24, 48 and 72 h	0, 300 mg/kg	Not reported	Negative	Chruscielska *et al*. (2000)	
Bone Marrow Micronucleus Test	Swiss Albino mice (males and females) Vehicle: corn oil	Intraperitoneal Injection (2 treatments, 24 h apart); sampling after 24 h (last treatment)	0, 15.62, 31.25, and 62.5 mg/kg (5/sex/dose)	980 g/kg Glyphosate technical	Negative#	Costa (2008)[1]	OECD guideline 474 #Was not tested up to limit dose and did not demonstrate that compound was tested up to toxic dose. No mention of BM toxicity or clinical signs.

Appendix 11 - Glyphosate: EPAs Table 5.6 (continued). In vivo tests for micronuclei induction in mammals: Glyphosate technical

Table 5.6. In Vivo Tests for Micronuclei Induction in Mammals- Glyphosate Technical.

Test/Endpoint	Test System	Route of Administration	Doses	Test Material Purity	Results	Reference	Comments
Bone Marrow Micronucleus Test	Crl:CD-1TM(ICR) BR mice (males only[1]) Vehicle: PBS	Intraperitoneal Injection (single treatment); sampling after 24 and 48 h (high dose only)	0, 150, 300 and 600 mg/kg (7/dose)	95.7%	Negative	Durward (2006) [MRID 49957411]	Clinical signs reported at ≥ 150 mg/kg. Significant ↓ in %PCEs reported at 24 h in 600 mg/kg group. ↑in MN PCEs observed at 600 mg/kg (1.9± 0.7 vs. 1.0 ± 1.2 control; p<0.05), at 24 h, but not 48 h, within historical control range.
Bone Marrow Micronucleus Test	Swiss Albino mice (males and females) Vehicle: water	Intraperitoneal Injection (2 treatments, 24 h apart); sampling after 24 h (last treatment)	0, 1008, 2016, and 3024 mg/kg 5/sex/dose	612.7 g/kg (glyphosate technical Nufarm)	Negative	Gava (2000)[1]	LD50 was 4032 mg/kg Mortality observed in 1 animal at high dose (only 4 m/f scored for MPCEs). No effect on PCE/NCE.
Bone Marrow Micronucleus Test	Swiss Albino mice (males and females) Vehicle: water	Intraperitoneal Injection (2 treatments, 24 h apart); sampling after 24 h (last treatment)	0, 187.5, 375 and 562.5 mg/kg 5/sex/dose	954.9 g/kg (glyphosate technical Nufarm)	Negative	Marques (1999) [MRID 49957412]	LD50 was 750 mg/kg No significant signs of toxicity observed in main study
Bone Marrow Micronucleus Test	NMRI-Bom mice	Intraperitoneal Injection (single treatment); sampling after 24 h (all doses) and 48 h (150 and 200 mg/kg)	0, 150, and 200 mg/kg (5/sex/dose)	glyphosate isopropyla mine (purity not specified)	Negative	Rank *et al*. (1993)	

Appendix 11 - Glyphosate: EPAs Table 5.6 (continued). In vivo tests for micronuclei induction in mammals: Glyphosate technical

Table 5.6. In Vivo Tests for Micronuclei Induction in Mammals- Glyphosate Technical.

Test/Endpoint	Test System	Route of Administration	Doses	Test Material Purity	Results	Reference	Comments
Bone Marrow Micronucleus Test	Swiss albino mice (males and females)	Intraperitoneal Injection (2 treatments, 24 h apart); sampling after 24 h (last treatment)	0, 68, 137, and 206 mg/kg (	360 g/L	Negative	Zaccaria (1996) [MRID 49961501]	Doses selected were reported as corresponding to 25, 50 and 75% LD_{50}
Bone Marrow Micronucleus Test	CD-1 mice (males and females) Vehicle: saline	Oral gavage (single treatment); sampling after 24 and 48 h	0, 5000 mg/kg 5/sex/dose	95.6%	Negative	Fox and Mackay (1996) [MRID 44320619]	No significant signs of toxicity observed
Bone Marrow Micronucleus Test	NMRI mice (males and females) Vehicle: PEG 400	Oral gavage (single treatment); sampling after 24 and 48 h (high dose only)	0, 500, 1000, and 2000 mg/kg 5 sex/dose	97.73%	Negative	Honarvar (2005)[1]	OECD guideline 474 No significant signs of toxicity observed
Bone Marrow Micronucleus Test	NMRI mice (males only) Vehicle: 0.5% carboxymethylcellulose	Oral gavage (single treatment); sampling after 24 and 48 h (high dose only)	0, 500, 1000, and 2000 mg/kg (5/dose)	99.1%	Negative	Honarvar (2008) [MRID 49961802]	No significant signs of toxicity observed
Bone Marrow Micronucleus Test	NMRI mice (males and females) Vehicle: 0.5% carboxymethylcellulose	Oral gavage (single treatment); sampling after 24, 48 and 72h	0, 5000 mg/kg; 5/sex/dose	98.6%	Negative	Jensen (1991c) [MRID 49961503]	No significant signs of toxicity observed
Bone Marrow Micronucleus Test	CD-1 mice (males only[1]) Vehicle: water	Oral gavage single treatment); sampling after 24 and 48 h	0, 2000 mg/kg 5/dose	59.3% potassium glyphosate salt	Negative	Jones (1999)[1]	OECD guideline 474 No significant signs of toxicity observed
Bone Marrow Micronucleus Test	Swiss albino mice; (males and females)	Oral gavage (2 treatments, 24 h apart); sampling	0, 50, 500, 5000 mg/kg 5/sex/dose	96.8% glyphosate acid	Positive in females at 5000	Suresh (1993b) [MRID 49987407]	No significant signs of toxicity observed

Appendix 11 - Glyphosate: EPAs Table 5.6 (concluded). In vivo tests for micronuclei induction in mammals: Glyphosate technical

Table 5.6. In Vivo Tests for Micronuclei Induction in Mammals- Glyphosate Technical.

Test/Endpoint	Test System	Route of Administration	Doses	Test Material Purity	Results	Reference	Comments
	Vehicle: peanut oil	after 24 h (last treatment)			mg/kg only. Negative in males at all doses		
Bone Marrow Micronucleus Test	Swiss mice (males only) Vehicle: corn oil	Oral gavage (2 treatments, 24 h apart); sampling after 24 h (last treatment)	0, 8, 15 and 30 mg/kg (6/dose)	980.1 g/kg	Negative	Zoriki Hosomi (2007) [MRID 50000901]	OECD guideline 474 No significant signs of toxicity observed
Bone Marrow Micronucleus Test	CD-1 mice (males and females) Vehicle: distilled water	Oral gavage , Sampling 24, 48 and 72 h after treatment	Males: 0, 700, 900 and 1100 mg/kg Females: 0, 400, 600 and 800 mg/kg	55.3% *Glyphosate trimesium salt*	Negative	Majeska (1987) [MRID 40214004]	
Bone Marrow Micronucleus Test	B6CF3 Mice (males and females)	Oral (dietary). MN assay conducted following 13 week feed study.	0, 205/213, 410/421, 811/844, 1678/1690 and 3393/3393 mg/kg (m/f) (10/sex/dose)	99%	Negative	NTP (1992)	
Bone Marrow Micronucleus Test	CD Rats (males and females) Vehicle: 0.8% hydroxypropylmethyl cellulose	Oral gavage (single treatment); sampling after 24 and 48 h (high dose only)	0, 500, 1000, and 2000 mg/kg (5/sex/dose)	98.8%	Negative	Flügge (2009b)[1]	OECD guideline 474 No significant signs of toxicity observed

[1] Study was cited in Kier and Kirkland (2013). Supplementary information about the study was provided online including test guideline followed, test material purity, control chemicals and summary data tables.
[2]Only males tested; report indicated that there were no difference between sexes seen in range finding study.
CA= chromosomal aberrations, MPCE= micronucleated polychromatic erythrocytes, NCE= normochromatic erythrocytes, PCE=polychromatic erythrocytes.

Appendix 12 - Glyphosate: EPAs Table 5.7. Assays for detecting primary DNA Damage - Glyphosate technical

Table 5.7 Assays for Detecting Primary DNA Damage- Glyphosate Technical.

Test/Endpoint	Test System	Route of Administration	Doses/ Concentrations	Test Material Purity	Results	Reference	Comments
DNA Adducts ^{32}P-postlabeling	Swiss CD1 mice (males and females) Liver and kidney evaluated	Intraperitoneal injection; 24 h exposure	0, 130 and 270 mg/kg	Not reported	Negative	Peluso *et al.* (1998)	
DNA oxidative damage: 8-OHdG formation	Swiss CD-1 mice (males) liver and kidney evaluated	Intraperitoneal injection (single dose); sampling 4 and 24 h after injection	0, 300 mg/kg (3/dose)	99.9%	Kidney: negative Liver: positive (24 h)	Bolognesi *et al.* (1997)	
Single-cell gel electrophoresis (SCGE) assays- Comet assay	TR146 cells (human-derived buccal epithelial cell line).	NA (*in vitro*)	-S9: 10-2000 mg/L; 20 minute exposure.	95%	Positive Increased DNA migration at >20 mg/L	Koller *et al.* (2012)	Also measured multiple cellular integrity parameters to assess cytotoxicity. No clear evidence of cytotoxicity seen except for increase in enzyme activity (indicative of membrane damage) in LDHe (extracellular lactate dehydrogenase) assay at >80 mg/L. No mention of monitoring pH
Single-cell gel electrophoresis (SCGE) assays- Comet assay	Hep-2 cells	NA (*in vitro*)	0, 3, 4.5, 6, 7.5, 9, 12 and 15 mM	96%	Positive Stat. significant increase in mean tail length, and tail intensity at all concs.	Manas *et al.* (2009)	The authors did not report a source for the Hep-2 cells. The agency presumes that this is a HeLa derived cervical carcinoma cell line.

Appendix 12 - Glyphosate: EPAs Table 5.7 (continued). Assays for detecting primary DNA Damage - Glyphosate technical

Table 5.7 Assays for Detecting Primary DNA Damage- Glyphosate Technical.

Test/Endpoint	Test System	Route of Administration	Doses/ Concentrations	Test Material Purity	Results	Reference	Comments
Single-cell gel electrophoresis (SCGE) assays- Comet assay	Human lymphocytes	NA (*in vitro*)	0, 0.7, 7, 70, 700 µM	96%	Positive at all doses (increase in tail length only)	Alvarez-Moya *et al*., (2014)	Issues were identified with this study resulting in a low quality ranking. These include: 1) blood was washed with PBS and then held at 4° C for an indeterminate amount of time before exposure to glyphosate. (2) Cells were treated for 20 hours at room temperature. (3) The same amount of damage was reported across 2 orders of magnitude concentration.
Single-cell gel electrophoresis (SCGE) assays- Comet assay	Human lymphocytes; ±S9 Alkaline and hOOG1 Comet assays performed	NA (*in vitro*)	0, 0.5, 2.91, 3.5, 92.8 and 580 µg/mL	98%	Positive ±S9	Mladinic *et al.* (2009a)	The alkaline comet assay -S9: ↑ in mean tail length at 580 µg/mL and ↑ in tail intensity at ≥ 3.5 µg/mL). +S9: ↑ DNA tail length at ≥3.5 µg/mL. Tail intensity ↑ only at 580 µg/mL hOOG1 comet assay: -S9 no effect on tail length, ↑tail intensity only at 3.50 µg/mL +S9: ↑ tail length at 580 µg/mL, no effect on tail intensity compared to controls at any conc.

Appendix 12 - Glyphosate: EPAs Table 5.7 (continued). Assays for detecting primary DNA Damage - Glyphosate technical

Table 5.7 Assays for Detecting Primary DNA Damage- Glyphosate Technical.

Test/Endpoint	Test System	Route of Administration	Doses/ Concentrations	Test Material Purity	Results	Reference	Comments
Single-cell gel electrophoresis (SCGE) assays- Comet assay with oxidative stress measures	Balb/C mice; evaluated blood and liver	Drinking water (14 days)	0, 40, and 400 mg/kg	96%	Positive Blood and liver at both doses	Manas et al. (2013)	Only minor effects seen on oxidative stress measurements (TBARs, SOD, CAT)
Sister Chromatid Exchange (SCE)	Bovine lymphocytes (3 donors)	NA (*in vitro*)	-S9: 0, 17, 85 and 170 µM; 72 h exposure	≥98%	Positive Significant (p>0.05) increase in SC/cell at all concentrations	Lioi (1998b)	1.8-, 2.1-, 1.6-fold increases, respectively
Sister Chromatid Exchange (SCE)	Human lymphocytes	NA (*in vitro*)	-S9: 0, 5, 8.5, 17 and 51 µM; 72 h exposure	≥98%	Positive Significant (p>0.05) increase in SCE/cell at ≥ 8.5 µM	Lioi (1998a)	1.9-, 2.8-, and 2.6-fold increase at 8.5, 17 and 51 µM, respectively
Sister Chromatid Exchange (SCE)	Human lymphocytes	NA (*in vitro*)	-S9: 0, 0.33, 1,3 and 6 mg/mL; 72 h exposure	99.9%	Positive	Bolognesi *et al.* (1997)	Very limited information was provided on the methods used in this paper. Authors report a dose –dependent increase in SCE frequency; however, no statistical analysis for dose response was reported. Data presented graphically with no error bars.
Sister Chromatid Exchange (SCE)	Human lymphocytes	NA (*in vitro*)	28, 56, 140, 280, 560 and 1120 µM; 24 h exposure ±S9	62%	Positive	Sivikova and Dianovsky (2006)	The increases in SCEs observed did not show a clear concentration related increase across a 40-fold increase in the concentrations tested

Table 5.7 Assays for Detecting Primary DNA Damage- Glyphosate Technical.

Test/Endpoint	Test System	Route of Administration	Doses/ Concentrations	Test Material Purity	Results	Reference	Comments
Alkaline elution assay- DNA single strand breaks	Swiss CD-1 mice (males) liver and kidney evaluated	Intraperitoneal injection (single dose); sampling 8 and 24 h after injection	0, 300 mg/kg (3/dose)	99.9%	Positive (Increased elution rate) at 4 hours in liver and kidney At 24 h, elution rate returned to control levels	Bolognesi *et al.* (1997)	Return to control values may indicate DNA repair or reflect rapid elimination of compound
DNA Repair Test (Rec-A test)	*B. subtilis* H17 (rec+) and M45 (rec-)	NA (*in vitro*)	20-2000 µg/disk	98.4%	Negative	Shirasu (1978) [MRID 00078619]	
Unscheduled DNA synthesis (DNA repair)	F-344 rat primary hepatocytes	NA (*in vitro*)	0, 0.0125, 0.0625, 0.125, 0.6.5, 1.25, 12.5, 125 µg/mL	98%	Negative	Li and Long (1988)	
Cell Transformation Assay	BALB/3T cells	NA (*in vitro*)	0.313-5.0 mg/mL	90% *Glyphosate trimesium salt*	Negative	Majeska (1982b) [MRID 00126616]	

h- hour; CAT= catalase, G6PD= glucose 6-phosphate dehydrogenase, NA= not applicable, hOOG1 =,TBARs= thiobarbituric acid reactive substances, SOD= superoxide dismutase

Attachment A

CURRICULUM VITAE

Jay Irwin Goodman

CURRENT POSITION: Professor
Department of Pharmacology and Toxicology
Michigan State University
East Lansing, MI 48824
[redacted]

HOME ADDRESS: [redacted]

Jay Irwin Goodman

EDUCATION: 1957-1958 Erasmus Hall High School, Brooklyn, NY
1958-1960 James Madison High School, Brooklyn, NY
1960-1965 B.S., Long Island University, College of Pharmacy, Brooklyn, NY
1965-1969 Ph.D. in Pharmacology, The University of Michigan, Ann Arbor, MI
1969-1971 Postdoctoral Fellow, McArdle Laboratory for Cancer Research, University of Wisconsin, Madison, WI

POSITIONS:

1965-1969 Predoctoral Fellow, Department of Pharmacology, The University of Michigan, Ann Arbor, MI
1969-1971 Postdoctoral Fellow, Recipient of a postdoctoral fellowship awarded by the National Institutes of Health, National Cancer Institute, McArdle Laboratory for Cancer Research, University of Wisconsin, Madison, WI
1971-1975 Assistant Professor, Department of Pharmacology, Michigan State University, East Lansing, MI
1975-1978 Associate Professor, Department of Pharmacology, Michigan State University, East Lansing, MI
1978-1982 Associate Professor, Department of Pharmacology and Toxicology, Michigan State University, East Lansing, MI
1980- Participating Faculty Member, Center for Environmental Toxicology, Michigan State University, East Lansing, MI
1982- Professor, Department of Pharmacology and Toxicology, Michigan State University, East Lansing, MI
2001-2002 Interim Chair, Department of Pharmacology and Toxicology, Michigan State University, East Lansing, MI

MEMBERSHIP IN PROFESSIONAL SOCIETIES:

Society of Toxicology
American Society for Pharmacology and Experimental Therapeutics
American Association for the Advancement of Science
American Chemical Society
International Society of Regulatory Toxicology and Pharmacology

CERTIFICATIONS:

Diplomate of the American Board of Toxicology, Inc.
Fellow of the Academy of Toxicological Sciences

HONORS AND AWARDS:

Distinguished Alumnus Award, Long Island University, College of Pharmacy, 1998
Elected President of the Society of Toxicology, 1999-2000
Distinguished Alumnus Award, Doctoral Program in Pharmacology, The University of Michigan, 2000
Recipient of the John Barnes Prize Lecture, awarded by the British Toxicology Society, 2005
Invited speaker, Annual John Doull Symposium, Department of Pharmacology, Toxicology and Therapeutics, University of Kansas, 2007
Recipient of the George H. Scott Memorial Award, awarded by the Toxicology Forum, 2007
Plenary Lecture, Annual Meeting of the European Societies of Toxicology (EUROTOX), 2009
Recipient of the Society of Toxicology's Merit Award, 2014
Recipient of the International Society of Regulatory Toxicology and Pharmacology's International Achievement Award, 2014

GOODMAN, JAY I. **SYNOPSIS OF RESEARCH INTERESTS**

My research interests are in the area of toxicology. These are concerned with discerning mechanisms involved in carcinogenesis, primarily those underlying tumor promotion.

Introduction. Inheritance should be considered on a dual level. The transmission of genes from generation to generation (i.e., inheritance of DNA base sequence) is distinct from the mechanisms involved in the transmission of alternative states of gene activity following cell division. Epigenetics is the term used to describe the latter. DNA methylation (the presence of 5-methylcytosine (5MeC) as compared to cytosine) is one epigenetic mechanism by which gene activity may be regulated. There is a persuasive body of evidence indicating that differential methylation of DNA (i.e., 5MeC v. cytosine) is a determinant of chromatin structure and that the methyl group provides a chemical signal which is recognized by transacting factors that regulate transcription. In general, hypomethylation (i.e., decreased content 5MeC) of a gene is necessary but not sufficient for its expression and, therefore, a hypomethylated gene can be considered to possess an increased potential for expression as compared to one which is hypermethylated. Changes in the methylation status of a gene provide a mechanism by which its potential for expression can be altered in an epigenetic heritable manner, and it is expected that modifications in DNA methylation would result from threshold-exhibiting events. Actually, alterations in DNA methylation may play multiple roles in carcinogenesis, involving mutation and epigenetic events, e.g., increased expression of oncogenes and silencing of tumor suppressor genes.

Carcinogenesis is a multistep process, involving initiation, promotion and progression stages. While mutation plays a role in the etiology of cancer, it is axiomatic that (with the exception of tumor suppressor genes) a mutated gene must be expressed in order to affect the phenotype of a cell. I have emphasized the view that hypomethylation of DNA is an epigenetic, nongenotoxic, mechanism underlying the aberrant gene expression involved in the tumor promotion stage of carcinogenesis. This provides as a **focal point** for a mechanism of action oriented approach for considering key aspects of carcinogenesis: aberrant gene expression, heritable epigenetic events, tumor promotion, thresholds and species to species extrapolation issues. We employ the liver tumor-prone B6C3F1 (C57BL/6♂ x C3H/He♀) mouse as our experimental model, focus upon oncogenes (e.g., Ha-ras and raf) relevant to mouse liver tumorigenesis and make relevant comparisons with the sensitive C3H/He paternal strain and the resistant C57BL/6 maternal strain. Our **results** indicate that differences in DNA methylation between the C57BL/6 and B6C3F1 mice could, in part, account for the unusually high propensity of the later strain to development of liver tumors. My working **hypothesis** is that susceptibility to tumorigenesis may be related inversely to the capacity to maintain normal patterns of DNA methylation.

A **unique aspect** of this research program is the fact that it combines the testing of an hypothesis which is shedding light on basic mechanisms involved in tumorigenesis while providing some of the fundamental knowledge required to take a rational approach towards risk assessment. This is related directly to three key questions: 1) dose setting for chronic studies, i.e., doses that affect DNA methylation may be considered as having caused the overriding of an important homeostatic mechanism and thus be viewed as excessive; 2) species to species extrapolation issues, e.g., liver tumors induced in B6C3F1 mice, especially those caused by nongenotoxic compounds, should not be regarded as an appropriate end point for human risk assessment; and 3) dose-response relationships, i.e., I view altered DNA methylation as a secondary mechanism underlying carcinogenesis. Carcinogens acting by this mode of action may be considered as exhibiting a threshold and, thus, should be regulated by a safety factor (or multiplicity of exposure) approach.

CURRENT RESEARCH SUPPORT

1. NIH-NIEHS Superfund Program "Environmental, Microbial, and Mammalian Bimolecular Responses to AhR Ligands," N.E. Kaminski, PI, J.I. Goodman, Co-Investigator on one Project"Characterization of the Pathways Linking Ah Receptor Activation with Altered B Cell Differentiation Using an Integrated Experimental and Computational Modeling Approach," and Core Leader, Training Core. Total direct costs: $14,100,00; 4-1-13 through 3-31-18.

2. NIH-NIEHS, ES007255-26. Multidisciplinary Training in Environmental Toxicology. R.A. Roth, Program Director; J.I. Goodman, Member of the Training Faculty; includes 19 additional MSU Faculty Members. Total Direct Costs for the current 5-year grant period): $1,454,780; 07/01/14 through 06/30/19.

3. R.J. Reynolds Tobacco Co. – Altered DNA Methylation During Specific Stages of Carcinogenesis. J.I. Goodman, Principal Investigator. Total Direct Costs – $515,000; November, 2001-open.

MEMBERSHIP ON ADVISORY COMMITTEES AND BOARDS

Consultant to the NIH, National Cancer Institute, Member of a site visit team, 1979.

Consultant to the NIH, National Institute of Environmental Health Sciences, Member of a site visit team, 1980.

State of Michigan, Department of Natural Resources, Member of the Rule 57 Advisory Committee for Implementation of Water Quality Standards, 1981-1983.

Michigan Regional Chapter of the Society of Toxicology

- Chairperson of the Nominating Committee, 1982
- Vice-President, 1983-1984
- President-Elect, 1984-1985
- Chairperson of the Program Committee, 1984-1985
- President, 1985-1986
- Counselor, 1986-1987

Member of the Professional Education Committee, American Cancer Society, Michigan Division, 1983-1985.

Ad-Hoc Consultant to the State of Michigan, Department of Natural Resources, November, 1983.

Member of the Technical Program Committee for the Annual Meeting of the Air Pollution Control Association, June, 1985.

Member of the Air Toxics Policy Committee for the State of Michigan, Technical Subcommittee to consider the use of toxicity and risk assessment data in the regulatory process, 1988-1989.

Consultant to the NIH, National Institute of Environmental Health Sciences, Member of a site visit team, 1988.

Consultant to the Pharmaceutical Manufacturer's Association Foundation, Inc., reviewer for the Research Starter Grant Program, 1988.

Member of the Board of Scientific Counselors, National Toxicology Program, Department of Health and Human Services, 1989-1992.

Consultant to the National Science Foundation, Biochemistry Program, Research Grant Proposal Reviewer, 1989.

Member of the Technical Reports Review Subcommittee, Board of Scientific Counselors, National Toxicology Program, Department of Health and Human Services, 1990-1992

Consultant to the Michigan Department of Natural Resources, Michigan Great Lakes Protection Fund, Research Grant Proposal Reviewer, 1990.

Consultant to the National Institute of Environmental Health Sciences, Division of Extramural Research and Training, Reviewer of Research Grant Proposals, 1991.

Member of the Scientific Review Committee, Program to investigate the mechanism(s) that relates peroxisome proliferation to rodent hepatocarcinogenicity, International Life Sciences Institute, Risk Science Institute, 1991-1993.

Member of the Board of Directors, American Board of Toxicology, Inc., 1992-1996.

Chairman of the Carcinogenesis Subcommittee, Committee for the Review of Functions and Purposes of the National Toxicology Program, Department of Health and Human Services, 1992.

Member of the Expert Working Group on Dose Selection Issues for the Carcinogen Bioassay, International Life Sciences Institute, Risk Science Institute, and U.S. Environmental Protection Agency, Office of Pesticide Programs, 1993-1996.

Consultant to the National Institute of Environmental Health Sciences, External Reviewer of the Intramural Program on Environmental Carcinogenesis and Mutagenesis, May, 1994.

Member of the Expert Review Group, U.S. Environmental Protection Agency Workshop on Cancer Risk Assessment Guideline Issues, Review of the draft revisions to the Guidelines for Carcinogen Risk Assessment, 1994

Member of the Siloxane Science Advisory Board, Dow Corning Corp., 1994-2003

Member of the Working Group on Transgenic Animals in Carcinogenicity Testing, International Life Sciences Institute, Risk Sciences Institute, 1995-2004

Expert Reviewer, Ad Hoc, National Toxicology Program, Board of Scientific Counselors, Technical Reports Review Committee, 1995.

Member of the Board of Directors, DNA Methylation Society, 1995-1996.

External Reviewer, Ad Hoc, Food and Drug Administration, National Center for Toxicological Research (NCTR), review of proposed NCTR research, August, 1995.

MEMBERSHIP ON ADVISORY COMMITTEES AND BOARDS (Continued)

External Examiner of a doctoral thesis, Faculty of Graduate Studies and Research, Department of Pharmacology and Therapeutics, McGill University, Montreal, Canada, July, 1995.

Member of the Flavor and Extract Manufacturers' Association (FEMA) Expert Panel for the Evaluation of Flavoring Materials, 1995-2005

Reviewer, Food and Drug Administration, National Center for Toxicological Research (NCTR), review of documents entitled "The Need for Dietary Control for the Reduction of Experimental Variability within Animal Assays" and "The Use of Dietary Restriction to Achieve Dietary Control," February, 1996.

Member of the Expert Panel to Evaluate Chloroform and Dichloroacetic Acid as Case Studies for the Application of EPA's Proposed Guidelines for Carcinogen Risk Assessment. Supported by the U.S. Environmental Protection Agency, The Chlorine Chemistry Council and The American Forest & Paper Association. Convened by the International Life Sciences Institute, Health and Environmental Sciences Institute, 1996-

Member of the Biological Effects of Low Level Exposures (Belle) Awards Committee to select the recipient of the Annual Belle Research Award, 1996-

Member of the Board of Trustees, Health and Environmental Sciences Institute, International Life Sciences Institute, 1997-2011.

Society of Toxicology

- President, 1999-2000
- Member of the Committee on Public Communications, 1984-1987
- Member of the Committee on Regulatory Affairs and Legislative Assistance, 1987-1989
- Counselor, Molecular Biology Specialty Section, 1990-1992
- Secretary-Elect and Member of Council, 1993-1994
- Secretary and Member of Council, 1994-1996
- Member of the Board of Trustees, Toxicology Education Foundation, 1994-1998
- Chairperson of the Chlorine Issue Working Group. This group led the development of the Society of Toxicology's position paper entitled "Toxicologic Principles Do Not Support the Banning of Chlorine," Fundamental and Applied Toxicology 24: 1-2, 1995.
- Member of the Task Force to Improve the Scientific Basis for Risk Assessment, 1996-1999
- Vice President-Elect, 1997-1998, and
- Co-Chairperson of the Program Committee for the 1998 Annual Meeting
- Vice President, 1998-1999
- Chairperson of the Program Committee for the 1999 Annual Meeting
- Immediate Past-President and Member of Council, 2000-2001
- Chairperson of the Steering Committee of the Mixtures Project, 2001-2003; Member, 2003-
- Chairperson of the Nominating Committee, 2001
- Member of the Nominating Committee, 2003-2004
- Member of the Awards Committee, 2009-2011
- Member of the Nominating Committee, 2017-2018

Member of the Science Advisory Panel for the Health and Environmental Sciences Institute, International Life Sciences Institute's Alternatives to Carcinogenicity Testing Committee, 1997-2001

Chairperson of the Publications Committee, Health and Environmental Sciences Institute, International Life Sciences Institute, 1997-2001

Member of a site visit team, Collaborative Research and Development Program, Research Council of Canada, re: Structure Function Analysis of DNA Methyltransferases, McGill University, in collaboration with Methylgene, Inc., Montreal, Canada, August, 1997.

Member of the Program Committee, Health and Environmental Sciences Institute, International Life Sciences Institute, Annual Scientific Meeting, 1998-2000

Member of the Subcommittee on Upper Reference Levels of Nutrients, Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutritional Board, Institute of Medicine, National Academy of Sciences, 1998-1999

Member of the Science Advisory Board, Phase-1 Molecular Toxicology, Inc., 1998-2002
Chairperson of the Communications Committee, Health and Environmental Sciences Institute, International Live Sciences Institute, 1999-2002

Member of the Nonclinical Studies Subcommittee of the Advisory Committee for Pharmaceutical Science, U.S. Food and Drug Administration, 1999-2002

Member of the Executive Committee, Health and Environmental Sciences Institute, International Life Sciences Institute, 1999-2004

Ad Hoc Research Grant Reviewer, Collaborative Research and Development Program, Research Council of Canada, re: Mechanism of DNA Demethylase Reaction, McGill University, Montreal, Canada, September, 1999

Vice Chairperson of the Executive Committee, Health and Environmental Sciences Institute, International Life Sciences Institute, 2000-2002

Member of the Global Environmental Advisory Council, Dow AgroSciences, 2000-2004

Chairperson of the Steering Committee "Support of Science-based Decisions Concerning the Evaluation of the Toxicology of Mixtures", Society of Toxicology, National Institute of Environmental Health Sciences, U.S. Environmental Protection Agency and the Chlorine Chemistry Council/ American Chemistry Council, 2000-2002

Chairperson, Society of Toxicology's Mixtures Project Steering Committee, 2001-2003; Member 2001-2004

Member of the Scientific Steering Committee of the Agricultural Chemicals Safety Assessment Committee, International Life Sciences Institute, Health and Environmental Sciences Institute, 2001-

Member of the Science Advisory Board, R.J. Reynolds Tobacco Co., 2001-2008; Co-Chair, 2007-2008

Member of Council, International Society of Regulatory Toxicology and Pharmacology, 2001-

Member, Alumni Steering Committee, Department of Pharmacology, The University of Michigan, 2001-

MEMBERSHIP ON ADVISORY COMMITTEES AND BOARDS (Continued)

Member of the Executive Committee, International Life Sciences Institute, Health and Environmental Sciences Institute, 1998-2008

Chairperson of the Executive Committee, International Life Sciences Institute, Health and Environmental Sciences Institute, 2002-2004

Member of the Board of Trustees, International Life Sciences Institute, 2002-2011

Member of Council, Academy of Toxicological Sciences, 2002-2005

Member of the Nominating Committee, Society of Toxicology, 2003-2004

Reviewer for the document entitled “Human Health Research Implementation Plan for the National Health and Environmental Effects Research Laboratory (NHEERL)”, U.S. Environmental Protection Agency, 2003.

Research Grant Reviewer, Canadian Liver Foundation, 2003

Member of the Pharmacology and Toxicology Subcommittee, Pharmaceutical Sciences Advisory Committee, U.S. Food and Drug Administration, 2003-2005

Research Grant Reviewer, Intramural Program, National Center for Toxicological Research, U.S. Food and Drug Administration, 2004

Participant in the Strategic Implementation Leadership Committee Meeting, American Chemistry Council, Chlorine Chemistry Council, 2004

Chair of the Toxicology Advisory Board, Division of Drug Safety and Disposition, Millenium Pharmaceuticals, Inc., 2004-2005

Member of the International Scientific Program Planning Committee for the International Congress of Toxicology (ICT XI), Montreal, Canada, July, 2007, 2005-2007

Member of the Advisory Committee to the Director, Centers for Disease Control and Prevention, Atlanta, GA, 2005-2009

Research Grant Reviewer, Canadian Liver Foundation, 2005

Member of the Science Advisory Board, Connetics Corp., 2006-2007

Research Grant Reviewer, U.S. Department of Energy, Office of Science, 2006

Member of the Board of Scientific Counselors, NIH, National Institute of Environmental Health Sciences, 2008-2013

Member of the Board of Trustees (and former Chair of the Board), International Life Sciences Institute. Health and Environmental Health Sciences Institute (term ended 2014)

MEMBERSHIP ON ADVISORY COMMITTEES AND BOARDS (Continued)

Member of the International Life Sciences Institute. Health and Environmental Health Sciences Institute's (HESI) Risk21 Project, an international effort aimed at transforming toxicity testing in the 21st century through the development of enhanced *in vitro* and high-throughput technologies, 2012 – 2014

Member of the International Life Sciences Institute's European Branch's "Threshold of Toxicological Concern Task Force, Expert Group on "Reanalysis of the cancer potency database underlying the 0.15 µg/day tier of the Threshold of Toxicological Concern (TTC)," 2013 -

Member of the EUROTOX (Association of the European Societies of Toxicology) Education Subcommittee, 2012-2018

Co-Chair, Toxicology Forum, Program Planning Committee, for the Annual Summer Meeting, 2015

Member of the Board of Directors, Toxicology Forum, 2015-2017

Member, 2015-2016, Michigan State University AFEX Review Team (AFEX is a biobased technology (patented by the Michigan Biotechnology Institute (MBI) that converts cellulose from crop residues into a sustainable source of cattle feed) chaired by George Smith, Associate Director, MSU AgBioResearch. This Team reviewed (and made suggestions for improvement) a proposal developed by Bobby Bringi (Chief Executive Officer, MBI) and colleagues for using AFEX to enhance the ability of cattle in India to produce milk. The proposal was submitted to the Gates Foundation, 2015-2016

Member of the Program Committee, Toxicology Forum, Rodent Liver Tumor Workshop, Washington, DC, October 2016

Member of the Steering Committee, Toxicoepigenetics Meeting, a Society of Toxicology Current Concepts in Toxicology meeting, Washington, DC, November 2016

Member of the Committee on Inorganic Arsenic, National Academies of Science, National Research Council, Board on Environmental Studies and Toxicology, 2015-

External peer reviewer, California Environmental Protection Agency, Office of Environmental Health Hazard Assessment, 2015-2016

CURRENT MEMBERSHIP ON MICHIGAN STATE UNIVERSITY COMMITTEES

Department:	Member of the Course and Curriculum Committee Member of the Alumni Relations and Development Committee
College:	Member of the Promotion and Tenure Committee
University:	Member of the Radiation Safety Committee

PREVIOUS MEMBERSHIP ON MICHIGAN STATE UNIVERSITY COMMITTEES

Department:
Chairman of the Graduate Committee (1979-1997)
Chairman of the Faculty Advisory Committee
Member of the Library Committee
Coordinator of the Seminar Program
Coordinator of the Medical Pharmacology Course
Coordinator of the Environmental Toxicology Course
Member of the Curriculum Committee
Member of the Faculty Advisory Committee
Member of the Graduate Committee
Member of the Laboratory Safety Committee
Member of the Search Committee, Molecular Toxicology position

College:
Member of the College Advisory Council
Member of the Committee on Student Evaluation
Member of the Agriculture Experiment Station's Cooperative Extension Service's Subcommittee on Environmental Quality and Toxicology
Member of the Committee for the Review of Toxic Drug Reactions
Member of the Search Committee for the selection of the Chairperson of the Department of Pharmacology and Toxicology
Member of the Cancer Education Committee and Chairman of its Basic Science Subcommittee
Member of the Promotion and Tenure Committee
Member of the Student Performance Committee
Member of the Biomedical Support Grant Review Committee

University:
Chairman of the Institutional Biosafety Committee
Member of the Radiation, Chemical and Biological Safety Committee
Member of the Search Committee for the Director of the Center for Environmental Toxicology
Member of the Task Force on Implementation in Graduate Students' Research of Regulations Regarding Human and Animal Subjects and Hazardous Materials
Member of the University Biohazards Committee
Member of the Safety and Health Operation Committee
Member of the Graduate Studies Committee
Member of the Strategic Partnership Grants Review Committee, Health and Biomedical Sciences Panel, Office of the Vice President for Research

TEACHING RESPONSIBILITIES

1) COLLEGES OF MEDICINE: I am responsible for the teaching of antibiotics, cancer chemotherapy, and viral chemotherapy in the Medical Pharmacology courses required for students enrolled in Michigan State University's College of Human and Osteopathic Medicine. I am the course coordinator for the Systems and Infectious Diseases Pharmacology course required for students enrolled in Michigan State University's College of Veterinary Medicine, and I teach the antibiotics section of this course. Additionally, I lecture on the topic of "Colon Cancer: An Example of Multistage Carcinogenesis" in the Medical School's Gastrointestinal Systems Course.

2) UNDERGRADUATE LEVEL: I am responsible for Introduction and the section dealing with risk/safety assessment in my Department's undergraduate course entitled Introduction to Chemical Toxicology.

3) GRADUATE SCHOOL: I am responsible for the sections dealing with mutagenesis, carcinogenesis, toxicology in drug development, risk/safety assessment of carcinogens, and transgenerational effects of chemicals in my Department's graduate course entitled Advanced Principles of Toxicology. I am responsible for the sections dealing with drugs that interact with nucleic acids, and cancer chemotherapy in my Department's graduate course entitled Cellular, Molecular and Integrated Pharmacology and Toxicology. I lecture on systems biology in my Department's graduate course entitled Current Topics in Molecular Pharmacology. Additionally, I present an on-line course entitled Concepts in Carcinogenesis.

   In addition, I was the Chair of the Department of Pharmacology and Toxicology's Graduate Committee from 1979-1997 and a member of the Committee from 1997-1998, and 2003-2005. This Committee oversees the Ph.D. program in Pharmacology and Toxicology at Michigan State University.

ASSOCIATE EDITOR: Regulatory Toxicology and Pharmacology, 2004-
Fundamental and Applied Toxicology, 1992-1997
Toxicological Sciences, 1997-2008

EDITORIAL BOARD MEMBERSHIP: Fundamental and Applied Toxicology, 1987-1992
Nonlinearity in Biology, Toxicology and Medicine, 2000-2003
Regulatory Toxicology and Pharmacology, 2000-
Toxicology, 2008 -
-

EDITOR: Society of Toxicology's Newsletter, 1993-1996.

REVIEWER OF MANUSCRIPTS

I have served as a reviewer of manuscripts submitted to the following journals:

Biochemical Pharmacology
BioTechniques
Blood
Cancer Epidemiology, Biomarkers and Prevention
Cancer Research
Carcinogenesis
Cell Biology and Toxicology
Chemico-Biological Interactions
Environmental Health Perspectives
Environmental Mutagenesis
FEBS Letters
Fundamental and Applied Toxicology
Genomics
Hepatology
Journal of Biological Chemistry
Journal of Hazardous Materials
Journal of Molecular Biology
Journal of the National Cancer Institute
Journal of Pharmacology and Experimental Therapeutics
Molecular Cancer Research
Molecular Carcinogenesis
Molecular Medicine Today
NeuroToxicology
Proceedings of the National Academy of Sciences
Regulatory Toxicology and Pharmacology
Science
Toxicologic Pathology
Toxicological Sciences
Toxicology and Applied Pharmacology
Toxicology *In Vitro*
Trends in Pharmacological Sciences, including Toxicological Sciences

GRADUATE EDUCATION

1. I have served as the major professor and thesis advisor for the following individuals who were enrolled in the graduate program of the Department of Pharmacology and Toxicology:

a. Masters Degree:

Rothenberg, R.J., M.S. (Pharmacology), 1974. "DNA Synthesis in Regenerating Liver *In Vivo." Current Position:* Resident Physician, 3420 Genessee St., B3, Cheektoweja, NY 14225.

Adams, M.P., M.S. (Pharmacology), 1976. "RNA Synthesis and DNA Template Activity in the Livers of Rats Fed the Hepatic Carcinogen 2-Acetylaminofluorene." *Current Position:* Department of Health Careers, Lansing Community College, Lansing, MI 48901.

McClure, Emily A., M.S., 2010. Microbiology and Molecular Genetics, Evaluation of Alterations in DNA Methylation Associated with the 2,3,7,8-Tetrachloro-p-Dioxin (TCDD)-Induced Inhibition of Differentiation in Lipopolysaccharide (LPS)-Stimulated Murine Splenocytes. *Current Position*: Graduate Student, Dept. Microbiology, University of Connecticut.

b. Doctoral Degrees:

Schwartz, Edward L., Ph.D. (Pharmacology and Toxicology), 1979. "Molecular Correlates of 2-Acetylaminofluorene Carcinogenicity." Recipient of a predoctoral fellowship awarded by The Procter and Gamble Company. *Current Position:* Professor of Medicine, Department of Oncology, Albert Einstein Comprehensive Cancer Center, Albert Einstein College of Medicine, 111 East 210th St., Bronx, NY 10467.

Faustman, Elaine M., Ph.D. (Pharmacology and Toxicology), 1981. "Qualitative and Quantitative Assessments of the Alkylation of DNA in Specific Hepatic Chromatin Fractions Following Exposure to Methylnitrosourea of Dimethylnitrosamine." Recipient of an advanced predoctoral fellowship awarded by the Pharmaceutical Manufacturer's Association Foundation, Inc. *Current Position:* Professor, Department of Environmental Health, University of Washington, Seattle, WA 98195.

Doolittle, David J., Ph.D. (Pharmacology and Toxicology), 1982. "Quantitative Cytotoxicity and Mutagenicity Studies Employing Mammalian Cells in Culture." *Current Position:* Vice President for Product Evaluation, R.J. Reynolds, Inc., Winston-Salem, NC 27102.

Baranyi-Furlong, Bonnie L., Ph.D. (Pharmacology and Toxicology),1982. "Factors Involved in Target Specificity of the Hepatocarcinogen N-2-Acetylaminofluorene with Regard to Cell Type and Location within the Genome." Postdoctoral Fellow, University of North Carolina; Staff Fellow, National Institute of Environmental Health Sciences, Research Triangle Park, NC 27790. *Current Position:* Time out for family.

Vorce, Roseann L., Ph.D. (Pharmacology and Toxicology), 1988. "Potential for Oncogene Expression in the Liver and in Spontaneous and Chemically-Induced Hepatomas of the B6C3F1 Mouse." Recipient of an advanced predoctoral fellowship awarded by the Pharmaceutical Manufacturer's Association Foundation, Inc. *Current Position:* Senior Scientist, Drug Safety Evaluation, Pfizer Global Research and Development, Ann Arbor, MI 48105.

GRADUATE EDUCATION (Continued)

Ray, Jean S., DVM, Ph.D. (Pharmacology and Toxicology), 1992. "Hypomethylation of the raf and Ha-ras Protooncogenes in Mouse Liver Following Cell Proliferation and in Mouse Liver Tumors." *Current Position:* Time out for family.

Counts (neé Pavlock), Jennifer L., Ph.D. (Pharmacology and Toxicology), 1995. "Hypomethylation of DNA May Underlie the Heightened Sensitivity of the B6C3F1 Mouse to Liver Tumorigenesis." Recipient of the Society of Toxicology (SOT), Carcinogenesis Specialty Section's First Place Award for a poster presentation at the 1993 Annual SOT Meeting; Recipient of a Society of Toxicology Predoctoral Fellowship. *Current Position:* Toxicologist, The Procter and Gamble Co., Cincinnati, OH 45241.

Watson, Rebecca E., Ph.D. (Pharmacology and Toxicology), 2003. "Characterization of DNA Methylation Patterns in Tumorigenesis and the Use of DNA Methylation of Gauge Toxic Potential." *Current Position:* Senior Scientist/Study Director, SNBL USA, Everett, WA 98203

Carnell-Bachman, Ammie N., Ph.D. (Pharmacology and Toxicology), 2006. "Progressive, Non-Random Altered Patterns of Methylation in Gene-Specific and GC-Rich Regions of DNA Underlie Tumorigenesis." *Current Position:* Toxicologist, Exxon Mobil Biomedical Sciences, Inc, Annandale, NJ.

Phillips, Jennifer M., Ph.D., Biochemistry and Molecular Biology, 2009. Identification of genes involved in tumorigenesis that are deregulated with an emphasis on altered DNA methylation. *Current Position:* Toxicologist, Wil research Laboratories, Ashland, OH 44805

2. Member of the Thesis Guidance Committee. I have served as a member of the thesis guidance committee for the following individuals who were enrolled in graduate programs at Michigan State University:

a. Masters Degree:

Constance Philipps, M.S., Interdepartmental Program in the Biological Sciences, 1976. "The Effects of Caffeine on the UV-Induced Frequency of Mutations in Chinese Hamster Fibroblasts."

b. Doctoral Degree:

Ronald C. Desrosiers, Ph.D., Biochemistry, 1975. "The Synthesis and Methylation of Messenger RNA in Novikoff Hepatoma Cells."

Robert W. Moore, Ph.D., Biochemistry, 1978. "Chemistry and Biochemical Pharmacology of Polybrominated Biphenyl Congeners."

Richard K. Jensen, DVM, Ph.D., Pathology, 1983. "Pathologic Effects and Hepatic Tumor Promoting Ability of Firemaster BP-6,3,3',4,4', 5,5'-Hexabromobiphenyl and 2,2',4,4',5,5'-Hexabromobiphenyl in the Rat."

Melanie O. Manis, Ph.D., Pharmacology and Toxicology, 1984. "Canine *In Vivo* and *In Vitro* Metabolism of the Bladder Carcinogen 4,4'-Methylenebis (2-chloroaniline)."

Benedict I. Kuslikis, Ph.D., Pharmacology and Toxicology, 1987. "Metabolic Activation of 4,4'-Methylenebis(2-Chloroaniline)."

Jeffrey M. Rosenberg, Ph.D., Pharmacology and Toxicology, 1988. "Messenger RNA as a Target for the Cytotoxic Action of the Antitumor Agent Cisplatin: Drug-Induced Inhibition of *In Vitro* Translation."**GRADUATE EDUCATION (Continued)**

Christopher P. Miller, Ph.D., Pharmacology and Toxicology, 1990. "Investigations into the Mechanism of Cyproheptadine-Induced Inhibition of Proinsulin Biosynthesis and Depletion of Pancreatic Insulin Content."

Cynthia M. Garcia-Hoorn, DVM, Ph.D., Pharmacology and Toxicology, 1992. "Effects of Monocrotaline Pyrrole on Cultured Endothelial Cell Function: Potential Role of Endothelial Changes in Vascular Remodeling and the Development of Pulmonary Hypertension."

Yi-Fan Zhai, Ph.D., Pharmacology and Toxicology, 1993. "Characterization of Protein Tyrosine Phosphatases in Human Breast Epithelial Cells Neoplastically Transformed by the New Oncogene: The Potential Role as a Tumor Suppressor."

Amy C. Herring, Ph.D., Pharmacology and Toxicology, 1999. "Inhibition of CREB, NF-κB, and Interleukin-2: A Mechanism of Immune Suppression by Cannabinol."

Coleen V. Dowling, Ph.D., Pharmacology and Toxicology, 1999. "The Relationship Between Gap Junctional Intercellular Communication and Differentiation in a Human Fetal Cell Line Isolated from the Central Nervous System."

Barbara L. Faubert Kaplan, Ph.D., Pharmacology and Toxicology, 2001. "Cannabinoid-induced Immune Suppression in Mouse Splenocytes Involves Both Cannabinoid Receptor-Dependent and -Independent Mechanisms."

Shawn J. Kinser, Ph.D., Pharmacology–Environmental Toxicology, 2001. Mechanisms of Enhanced Allyl Alcohol Hepatotoxicity by Endotoxin.

Nestor D. Deocampo, Ph.D., Genetics, 2001. "The Role of Bcl_2 in Gap Junction-Mediated Cell-Cell Communication and Transformation."

Evan L. Kaplan, Ph.D., Pharmacology–Environmental Toxicology, 2002. "Introduction of Chromosome 15 Into the Immortalized Fibroblast Cell Strain MSU-1.1 Prevents Malignant Transformation by the T24 H-ras Oncogene.

Carrie Northcott, Ph.D., Pharmacology and Toxicology, 2003. "Phosphoinositide-3-Kinase Upregulation in Hypertension: A Reason for Enhanced Arterial Contraction and Tone."

Darrell Boverhof, Ph.D., Biochemistry and Molecular Biology, 2006. "In Vivo Examination of the Inhibitory Effects of 2,3,7,8-Tetrachlorodibenzo-p-dioxin on Estrogen-Mediated Gene Expression Responses."

Dina Shnaider, Ph.D., Pharmacology and Toxicology, 2008. "The Role of Paired Box 5, B Lymphocyte-Induced Maturation of Protein-1 and Activation of Protein-1 in the Suppression of B Cell Differentiation by 2,3,7,8-Tetrachlorodibenzo-p-dioxin

TRAINING OF POSTDOCTORAL FELLOWS

Paula S. Samiec, Ph.D., 1995, Pharmacology and Physiology, Emory University. 1995-1997. *Current Position:* Assistant Professor, School of Natural and Health Sciences, Barry University, Miami Shores, FL

PUBLICATIONS

1. **Goodman, J.I.** and Tephly, T.R.: The role of hepatic microbody and soluble oxidases in the peroxidation of methanol in the rat and monkey. Mol. Pharmacol. 4: 492-501, 1968.

2. Mannering, G.J., Van Harken, D.R., Makar, A.B., Tephly, T.R., Watkins, W.D. and **Goodman, J.I.**: Role of the intracellular distribution of hepatic catalase in the peroxidative oxidation of methanol. Ann. N.Y. Acad. Sci. 168: 265-280, 1969.

3. **Goodman, J.I.** and Tephly, T.R.: Peroxidative oxidation of methanol in human liver: The role of hepatic microbody and soluble oxidases. Res. Commun. Chem. Pathol. Pharmacol. 1: 441-450, 1970.

4. Watkins, W.D., **Goodman, J.I.** and Tephly, T.R.: Inhibition of methanol and ethanol oxidation by pyrazole in the rat and monkey *in vivo.* Mol. Pharmacol. 6: 567-572, 1970.

5. **Goodman, J.I.** and Tephly, T.R.: A comparison of rat and human liver formaldehyde dehydrogenase. Biochem. Biophys. Acta 252: 489-505, 1971.

6. **Goodman, J.I.** and Potter, V.R.: Studies on oncogeny as blocked ontogeny: Increased turnover of DNA in livers of rats fed 3'-methyl-4-dimethylaminoazobenzene. In: Proceedings of the First Conference and Workshop on Embryonic and Fetal Antigens in Cancer (N.G. Anderson and J.H. Coggins, Jr., eds.). Springfield, VA, National Technical Information Service, U.S. Department of Commerce, pp. 39-57, 1971.

7. **Goodman, J.I.** and Potter, V.R.: Increased turnover of DNA in precancerous liver: Evidence for DNA repair synthesis as an early consequence of 3'-methyl-4-dimethylaminoazobenzene ingestion. Cancer Res. 32: 766-775, 1972.

8. Potter, V.R., Walker, P.R. and **Goodman, J.I.**: Survey of current studies on oncogeny as blocked ontogeny: lysozyme changes in livers of rats fed 3'-methyl-4-dimethylaminoazobenzene with collateral studies on DNA stability. Symposium on lysozymes and Enzyme Regulation in Cancer. GANN Monograph on Cancer Research 13: 121-134, 1973.

9. **Goodman, J.I.** and Potter, V.R.: The effect of 5-fluorodeoxyuridine on the synthesis of deoxyribonucleic acid pyrimidines in precancerous rat liver. Mol. Pharmacol. 9: 297-303, 1973.

10. Balis, E.M., **Goodman, J.I.**, Sarma, D.S.R. and Stick, H.F.: Report on indicator tests: Chemical interaction measurements. Conference on Carcinogenesis Testing in the Development of New Drugs, May 23-25, 1973, Washington, D.C., National Academy of Sciences Monograph. In: Carcinogenesis Testing of Chemicals (L. Golberg, ed.). Chemical Rubber Co., OH, 1974.

PUBLICATIONS (Continued)

11. Tephly, T.R., Watkins, W.D. and **Goodman, J.I.**: The biochemical toxicology of methanol. In: Essays in Toxicology, Vol. 5 (W. Hayes, ed.). Academic Press, NY, pp. 149-177, 1974.

12. **Goodman, J.I.**: Hepatic DNA repair in rats fed 3'-methyl-4-dimethylaminoazobenzene. Biochem. Biophys. Res. Commun. 56: 52-59, 1974.

13. **Goodman, J.I.**: A comparison of the utilization of thymine and thymidine for the synthesis of DNA-thymine in Novikoff hepatoma cells. Exp. Cell Res. 85: 415-423, 1974.

14. **Goodman, J.I.**, Trosko, J.E. and Yager, J.D., Jr.: Studies on the mechanism of inhibition of 2-acetylaminofluorene toxicity by butylated hydroxytoluene. Chem.-Biol. Interactions 12: 171-182, 1976.

15. **Goodman, J.I.**: Separation of the products of the reaction of deoxyguanosine with N-acetoxy-2-acetylaminofluorene by high pressure liquid chromatography. Analyt. Biochem. 70: 203-207, 1976.

16. Adams, M.P. and **Goodman, J.I.**: RNA synthesis and RNA polymerase activity in hepatic nuclei isolated from rats fed the carcinogen 2-acetylaminofluorene. Biochem. Biophys. Res. Commun. 68: 850-857, 1976.

17. **Goodman, J.I.** and Rothenberg, R.J.: A procedure for examining deoxyribonucleic acid synthesis in regenerating liver *in vitro.* J. Pharmacol. Meth. 1: 299-310, 1978.

18. Schwartz, E.L. and **Goodman, J.I.**: A comparison of procedures for fractionating hepatic chromatin. J. Pharmacol. Meth. 2: 161-174, 1979.

19. Schwartz, E.L. and **Goodman, J.I.**: Quantitative and qualitative aspects of the binding of N-hydroxy-2-acetylaminofluorene to hepatic chromatin fractions. Chem.-Biol. Interactions 26: 287-303, 1979.

20. Schwartz, E.L. and **Goodman, J.I.**: Non-random nature of 2-acetylaminofluorene-induced alterations of DNA template activity. Chem.-Biol. Interactions 27: 1-15, 1979.

21. Schwartz, E.L., Kluwe, W.M., Sleight, S.D., Hook, J.B. and **Goodman, J.I.**: Inhibition of N-2-fluorenylacetamide-induced mammary tumorigenesis in the rat by dietary polybrominated biphenyls. J. Natl. Cancer Inst. USA 64: 63-67, 1980.

22. Faustman, E.M. and **Goodman, J.I.**: A method for the rapid quantitation of methylated hepatic DNA-purines using high pressure liquid chromatography. J. Pharmacol. Meth. 4: 305-312, 1980.

23. Schwartz, E.L., Braselton, W.E., Jr. and **Goodman, J.I.**: Factors influencing the binding of N-2-fluorenylacetamide to specific areas of the hepatic genome *in vivo.* J. Natl. Cancer Inst., USA 66: 667-672, 1981.

24. Faustman, E.M. and **Goodman, J.I.**: Alkylation of DNA in specific hepatic chromatin fractions following exposure to methylnitrosourea or dimethylnitrosamine. Toxicol. Appl. Pharmacol. 58: 379-388, 1981.

PUBLICATIONS (Continued)

25. Warren, S.T., Doolittle, D.J., Chang, C.C., **Goodman, J.I.** and Trosko, J.E.: Evaluation of the carcinogenic potential of 2,4-dinitrofluorobenzene and its implications regarding mutagenicity testing. Carcinogenesis 3: 139-145, 1982.

26. Jensen, R.K., Sleight, S.D., **Goodman, J.I.**, Aust, S.D. and Trosko, J.E.: Polybrominated biphenyls as promoters in experimental hepatocarcinogenesis in rats. Carcinogenesis 3: 1183-1186, 1982.

27. **Goodman, J.I.**: Concepts in toxicology and carcinogenesis: A basis for discussing the potential environmental hazard posed by PCBs. In: PCBs: Human and Environmental Hazards (F.M. D'Itri and M.A. Kamrin, eds.). Butterworth Publishers, Boston, pp. 179-187, 1983.

28. Doolittle, D.J., Newton, J.F. and **Goodman, J.I.**: Quantitative studies on metabolic activation *in vitro* employing benzo(a)pyrene as the test compound. Mutation Res. 108: 29-44, 1983.

29. Swenberg, J.A., Rickert, D.E., Baranyi, B.L. and **Goodman, J.I.**: Cell specificity in DNA binding and repair of chemical carcinogens. Environ. Hlth. Perspec. 49: 155-163, 1983.

30. Jensen, R.K., Sleight, S.D., Aust, S.D., **Goodman, J.I.** and Trosko, J.E.: Hepatic tumor promotion by 3,3',4,4',5,5'-hexabromobiphenyl: The interrelationship between toxicity. Induction of microsomal drug metabolizing enzymes and tumor promotion. Toxicol. Appl. Pharmacol. 71: 163-176, 1983.

31. Baranyi-Furlong, B.L. and **Goodman, J.I.**: Damage to specific hepatic DNA base sequences following exposure to the hepatocarcinogen 2-acetylaminofluorene. In: Proceedings of the Third International Congress on Toxicology, Developments in the Science and Practice of Toxicology (A.W. Hayes, R.C. Schnell and T.S. Miya, eds.). Elsevier Biomedical Press, Amsterdam, pp. 363-366, 1983.

32. Baranyi-Furlong, B.L. and **Goodman, J.I.**: Nonrandom interaction of N-2-acetylaminofluorene and its N-hydroxy metabolite with DNA of rat hepatic parenchymal and nonparenchymal cell nuclei following *in vivo* administration of carcinogen. Chem.-Biol. Interactions 48: 15-28, 1984.

33. Faustman-Watts, E.M. and **Goodman, J.I.**: DNA purine methylation in hepatic chromatin following exposure to dimethylnitrosamine or methylnitrosourea. Biochem. Pharmacol. 33: 585-590, 1984.

34. Doolittle, D.J. and **Goodman, J.I.**: Quantitative studies on the *in vitro* metabolic activation of dimethylnitrosamine by rat liver postmitochondrial supernatant. Environ. Hlth. Perspec. 57: 327-332, 1984.

35. Vorce, R.L. and **Goodman, J.I.**: Methylation of DNA in the vicinity of the serum albumin gene as compared to the Kirsten-ras oncogene in hepatocytes and nonparenchymal cells of rat liver. Biochem. Biophys. Res. Commun. 126: 879-883, 1985.

36. **Goodman, J.I.**, Vorce, R.L. and Baranyi-Furlong, B.L.: Genetic toxicology: Chemical carcinogens modify DNA in a non-random fashion. Trends in Pharmacol. Sci. 7: 354-357, 1986.

37. **Goodman, J.I.**: The Ames test in perspective, Letter to the Editor. Fundam. Appl. Toxicol. 8: 132-133, 1987.

PUBLICATIONS (Continued)

38. Vorce, R.L. and **Goodman, J.I.**: Investigation of parameters associated with activity of the Kirsten-ras, Harvey-ras and myc oncogenes. Toxicol. Appl. Pharmacol. 90: 86-95, 1987.

39. Vorce, R.L. and **Goodman, J.I.**: Altered methylation of ras oncogenes in benzidine-induced B6C3F1 mouse liver tumors. Toxicol. Appl. Pharmacol. 100: 398-410, 1989.

40. Vorce, R.L. and **Goodman, J.I.**: Alteration in the methylation status of ras oncogenes in B6C3F1 mouse liver tumors. In: Mouse Liver Carcinogenesis: Mechanisms and Species Comparisons (D.E. Stevenson, R.M. McClain, J.A. Popp, T.J. Slaga, J.M. Ward and H.C. Pitot, eds.), pp. 335-344. Wiley-Liss, NY, 1990.

41. **Goodman, J.I.**: The carcinogen bioassay in perspective: A requirement for incorporation of biological information. In Vitro Toxicology: A J. Molec. Cell. Toxicol. 3: 1-7, 1990.

42. DeFeijter, A.W., Ray, J.S., Weghorst, C.M., Klaunig, J., **Goodman, J.I.**, Chang, C.C., Ruch, R.J. and Trosko, J.E.: Infection of rat liver epithelial cells with v-Ha-ras: Correlation between oncogene expression, gap junctional communication and tumorigenicity. Molecular Carcinogenesis 3: 54-67, 1990.

43. Vorce, R.L. and **Goodman, J.I.**: Hypomethylation of ras oncogenes in chemically-induced and spontaneous B6C3F1 mouse liver tumors. J. Toxicol. Environ. Hlth. 34: 367-384, 1991.

44. Vorce, R.L. and **Goodman, J.I.**: Differential DNase I hypersensitivity of ras oncogenes in B6C3F1, C3H/He and C57BL/6 mouse liver. J. Toxicol. Environ. Hlth. 34: 385-395, 1991.

45. **Goodman, J.I.**, Ward, J.M., Popp, J.A., Klaunig, J.E. and Fox, T.R.: Mouse liver carcinogenesis: Mechanisms and relevance. Fundam. Appl. Toxicol. 17: 651-665, 1991.

46. **Goodman, J.I.**: Mouse liver tumor status report. Proceedings of the Annual Summer Meeting of the Toxicology Forum, 1992, pp. 391-396.

47. **Goodman, J.I.** and Counts, J.L.: Hypomethylation of DNA: A possible mechanism underlying the role of cell proliferation in carcinogenesis. Environ. Hlth. Perspec. 101(Suppl. 5): 169-172, 1993.

48. Counts, J.L. and **Goodman, J.I.**: Comparative analysis of the methylation status of the 5' flanking region of Ha-ras in B6C3F1, C3H/He and C57BL/6 mouse liver. Cancer Letters 75: 129-136, 1993.

49. **Goodman, J.I.**: A rational approach to risk assessment requires the use of biological information: An analysis of the National Toxicology Program (NTP). Final Report of the Advisory Review by the NTP Board of Scientific Counselors. Regulatory Toxicology and Pharmacology 19: 51-59, 1994.

50. Ray, J.S., Harbison, M.L., McClain, R.M. and **Goodman, J.I.**: Hypomethylation of the raf proto-oncogene in phenobarbital-induced mouse liver tumors. Molecular Carcinogenesis 9: 155-166, 1994.

51. Trosko, J.E. and **Goodman, J.I.**: Intercellular communication may facilitate apoptosis: Implications for tumor promotion. Molecular Carcinogenesis 11: 8-12, 1994.

PUBLICATIONS (Continued)

52. Moulds, B.A. and **Goodman, J.I.**: Spontaneous mutation at codon 61 of the Ha-ras gene in the nascent liver of B6C3F1, C3H/He and C57BL/6 mice. Mutation Research (Molecular Mechanisms of Mutagenesis) 311: 1-7, 1994.

53. Counts, J.L. and **Goodman, J.I.**: Hypomethylation of DNA: An epigenetic mechanism involved in tumor promotion. Molecular Carcinogenesis 11: 185-188, 1994.

54. Counts, J.L. and **Goodman, J.I.**: Hypomethylation of DNA: A possible epigenetic mechanism involved in tumor promotion. In "Growth Factors and Tumor Promotion: Implications for Risk Assessment," R.M. McClain and T.J. Slaga (Eds.), Wiley-Liss, NY, 1995, pp. 81-101.

55. **Goodman, J.I.**: An analysis of the National Toxicology Program's (NTP) Technical Report (NTP TR 421) on the toxicology and carcinogenesis studies of talc. Regulatory Toxicology and Pharmacology 21: 244-249, 1995.

56. Counts, J.L. and **Goodman, J.I.**: Hypomethylation of DNA: An epigenetic mechanism that can facilitate the aberrant oncogene expression involved in carcinogenesis. In: "Liver Regeneration and Carcinogenesis," R.L. Jirtle (Ed.), Academic Press, New York, Chapter 10, 1995, pp. 227-255.

57. Counts, J.L. and **Goodman, J.I.**: Principles underlying dose selection for, and extrapolation from, the carcinogen bioassay: Dose influences mechanism. Regulatory Toxicology and Pharmacology 21: 418-421, 1995.

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Jay I. Goodman. Non-random Gene Damage Following Exposure to the Hepatocarcinogen 2-Acetylaminofluorene. Seminar presented to the School of Public Health, The University of Michigan, Ann Arbor, MI, April, 1984.

Jay I. Goodman. Non-random DNA Damage Following Carcinogen Exposure. Seminar presented to the Department of Pathology and Experimental Toxicology, Warner-Lambert/Parke-Davis, Pharmaceutical Research Division, Ann Arbor, MI, May, 1984.

Jay I. Goodman. Modification of Hepatic DNA Following Exposure to 2-Acetylaminofluorene. Seminar presented at the Warner-Lambert Research Institute, Mississauga, Ontario, Canada, June, 1984.

Jay I. Goodman. Invited participant, symposium entitled "Toxic Chemicals and the Media." Cornell University Institute for Comparative and Environmental Toxicology, Ithaca, NY, October, 1984.

Jay I. Goodman. Moderator of the symposium entitled "Risk Assessment: Yesterday, Today and Tomorrow." Presented at the Annual Fall Meeting of the Michigan Regional Chapter of the Society of Toxicology, Midland, MI, October, 1984.

Jay I. Goodman. Modification of Hepatic DNA Following Carcinogen Exposure. Seminar presented to the Department of Pharmacology and Toxicology, Michigan State University, East Lansing, MI, October, 1984.

Jay I. Goodman. Participant, symposium entitled "Experimentation, Experience and the Media." Dow Chemical USA, Midland, MI, October, 1984.

Jay I. Goodman. Invited participant in the workshop entitled "Toxicology and Environmental Risk." Sponsored by the Michigan Department of Natural Resources and presented by the Michigan State University Center for Environmental Toxicology, Hamburg, MI, October, 1984.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. The Role of Non-random Gene Damage in Chemical Carcinogenesis. Seminar presented to the Department of Pathology, Michigan State University, East Lansing, MI, November, 1984.

Jay I. Goodman. Concepts in Toxicology: A Basis for Discussing the Carcinogenic Potential of Chemicals. Seminar presented as part of the Symposium entitled "Food Product-Package Compatibility." Sponsored by the Department of Food Science and Human Nutrition, Michigan State University, East Lansing, MI, and the Food and Drug Administration, Lansing, MI, May 1985.

Jay I. Goodman. Genetic and Teratogenic Effects: Interactions Between Genes and Chemicals. Lecture presented in Toxic Chemicals and Human Health; a Continuing Education course administered by the Center for Environmental Toxicology, Michigan State University, Birmingham, MI, May, 1985.

Jay I. Goodman. Cancer: Initiation vs. Promotion, Relevance of Animal Studies, Causative Agents. Lecture presented in Toxic Chemicals and Human Health; a Continuing Education course administered by the Center for Environmental Toxicology, Michigan State University, Birmingham, MI, May, 1985.

Jay I. Goodman. Organizer of the meeting and moderator of the symposium entitled "Toxicology in Michigan Today: Symposium on Immunotoxicology plus Open Poster Presentations." Presented at Michigan State University, May, 1985.

Jay I. Goodman. Member of the Organizing Committee and Keynote Speaker, symposium on Chemical Carcinogenesis. Presented by the Michigan Regional Chapter of the Society of Toxicology and the Society of Toxicologic Pathologists in Ann Arbor, MI, September, 1985.

Jay I. Goodman. Chemicals and Cancer. Lecture presented to the Michigan High School Science Teachers, Michigan State University, October, 1985.

Jay I. Goodman. Carcinogens Modify DNA in a Non-random Manner: Theoretical and Practical Implications. Seminar presented at Adria Laboratories, Dublin, OH, January, 1986.

Jay I. Goodman. Toxicity Assessment: What We Learn and Do Not Learn from Animal Testing. Seminar presented at the meeting of the American Association for Laboratory Animal Science, Laboratory Animal Care Service, Michigan State University, East Lansing, MI, February, 1986.

Jay I. Goodman. Concepts in Toxicology: The Use of Animals in Safety Assessment. Presentation in the Veterinary Technology Program, Michigan State University, East Lansing, MI, May, 1986.

Jay I. Goodman. Keynote Speaker, symposium on *In Vitro* Approaches for Studying Toxic Cell Injury and Open Poster Sessions. Presented by the Michigan Regional Chapter of the Society of Toxicology, Western Michigan University, Kalamazoo, MI, May, 1986.

Jay I. Goodman. Hepatocarcinogenesis Induced by Chemicals: A Multistep Process. Seminar presented at Ingham Medical Center, Lansing, MI, July, 1986.

Jay I. Goodman. Participant in a news media workshop dealing with effective communication issues in environmental toxicology. Sponsored by the Center for Environmental Toxicology, Michigan State University, East Lansing, MI, February, 1987.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Symposium entitled "Oncogenes, Their Role in Normal and Aberrant Cell Proliferation." Organized and Co-Chaired by Jay I. Goodman and Ann E. Aust, presented at the 1987 Annual Meeting of the Society of Toxicology, Washington, D.C., February, 1987.

Jay I. Goodman. Parameters Associated with Oncogene Expression. Symposium address presented at the 1987 Annual Meeting of the Society of Toxicology, symposium entitled "Oncogenes, Their Role in Normal and Aberrant Cell Proliferation." Washington, D.C., February, 1987.

Jay I. Goodman. Chemicals and Cancer: What We Learn and Do No Learn from Animal Testing. Seminar presented at the Meeting of the Western Michigan Section of the American Chemical Society, Grand Rapids, MI, March, 1987.

Jay I. Goodman. Alteration of Gene Expression as an Indication of Potential Target Organ Toxicity. Presentation at The Upjohn Company/Michigan State University Collaborative Research Meeting, Kalamazoo, MI, May, 1987.

Jay I. Goodman. Incorporation of Biological Data in the Carcinogen Risk Assessment Process. Symposium address presented at the conference and Workshop entitled "Reducing Uncertainty in Risk Assessment," sponsored by the Center for Environmental Toxicology, Michigan State University, East Lansing, MI, May, 1987.

Jay I. Goodman. New Approaches to the Use of Biological Data in Risk Assessment. Discussion Leader of a workshop presented at the Conference and Workshop entitled "Reducing Uncertainty in Risk Assessment," sponsored by the Center for Environmental Toxicology, Michigan State University, East Lansing, MI, May, 1987.

Jay I. Goodman. Assessment of the Carcinogenic Potential of Chemicals: Incorporation of Biological Data into the Process." Presentation delivered at the symposium entitled "Drug and Chemical Safety," sponsored by The Upjohn Company, Kalamazoo, MI, July, 1987.

Jay I. Goodman. The Potential for Oncogene Expression in the Liver of the Hepatoma-Prone B6C3F1 Mouse. Presentation delivered at the symposium entitled "Pathobiology of the Liver," sponsored by The Upjohn Company, Kalamazoo, MI, October, 1987.

Jay I. Goodman. Carcinogen Risk Assessment: A Rational Approach Requires the Incorporation of Biological Information. Seminar presented to the Department of Civil and Environmental Engineering, Michigan State University, East Lansing, MI, January, 1988.

Jay I. Goodman. Mechanisms of Chemical Carcinogenesis: Implications for Rational Risk Assessment. Presentation delivered at the symposium entitled "Water Quality: A Realistic Perspective," sponsored by the American Water Works Association, Michigan Section, The University of Michigan, College of Engineering, Ann Arbor, MI, February, 1988.

Roseann L. Vorce and **Jay I. Goodman**. Differential Potential for Expression of the Harvey-ras Oncogene in B6C3F1, C3H/He, and C57BL/6 Mice. Presentation at the Society of Toxicology Program Committee's Plenary Session to highlight research that holds promise for advancing the discipline of toxicology, Annual Meeting of the Society of Toxicology, Dallas, TX, February, 1988.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. The Role of Oncogene Activation in Multistep Carcinogenesis. Presentation delivered at the symposium entitled "Genetic Toxicology," Toxicology Program, Duke University, Durham, NC, February, 1988.

Jay I. Goodman. Alteration of Gene Expression as an Indication of Potential Target Organ Toxicity. Presentation at The Upjohn Company/Michigan State University Collaborative Research Meeting, Kalamazoo, MI, June, 1988.

Jay I. Goodman. The Biology of Chemical Carcinogenesis: Implications for Rational Risk Assessment. Seminar presented at the Simpson Engineering Meeting, Simpson Paper Co., Kalamazoo, MI, June, 1988.

Jay I. Goodman. Invited participant and co-session leader. Gordon Research Conference entitled "Risk Assessment of Chemical Substances." Wolfeboro, NH, June, 1988.

Jay I. Goodman. Implications of Chemical Modulators of Gap Junctions for Chemical Risk Assessment Models. Panel Discussion at the symposium entitled "Toxicological Implications of Altered Gap Junctional Intercellular Communication," Michigan State University, East Lansing, MI, September, 1988.

Jay I. Goodman. Hepatotumorigenesis in the B6C3F1 Mouse: The Role of Alterations in the Methylation Status of Oncogenes. Presentation at the Annual Fall symposium entitled "Mechanisms of Carcinogenesis: Implications for Risk Assessment," sponsored by the Michigan Regional Chapter of the Society of Toxicology, Western Michigan University, Kalamazoo, MI, October, 1988.

Jay I. Goodman. Alterations in the Methylation Status of the ras Oncogenes in B6C3F1 Mouse Liver Tumors. Presentation delivered at the Mouse Liver Carcinogenesis Conference, M.D. Anderson Research Division, The University of Texas, Austin, TX, November, 1988.

Jay I. Goodman. Understanding Mechanisms Involved in Chemical Carcinogenesis: A Requirement for a Rational Approach Towards Risk Assessment. Seminar presented to the Department of Chemistry, Eastern Michigan University, Ypsilanti, MI, December, 1988.

Jay I. Goodman. Co-Chairman, Genetic Toxicology/Mutagenesis Session, Annual Meeting of the Society of Toxicology, Atlanta, GA, February, 1989.

Jay I. Goodman. Carcinogen Risk Assessment: What We Know and What We Do Not Know. Seminar presented at the Annual Spring Meeting of the Environmental Law Section of the Michigan State Bar, Ann Arbor, MI, May, 1989.

Jay I. Goodman. Chemical Carcinogenesis and Risk Assessment. Lecture presented to the Michigan Forest Products Industry Development Council, Manufacturing and Development Group, Michigan Department of Commerce, Detroit, MI, September, 1989.

Jay I. Goodman. Carcinogen Risk Assessment: A Scientific Perspective. Lecture presented to a meeting of the Michigan Coalition for Clean Water, Michigan State University, East Lansing, MI, October, 1989.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Alterations in the Methylation Status of the Ha-ras Oncogene May Facilitate the Development of Mouse Liver Tumors. Seminar presented at the Workshop on Mouse Liver Tumors, International Life Sciences Institute, Washington, DC, November, 1989.

Jay I. Goodman. Carcinogen Risk Assessment: The Need to Incorporate Biological Information. Lecture presented at the Environmental Real Estate Issues Seminar, sponsored by the Institute of Continuing Legal Education, The University of Michigan, Grand Rapids, MI and Southfield, MI, December, 1989.

Jay I. Goodman. Participant in the meeting of the Board of Scientific Counselors of the National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC, November, 1989.

Jay I. Goodman. Chairman, "Oncogenes/Growth Factors" Poster Discussion Session, Annual Meeting of the Society of Toxicology, Miami, FL, February, 1990.

Jay I. Goodman. Water Quality and Health. Seminar presented to the Department of Resource Development and Agricultural Experiment Station Extension Service, Michigan State University, East Lansing, MI, February 1990.

Jay I. Goodman. Hypomethylation of the Ha-ras oncogene may facilitate tumorigenesis. Seminar presented to the Department of Medicine, Michigan State University, East Lansing, MI, March, 1990.

Jay I. Goodman. "Hypomethylation of proto-oncogenes: A possible mechanism involved in tumor promotion". Seminar presented to The Chemical Industry Institute of Toxicology, Research Triangle Park, NC, March, 1990.

Jay I. Goodman. Participant in the meeting of the Board of Scientific Counselors, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC, March, 1990.

Jay I. Goodman. Member of the Panel of Judges, Annual Phi Zeta Research Day, Honor Society of Veterinary Medicine, College of Veterinary Medicine, Michigan State University, East Lansing, MI, April, 1990.

Jay I. Goodman. Participant in the meeting of the Technical Reports Review Subcommittee and Panel of Experts, Board of Scientific Counselors, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC, April, 1990.

Jay I. Goodman. Invited participant in the Discussion Workshop on Human Biomarkers for Exposure to Mutagenic and Carcinogenic Chemicals, The Dow Chemical Company, Midland, MI, July, 1990.

Jay I. Goodman. "Hypomethylation of the Ha-ras oncogene may facilitate tumorigenesis in the liver of the B6C3F1 mouse". Seminar presented to the Toxicology Program, School of Public Health, The University of Michigan, Ann Arbor, MI, September, 1990.

Jay I. Goodman. Participant in the meeting of the Board of Scientific Counselors, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC, October, 1990.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Invited participant in the Mouse Liver Tumor meeting, National Institute of Environmental Health Sciences, Research Triangle Park, NC, October, 1990.

Jay I. Goodman. Altered methylation status of the Ha-ras and ras oncogenes in mouse liver after cell proliferation. Seminar presented at the Second Workshop on Mouse Liver Tumors, International Life Sciences Institute, Health and Environmental Sciences Institute, Washington, DC, November, 1990.

Jay I. Goodman. Participant in the meeting of the Technical Reports Review Subcommittee and Panel of Experts, Board of Scientific Counselors, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC, November, 1990.

Jay I. Goodman. Organizer and Chairman of the symposium entitled "Mouse Liver Carcinogenesis: Mechanisms and Relevance." Presented at the 1991 Annual Meeting of the Society of Toxicology, Dallas, TX, February, 1991.

Jay I. Goodman. Hypomethylation of Proto-oncogenes: A Possible Mechanism Involved in the Promotion Stage of Carcinogenesis. Symposium address presented at the 1991 Annual Meeting of the Society of Toxicology Symposium entitled "Mouse Liver Carcinogenesis: Mechanisms and Relevance," Dallas, TX, February 1991.

Jay I. Goodman. Co-Chairperson, Poster Discussion Session entitled "Gap Junctions" at the 1991 Annual Meeting of the Society of Toxicology, Dallas, TX, February, 1991.

Jay I. Goodman. Participant in the meeting of the Board of Scientific Counselors, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC, March, 1991.

Jay I. Goodman. Carcinogen Risk Assessment: A Rational Approach Requires the Incorporation of Biological Information. Symposium address presented at the National Meeting of the American Chemical Society, Atlanta, GA, April, 1991.

Jay I. Goodman. Hypomethylation of proto-oncogenes: A possible mechanism underlying the role of cell proliferation in carcinogenesis. Seminar presented at the Procter and Gamble Co., Cincinnati, OH, June, 1991.

Jay I. Goodman. Participant in the meeting of the Technical Reports Review Subcommittee and Panel of Experts, Board of Scientific Counselors, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC, July, 1991.

Jay I. Goodman. Invited participant, the Summer Meeting of the Toxicology Forum, Aspen, CO, July, 1991.

Jay I. Goodman. Invited participant, Mouse Liver Tumor Meeting, International Life Sciences Institute, Risk Science Institute, Washington, DC, August, 1991.

Jay I. Goodman. Hypomethylation of DNA: A possible mechanism underlying the role of cell proliferation in mouse liver tumorigenesis. Presentation at the International Life Sciences Institute, Health and Environmental Sciences Institute, Third Annual Workshop on Mouse Liver Tumorigenesis, Arlington, VA, October, 1991.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Incorporation of biological information into carcinogen risk assessment: A role for cell proliferation and hypomethylation of DNA. Symposium presentation, Annual Meeting of the American College of Toxicology, Savannah, GA, October, 1991.

Jay I. Goodman. Participant in the meeting of the Board of Scientific Counselors, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC, October, 1991.

Jay I. Goodman. Participant in the meeting of the Technical Reports Review Subcommittee and Panel of Experts, Board of Scientific Counselors, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC, November, 1991.

Jay I. Goodman. Participant in the meeting of the Scientific Review Committee, Peroxisome Proliferation Working Group, International Life Sciences Institute, Risk Science Institute, Washington, DC, December, 1991.

Jay I. Goodman. Carcinogen risk assessment. Presentation in the Environmental Science for Lawyers Seminar, University of Detroit, School of Law, Detroit, MI, December, 1991.

Jay I. Goodman. Hypomethylation of DNA: A possible mechanism underlying the role of cell proliferation in carcinogenesis. Presentation at the Symposium entitled "Cell Proliferation and Chemical Carcinogenesis," National Institute of Environmental Health Sciences, Research Triangle Park, NC, January, 1992.

Jay I. Goodman. Alterations in the methylation status of proto-oncogenes in mouse liver tumors. Seminar presented to the Department of Food Science and Human Nutrition, Michigan State University, East Lansing, MI, January, 1992.

Jay I. Goodman. Hypomethylation of DNA: A possible mechanism underlying the role of cell proliferation in carcinogenesis. Seminar presented to the Department of Pharmacology and Toxicology, Indiana University Medical School, Indianapolis, IN, January, 1992.

Jay I. Goodman. Chairperson of the poster session entitled "Oncogenes". Annual Meeting of the Society of Toxicology, Seattle, WA, February, 1992.

Jay I. Goodman. Participant in the meeting of the Board of Scientific Counselors, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC, April, 1992.

Jay I. Goodman. The requirement for incorporation of biological information into the carcinogen risk assessment process. Seminar presentation, Institute of Environmental Toxicology, Michigan State University, East Lansing, May, 1992.

Jay I. Goodman. Hypomethylation of DNA: A possible nongenotoxic mechanism underlying the role of cell proliferation in mouse liver carcinogenesis. Seminar presentation, Department of Toxicology and Pathology, Hoffmann-La Roche, Inc., Nutley, NJ, May, 1992.

Jay I. Goodman. Hypomethylation of DNA: A possible nongenotoxic mechanism underlying the role of cell proliferation in mouse liver carcinogenesis. Seminar presentation, Research and Development Division, RJR-Nabisco, Winston-Salem, NC, June, 1992.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Participant in the meeting of the Technical Reports Review Subcommittee and Panel of Experts, Board of Scientific Counselors, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC, June, 1992.

Jay I. Goodman. Mouse liver carcinogenesis: An update. Seminar presented at the Procter and Gamble Co., Cincinnati, OH, June, 1992.

Jay I. Goodman. Mouse Liver Tumorigenesis Status Report. Invited speaker, The Summer Meeting of the Toxicology Forum, Aspen, CO, July, 1992.

Jay I. Goodman. Participant in the Annual Summer Meeting of the Board of Directors of the American Board of Toxicology, Inc., Pinehurst, NC, July, 1992.

Jay I. Goodman. Participant in the Planning Meeting for the Fall 1992 Workshop on Mouse Liver Tumors. International Life Sciences Institute, Health and Environmental Sciences Institute, Washington, DC, July, 1992.

Jay I. Goodman. Evaluating the carcinogenic potential of chemicals. Presentation in the MSU course entitled "Environmental Contaminants: What are Your Health Risks?", Michigan State University, East Lansing, MI, October, 1992.

Jay I. Goodman. Participant in the Annual Fall Meeting of the Board of Directors of the American Board of Toxicology, Inc., Raleigh, NC, October, 1992.

Jay I. Goodman. Hypomethylation of DNA: A Possible nongenotoxic Mechanism Underlying the Role of Cell Proliferation in Mouse Liver Carcinogenesis. Presentation at the International Life Sciences Institute, Health and Environmental Sciences Institute, and the U.S. Environmental Protection Agency, Fourth Annual Workshop on Mouse Liver Tumorigenesis, Washington, DC, November, 1992.

Jay I. Goodman. Chairman of the session entitled "Nongenotoxic Mechanisms: Biologically-Plausible Threshold Events Underlying Mouse Liver Tumorigenesis." International Life Sciences Institute, Health and Environmental Sciences Institute, and the U.S. Environmental Protection Agency, Fourth Annual Workshop on Mouse Liver Tumorigenesis, Washington, DC, November, 1992.

Jay I. Goodman. Rational carcinogen risk assessment requires the use of biological information: Hypomethylation of DNA and cell proliferation as an example. Presentation in the Symposium entitled "Current Issues in Risk Assessment," Annual Meeting of the Gulf Coast Regional Chapter of the Society of Toxicology, Texas A&M University, College Station, TX, November, 1992.

Jay I. Goodman. Cancer biology and carcinogen risk assessment: Fact and fiction. Presentation in the Symposium entitled "Innovations in Water and Waste Water in the 90s." Sponsored by the Michigan Department of Public Health, The American Waterworks Association, and the University of Michigan, College of Engineering, Ann Arbor, MI, February, 1993.

Jay I. Goodman. The Recent Advisory Review of the National Toxicology Program (NTP) by the NTP Board of Scientific Councilors: Report of the Carcinogenesis Working Group (chaired by J.I. Goodman). Symposium presentation at the Annual Winter Meeting of the Toxicology Forum, Washington, DC, February, 1993.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Chemically-induced alterations in proto-oncogenes: Significant end-points for toxicological evaluation. Presentation in the Symposium entitled "Role of Toxicologic Pathology in Safety Evaluation" sponsored by the National Research Council, National Academy of Sciences, Washington, DC, February, 1993.

Jay I. Goodman. Co-Chairman of the Poster Discussion Session entitled "Oncogenes and Tumor Suppressor Genes," 1993 Annual Meeting of the Society of Toxicology, New Orleans, LA, March, 1993.

Jay I. Goodman. Organizer and Chairperson of the Continuing Education course entitled "Experimental approaches to assess chemically-induced alterations in gene expression." Presented at the 1993 Annual Meeting of the Society of Toxicology, New Orleans, LA, March, 1993.

Jay I. Goodman. Hypomethylation of DNA: A cell proliferation-linked mechanism that can facilitate aberrant gene expression. Presentation as part of the Continuing Education course entitled "Experimental approaches to assess chemically-induced alterations in gene expression." Presented at the 1993 Annual Meeting of the Society of Toxicology, New Orleans, LA, March, 1993.

Jay I. Goodman. Participant in the Meeting of the Council of the Society of Toxicology, New Orleans, LA, March, 1993.

Jay I. Goodman. Participant in the Annual Winter Meeting of the American Board of Toxicology, New Orleans, LA, March, 1993.

Jay I. Goodman. Hypomethylation of DNA: A possible epigenetic mechanism underlying the role of cell proliferation in carcinogenesis. Seminar presentation, Cancer Center Program, Michigan State University, East Lansing, MI, April, 1993.

Jay I. Goodman. Hypomethylation of DNA: A possible epigenetic mechanism underlying the role of cell proliferation in carcinogenesis. Seminar presentation, Department of Pharmacology and Toxicology, Purdue University, West Lafayette, IN, April, 1993.

Jay I. Goodman. Participant in the Meeting of the Council of the Society of Toxicology, Washington, DC, May, 1993.

Jay I. Goodman. Invited participant -- International Workshop on Predicting Chemical Carcinogenesis in Rodents. National Institute of Environmental Health Sciences, Research Triangle Park, NC, May, 1993.

Jay I. Goodman. Participant in the Annual Summer Meeting of the Board of Directors of the American Board of Toxicology, Inc., Raleigh, NC, July, 1993.

Jay I. Goodman. Participant in the Meeting of the Council of the Society of Toxicology, Washington, DC, July, 1993.

Jay I. Goodman. A scientific basis for selection of the high dose to be employed in the carcinogen bioassay. Presentation made at the Toxicology Roundtable Meeting of the National Agricultural Chemicals Associations, Washington, DC, July, 1993.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Invited participant, Federation of the American Society for Experimental Biology, 1993 FASEB Summer Research Conference entitled "Biochemistry and Pharmacology of S-Adenosylmethionine and Methylation," Copper Mountain, CO, August, 1993.

Jay I. Goodman. Participant in the meeting of the Council of the Society of Toxicology, Annapolis, MD, September, 1993.

Jay I. Goodman. Carcinogen risk assessment: A rational approach requires the use of biological information. Invited presentation at the Ceres-American Association for the Advancement of Science Workshop entitled "Eating and Health: Current and Future Issues," Georgetown University, Washington, DC, November, 1993.

Jay I. Goodman. Participant in the meeting of the Council of the Society of Toxicology, Washington, DC, November, 1993.

Jay I. Goodman. Chairperson, Session on Mechanisms. The 7th International Conference on Carcinogenesis and Risk Assessment; Growth Factors and Tumor Promotion: Implications for Risk Assessment. University of Texas, M.D. Anderson Cancer Center, Dallas, TX, December, 1993.

Jay I. Goodman. Hypomethylation of DNA: A Possible Epigenetic Mechanism Underlying Tumor Promotion. Invited presentation at the 7th International Conference on Carcinogenesis and Risk Assessment; Growth Factors and Tumor Promotion: Implications for Risk Assessment. University of Texas, M.D. Anderson Cancer Center, Dallas, TX, December, 1993.

Jennifer L. Counts and **Jay I. Goodman**. Site specific methylation in the 5' flanking region of Ha-ras in the liver of the B6C3F1 mouse. Invited poster presentation at the 7th International Conference on Carcinogenesis and Risk Assessment; Growth Factors and Tumor Promotion: Implications for Risk Assessment. University of Texas, M.D. Anderson Cancer Center, Dallas, TX, December, 1993.

Jay I. Goodman. Invited Participant, Meeting of the Planning Committee for the Spring 1994 Mouse Liver Tumor Conference, International Life Sciences Institute, Health and Environmental Sciences Institute, Washington, DC, December, 1993.

Jay I. Goodman. Participation as a member of the Expert Working Group on Dose Selection Issues for the Carcinogen Bioassay. International Life Sciences Institute, Risk Science Institute, and U.S. Environmental Protection Agency, Office of Pesticide Programs, Washington, DC, December, 1993.

Jay I. Goodman. Review of the National Toxicology Program Chronic Studies in Rodents. Workshop entitled "Talc: Consumer Uses and Health Perspectives. Sponsored by the International Society of Regulatory Toxicology and Pharmacology and the U.S. Food and Drug Administration, National Library of Medicine, Bethesda, MD, January, 1994.

Jay I. Goodman. Participant in the Meeting of the Board of Directors of the American Board of Toxicology, Inc., Dallas, TX, March, 1994.

Jay I. Goodman. Participant in the Meeting of the Council of the Society of Toxicology, Dallas, TX, March, 1994.

Jay I. Goodman. Co-Chairperson of the Poster Discussion Session entitled "Oncogenes and Tumor Suppressor Genes," 1994 Annual Meeting of the Society of Toxicology, Dallas, TX, March, 1994.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Participant in the Meeting of the Council of the Society of Toxicology, Reston, VA, May, 1994.

Jay I. Goodman. DNA methylation and oncogene expression in mouse liver tumors. Invited speaker, Hoffmann-La Roche, Inc., Department of Toxicology and Pathology, Workshop entitled "Molecular Mechanisms for Mouse Hepatocarcinogenicity: Implications for Drug Discovery and Development", Nutley, NJ, June, 1994

Jay I. Goodman. Participant in the Meeting of the Board of Directors of the American Board of Toxicology, Inc., Raleigh, NC, July, 1994.

Jay I. Goodman. Participant in the Meeting of the Council of the Society of Toxicology, Reston, VA, July, 1994.

Jay I. Goodman. Hypomethylation of protooncogenes/oncogenes: A possible mechanism involved in the promotion stage of carcinogenesis. Invited Symposium speaker, XIIth International Congress of Pharmacology, Montreal, Canada, July, 1994.

Jay I. Goodman. Invited expert reviewer, U.S. Environmental Protection Agency Workshop on Cancer Risk Assessment Guideline Issues, Review of the draft revisions to the Guidelines for Carcinogen Risk Assessment, Reston, VA, September, 1994.

Jay I. Goodman. Participant in the Meeting of the Council of the Society of Toxicology, Reston, VA, September, 1994.

Jay I. Goodman. Hypomethylation of DNA: An epigenetic mechanism involved in tumor promotion. Seminar speaker, Meeting of the Expert Panel of the Flavor and Extract Manufacturers' Association (FEMA) of the United States, Washington, DC, September, 1994.

Jay I. Goodman. A decreased capacity to maintain the nascent DNA methylation status may affect an increased susceptibility to carcinogenesis. Seminar presentation, Department of Radiation Oncology, Duke University, Durham, NC, October, 1994.

Jay I. Goodman. Hypomethylation of DNA is a mechanism underlying tumor promotion. Invited speaker, American College of Toxicology Symposium on Risk Assessment, Reston, VA, October, 1994.

Jay I. Goodman. Co-Chair of the Program Committee and Chair of the Session entitled "Non-Genotoxic Mechanisms in Mouse Liver Carcinogenesis. Fifth Workshop on Mouse Liver Tumors, Organized by the International Life Sciences Institute, Arlington, VA, November, 1994.

Jay I. Goodman. Hypomethylation of DNA and tumor promotion. Presented in the Session entitled "Non-Genotoxic Mechanisms in Mouse Liver Carcinogenesis. Fifth Workshop on Mouse Liver Tumors, Organized by the International Life Sciences Institute, Arlington, VA, November, 1994.

Jennifer L. Counts, R. Michael McClain, Margaret L. Harbison and **Jay I. Goodman**. Differences in DNA methylation induced by a choline-devoid, methionine-deficient diet or by phenobarbital correlate with liver tumor susceptibility in mice. Invited poster-discussion presentation in the Session entitled "Non-Genotoxic Mechanisms in Mouse Liver Carcinogenesis. Fifth Workshop on Mouse Liver Tumors, Organized by the International Life Sciences Institute, Arlington, VA, November, 1994.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Participant in a meeting of the Siloxane Science Advisory Board, Dow Corning Corporation, Midland, MI, December, 1994.

Jay I. Goodman. Participant in the Meeting of the Board of Directors of the American Board of Toxicology, Inc., Baltimore, MD, March, 1995.

Jay I. Goodman. Participant in the Meeting of the Council of the Society of Toxicology, Baltimore, MD, March, 1995.

Jay I. Goodman. Biological processes relevant to dose selection. Presented at the 1995 Annual Meeting of the Society of Toxicology, in the workshop entitled "National Toxicology Program Studies: Principles Of Dose Selection And Application To Mechanism-Based Risk Assessment, Baltimore, MD, March, 1995.

Jay I. Goodman. Hypomethylation of DNA: An epigenetic mechanism involved in tumor promotion. Seminar presented to the Department of Pathology and Experimental Toxicology, Warner-Lambert, Parke-Davis Pharmaceutical Research Division, Ann Arbor, MI, March, 1995.

Jay I. Goodman. Participant in a meeting of the Siloxane Science Advisory Board, Dow Corning Corporation, Midland, MI, April, 1995.

Jay I. Goodman. Participant in a Long Range Planning Meeting, Society of Toxicology, Alexandria, VA, May, 1995.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Reston, VA, May, 1995.

Jennifer L. Counts, R. Michael McClain, Margaret L. Harbison, Juan I. Sarmiento and **Jay I. Goodman**. Hypomethylation of DNA and the heightened sensitivity of the B6C3F1 mouse to liver tumorigenesis. Presented at the meeting of the International Congress of Toxicology - VII, Seattle, WA, July, 1995.

Jay I. Goodman and Jennifer L. Counts. Hypomethylation of DNA: A nongenotoxic mechanism involved in tumor promotion. Invited presentation at the meeting of the International Congress of Toxicology - VII, in the workshop entitled "Nongenotoxic Chemical Carcinogenesis", Seattle, WA, July, 1995.

Jay I. Goodman. The current approach to the rodent bioassay is no longer needed. Invited participant in the debate regarding the rodent bioassay at the meeting of the International Congress of Toxicology - VII, Seattle, WA, July, 1995.

Jay I. Goodman. Participant in the Meeting of the Board of Directors of the American Board of Toxicology, Inc., Flat Rock, NC, July, 1995.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, McLean, VA, July, 1995.

Jay. I. Goodman. Participant in a meeting of the Dose Selection for the Bioassay Working Group, International Life Sciences Institute, Risk Science Institute, and U.S. Environmental Protection Agency, Washington, DC, September, 1995.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Participant in a meeting of the Siloxane Science Advisory Board, Dow Corning Corporation, Midland, MI, September, 1995.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Herndon, VA, September, 1995.

Jay I. Goodman. Participant in meeting of the Flavor and Extract Manufacturers' Association (FEMA) Expert Panel for the Evaluation of Flavoring Materials, Toronto, Canada, September, 1995.

Jay I. Goodman. Are transgenic animals an alternative to the bioassay? A focus on non-genotoxic carcinogenic mechanisms is more appropriate. Invited presentation in the workshop entitled "Nurturing New Technologies in a Regulatory Environment," sponsored by the Pharmaceutical Research Manufacturers Association and the U.S. Food and Drug Administration, Washington, DC, October, 1995.

Jay I. Goodman. Participant in a meeting of the Board of Directors of the American Board of Toxicology, Inc., Raleigh, NC, October, 1995.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Reston, VA, November, 1995.

Jay I. Goodman. Participant in meeting of the Flavor and Extract Manufacturers' Association (FEMA) Expert Panel for the Evaluation of Flavoring Materials, Tucson, AZ, January, 1996.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Nashville, TN, January, 1996.

Jay I. Goodman. Participant in a meeting of the Siloxane Science Advisory Board, Dow Corning Corporation, Midland, MI, January, 1996.

Jay I. Goodman. Participant in a meeting to discuss the role of transgenic/knockout animals in carcinogenicity testing. Laboratory of Environmental Carcinogenesis and Mutagenesis, National Institute of Environmental Health Sciences, Research Triangle Park, NC, February, 1996.

Jay I. Goodman. Participant in a meeting of the Board of directors of the American Board of Toxicology, Inc., Anaheim, CA, March, 1996.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Anaheim, CA, March, 1996.

Jay I. Goodman. Participant in a meeting of the Board of Directors of the Toxicology Education Foundation, Anaheim, CA, March, 1996.

Jay I. Goodman. The current academic approach to training graduate students in toxicology. Invited presentation made in a debate sponsored by the Education Committee, Annual Meeting of the Society of Toxicology, Anaheim, CA, March, 1996.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Use of mode of action information in cancer risk assessment. Invited speaker, workshop entitled Implementation of the EPA's Revised Cancer Risk Assessment Guidelines: Incorporation of Mechanistic/Pharmacokinetic Data, Annual Meeting of the Society of Toxicology, Anaheim, CA, March, 1996.

Jay I. Goodman. A biologically-based approach to risk assessment: Revision of the Environmental Protection Agency's cancer risk assessment guidelines. Invited speaker, International Conference on "Food Safety in North America: Regulatory and Scientific Issues," sponsored by the National Food Safety and Toxicology Center, Michigan State University, and The University of Guelph/Ontario, East Lansing, MI, March, 1996.

Jay I. Goodman. Participant in a meeting of the Society of Toxicology's Task Force to Improve the Scientific Basis for Risk Assessment, Anaheim, CA, March, 1996.

Jay I. Goodman. Invited participant in the "Toxicological Assessment" Work Group, in the symposium entitled "Harmonization of State/Federal Approaches to Environmental Risk," Institute for Environmental Toxicology, Michigan State University, East Lansing, MI, May, 1996.

Jay I. Goodman. Participant in a meeting of the Flavor and Extract Manufacturers' Association (FEMA) Expert Panel for the Evaluation of Flavoring Materials, Washington, DC, May, 1996.

Jay I. Goodman. Participant in a meeting of the Siloxane Science Advisory Board, Dow Corning Corporation, Midland, MI, May, 1996.

Jay I. Goodman. Participant in a meeting of the Society of Toxicology's Task Force to Improve the Scientific Basis for Risk Assessment, St. Louis, MO, June, 1996.

Jay I. Goodman. A rational approach to carcinogen risk assessment requires the use of biological information. Invited speaker, workshop entitled "Risk Assessment in Establishing Upper Reference Levels of Nutrients". Sponsored by the National Academy of Sciences, Institute of Medicine, Food and Nutrition Board, Washington, D.C., July, 1996.

Jay I. Goodman. Seminar entitled "Altered DNA Methylation: A Secondary Mechanism Involved in Carcinogenesis," Sanofi Winthrop Research Division, Sanofi Winthrop, Inc., Collegeville, PA, July, 1996.

Jay I. Goodman. Organizer of the session entitled "Role of DNA Methylation in Normal and Aberrant Gene Expression," Gordon Conference on Mechanisms of Toxicity, New England College, Henniker, NH, July-August, 1996.

Jay I. Goodman. "Hypomethylation and Tumor Promotion," presentation in the session entitled "Role of DNA Methylation in Normal and Aberrant Gene Expression," Gordon Conference on Mechanisms of Toxicity, New England College, Henniker, NH, July-August, 1996.

Samiec, P.S., Counts, J.L., McClain, R.M. and **Goodman, J.I.** "Hypomethylation and increased expression of myc in mouse liver in response to a choline-devoid, methionine-deficient diet." Poster presentation, Gordon Conference on Mechanisms of Toxicology, New England College, Henniker, NH, July-August, 1996.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Participant in a meeting of the Expert Panel to Evaluate Chloroform and Dichloroacetic Acid as Case Studies for the Application of EPA's Proposed Guidelines for Carcinogen Risk Assessment. Supported by the U.S. Environmental Protection Agency, The Chlorine Chemistry Council and The American Forest & Paper Association. Convened by the International Life Sciences Institute, Health and Environmental Sciences, Washington, DC, September, 1996.

Jay I. Goodman. Participant in a meeting of the Flavor and Extract Manufacturers' Association (FEMA) Expert Panel for the Evaluation of Flavoring Materials, Washington, DC, September, 1996.

Jay I. Goodman. Participant in a meeting of the Siloxane Science Advisory Board, Dow Corning Corporation, Midland, MI, September, 1996.

Jay I. Goodman. "Altered DNA methylation: A secondary mechanism involved in carcinogenesis," seminar presentation. Environmental Toxicology Center, University of Wisconsin, Madison, WI, October, 1996.

Jay I. Goodman. Participant in a meeting of the Expert Panel to Evaluate Chloroform and Dichloroacetic Acid as Case Studies for the Application of EPA's Proposed Guidelines for Carcinogen Risk Assessment. Supported by the U.S. Environmental Protection Agency, The Chlorine Chemistry Council and The American Forest & Paper Association. Convened by the International Life Sciences Institute, Health and Environmental Sciences, Washington, DC, November, 1996.

Jay I. Goodman. The traditional toxicological paradigm is correct: Dose influences mechanism. Plenary session presentation, Third BELLE Conference on "Toxicological Defense Mechanisms and the Shape of Dose-Response Relationships," National Institute of Environmental Health Sciences, Research Triangle Park, NC, November, 1996.

Jay I. Goodman. Chairperson of the session entitled "Molecular and Biochemical Processes Including Antioxidant Defensive Mechanisms," Third BELLE Conference on "Toxicological Defense Mechanisms and the Shape of Dose-Response Relationships," National Institute of Environmental Health Sciences, Research Triangle Park, NC, November, 1996.

Jay I. Goodman. Participant in a meeting of the Flavor and Extract Manufacturer's Association (FEMA) Expert Panel for the Evaluation of Flavoring Materials, Washington, DC, January, 1997.

Jay I. Goodman. Participant in a meeting of the Siloxane Science Advisory Board, Dow Corning Corporation, Midland, MI, January, 1997.

Jay I. Goodman. Participant in a meeting of the Board of Trustees, Health and Environmental Sciences Institute, International Life Sciences Institute, Miami, FL, January, 1997.

Jay I. Goodman. Mouse Liver Tumors Belong in the Laboratory. Article published in the Society of Toxicology's Carcinogenesis Specialty Section's Newsletter, January, 1997.

Jay I. Goodman. Participant in a meeting of the Expert Panel to Evaluate Chloroform and Dichloroacetic Acid as Case Studies for the Application of EPA's Proposed Guidelines for Carcinogen Risk Assessment. Supported by the U.S. Environmental Protection Agency, The Chlorine Chemistry Council and The American Forest & Paper Association. Convened by the International Life Sciences Institute, Health and Environmental Sciences, Washington, DC, February, 1997.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Pitfalls in the application of data from transgenics in regulation. Invited speaker, Roundtable Discussion entitled "Should carcinogenesis data from transgenic animals be applied in regulation, if so, how?" Annual Meeting of the Society of Toxicology, Cincinnati, OH, March, 1997.

Jay I. Goodman. Participant in a meeting of the Flavor and Extract Manufacturer's Association (FEMA) Expert Panel for the Evaluation of Flavoring Materials, New York City, NY, April, 1997.

Jay I. Goodman. Altered DNA methylation: A secondary mechanism involved in carcinogenesis. Invited presentation in the Symposium entitled "Molecular Toxicology: Utilization of Molecular and Mechanistic Toxicology in Accelerated Drug Discovery and Chemical Safety Analysis; Basic and Applied Science", sponsored by International Business Communications, Rockville, MD, April, 1997.

Jay I. Goodman. Participant in a meeting of the Siloxane Science Advisory Board, Dow Corning Corporation, Midland, MI, May, 1997.

Jay I. Goodman. Participant in a meeting of the Expert Panel to Evaluate Chloroform and Dichloroacetic Acid as Case Studies for the Application of EPA's Proposed Guidelines for Carcinogen Risk Assessment. Supported by the U.S. Environmental Protection Agency, The Chlorine Chemistry Council and The American Forest & Paper Association. Convened by the International Life Sciences Institute, Health and Environmental Sciences, Washington, DC, May, 1997.

Jay I. Goodman. Co-Chaired a meeting of the Program Committee, Society of Toxicology, Tysons Corner, McLean, VA, May, 1997.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Tysons Corner, McLean, VA, May, 1997.

Jay I. Goodman. Invited participant, Discussion Leader, session entitled "DNA Methylation and Cancer", Federation of American Societies for Experimental Biology (FASEB) meeting on Biological Methylation, Saxon River, VT, June, 1997.

Jay I. Goodman. Use of transgenic animals for carcinogenicity testing: Possibilities and Pitfalls. Invited presentation in the session entitled “Transgenic Models for Assessing Carcinogenic Potential of Chemicals”, 1997 Annual Summer Meeting of the Toxicology Forum, Aspen, CO, July, 1997.

Jay I. Goodman. Participant in a Meeting of the Council of the Society of Toxicology, Tysons Corner, McLean, VA, July, 1997.

Jay I. Goodman. Use of transgenic animals for carcinogenicity testing: Possibilities and pitfalls. Seminar presentation, Toxicology Laboratory, Dow Chemical Co., Midland, MI, August, 1997.

Jay I. Goodman. DNA methylation and cancer. Seminar presentation, Transcriptional Regulation Journal Club, Biochemistry Department, Michigan State University, East Lansing, MI, August, 1997.

Jay I. Goodman. Participant in a meeting of the Board of Trustees, Toxicology Education Foundation, Society of Toxicology, Reston, VA, August, 1997.

Jay I. Goodman. Stability of DNA methylation and susceptibility to liver carcinogenesis. Invited presentation, Conference entitled “Mechanisms of Susceptibility to Mouse Liver Carcinogenesis, Chapel Hill, NC, September, 1997.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Participant in a meeting of the Science Advisory Panel for the Health and Environmental Sciences Institute, International Life Sciences Institute's Alternatives to Carcinogenicity Testing Committee, September, 1997.

Jay I. Goodman. Participant in a meeting of the Siloxane Science Advisory Board, Dow Corning Corporation, Midland, MI, September, 1997.

Jay I. Goodman. Participant in a meeting of the Flavor and Extract Manufacturer's Association (FEMA) Expert Panel for the Evaluation of Flavoring Materials, Washington, DC, September, 1997.

Jay I. Goodman. Co-Chaired a meeting of the Program Committee, Society of Toxicology, Tysons Corner, McLean, VA, September, 1997.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Tysons Corner, McLean, VA, September, 1997.

Jay I. Goodman. Co-chaired a meeting of the Program Committee, Society of Toxicology, Tysons Corner, McLean, VA, November, 1997.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Tysons Corner, McLean, VA, November, 1997.

Jay I. Goodman. Participant in a meeting of the Society of Toxicology's Task Force to Improve the Scientific Basis of Risk Assessment, Tysons Corner, McLean, VA, December, 1997.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, San Diego, CA, January, 1998.

Jay I. Goodman. Participant in a meeting of the Flavor and Extract Manufacturer's Association (FEMA) Expert Panel for the Evaluation of Flavoring Materials, Key Biscayne, FL, January, 1998.

Jay I. Goodman. Use of mechanistic data in risk assessment: Case studies using EPA's new proposed cancer risk assessment guidelines. Invited presentation in the session entitled “Emerging Issues in Risk Assessment,” Annual Meeting of the International Life Sciences Institute, Health and Environmental Sciences Institute, St. Petersburg, FL, January, 1998.

Jay I. Goodman. Participant in a meeting of the Siloxane Science Advisory Board, Dow Corning Corporation, Midland, MI, February, 1998.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Seattle, WA, March, 1998.

Jay I. Goodman. Epigenetic mechanisms in toxicology. Introductory presentation and Co-Chair (with J.E. Trosko), symposium entitled “Epigenetic Mechanisms in Toxicology,” Annual Meeting of the Society of Toxicology, Seattle, WA, March, 1998.

Jay I. Goodman. Participant in a meeting of the Flavor and Extract Manufacturers' Association (FEMA) Expert Panel for the Evaluation of Flavoring Materials, Washington, DC, April, 1998.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Toxicology and epidemiology: Focusing on the basics to avoid pitfalls. Invited presentation in the conference entitled "Epidemiology and Toxicology: Critical Partnerships in Assessing Human Environmental Risks," International Business Conferences, USA, co-sponsored by the NIH, National Institute of Environmental Health Sciences, Washington, DC, May, 1998.

Jay I. Goodman. Chaired a meeting of the Program Committee, Society of Toxicology, Baltimore, MD, May, 1998.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Baltimore, MD, May, 1998.

Jay I. Goodman. Invited Presentation: "Use of mode of action information in cancer risk assessment," Conference entitled "Comparative Risk in Food Safety", sponsored by the Michigan State University National Center for Food Safety and Toxicology, East Lansing, MI, June, 1998.

Jay I. Goodman. Altered DNA methylation and carcinogenesis: Implications for safety assessment, and alternative methods in carcinogenesis testing. Seminar presentations, Sanofi Recherche, Pharmaceutical Division, Montpellier, France, July, 1998.

Jay I. Goodman. Debate: Transgenic animal models are an appropriate alternative to the second species in testing for carcinogenicity of pharmaceuticals - Against. Invited presentation, International Congress of Toxicology - VIII, Paris, France, July, 1998.

Jay I. Goodman. Invited participant, Strategic Planning Retreat, Health and Environmental Sciences Institute, International Life Sciences Institute, Reston, VA, July, 1998.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Baltimore, MD, July, 1998.

Jay I. Goodman. Participant in meetings of the International Life Sciences Institute, Health and Environmental Sciences Institute, Alternatives to Carcinogenicity Testing Steering Committee and Research Grant Review Committee, Washington, DC, August, 1998.

Jay I. Goodman. Participant in a meeting of the Flavor and Extract Manufacturers' Association (FEMA) Expert Panel for the Evaluation of Flavoring Materials, Montreal, Canada, September, 1998.

Jay I. Goodman. Chaired a meeting of the Program Committee, Society of Toxicology, Research Triangle Park, NC, September, 1998.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Research Triangle Park, NC, September, 1998.

Jay I. Goodman. Chaired a meeting of the Program Committee, Society of Toxicology, Baltimore, MD, November, 1998.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Baltimore, MD, November, 1998.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Susceptibility to carcinogenesis is inversely proportional to the capacity to maintain DNA methylation status. Seminar presentation, Cancer Center, Wayne State University, Detroit, MI, November, 1998.

Jay I. Goodman. Use of carcinogenicity data from transgenic animals in toxicology and safety assessment, Session Chair, Annual meeting of the Canadian Society of Toxicology, Montreal, Canada, December, 1998.

Jay I. Goodman. Altered DNA methylation: A secondary mechanism involved in carcinogenesis. Invited presentation, Annual Meeting of the Canadian Society of Toxicology, Montreal, Canada, December, 1998.

Jay I. Goodman. Participant in a meeting of the Expert Panel of the Flavor and Extract Manufacturers' Association, Miami, FL, January, 1999.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Phoenix, AZ, January, 1999.

Jay I. Goodman. Co-Organizer and co-chair of the session entitled “Risk Assessment of Receptor Mediated Toxicity,” 1999 Annual Meeting, International Life Sciences Institute, Health and Environmental Sciences Institute, Nassau, Bahamas, January, 1999.

Jay I. Goodman. Chloroform cancer risk assessment: Use of mechanistic information. Invited presentation, Annual Winter Meeting of the Toxicology Forum, Washington, DC, February, 1999.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, New Orleans, LA, March, 1999.

Jay I. Goodman. Chair of a meeting of the Program Committee, Society of Toxicology, New Orleans LA, March, 1999.

Jay I. Goodman. Altered DNA methylation: An epigenetic mechanism involved in carcinogenesis. Seminar presentation, Center for Environmental Health Sciences, College of Veterinary Medicine, Mississippi State University, Mississippi State, MS, March, 1999.

Jay I. Goodman. Use of transgenic animals and other alternative approaches for carcinogenicity testing. Invited presentation, University of Connecticut, School of Pharmacy, Center for Biochemical Toxicology, Storrs, CT, April, 1999.

Jay I. Goodman. Altered DNA methylation: An epigenetic mechanism involved in carcinogenesis. Invited presentation, Toxicology Scholars Program, University of Connecticut, School of Pharmacy, Center for Biochemical Toxicology, Storrs, CT, April, 1999.

Jay I. Goodman. Altered DNA methylation: An epigenetic mechanism involved in carcinogenesis. Presented at the Workshop on Computational and Theoretical Biology, Michigan State University, East Lansing, MI, April, 1999.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. The Society of Toxicology's initiatives to promote science-based risk assessment; and altered DNA methylation: An epigenetic mechanism involved in carcinogenesis. Invited presentation, Annual Meeting of the Michigan Chapter of the Society of Toxicology, Michigan State University, East Lansing, MI, April, 1999.

Jay I. Goodman. Participant in a meeting of the Expert Panel of the Flavor and Extract Manufacturers' Association, Washington, DC, May, 1999.

Jay I. Goodman. Chair of a meeting of the Council of the Society of Toxicology, Baltimore, MD, May, 1999.

Jay I. Goodman. Chair of a leadership meeting of the Society of Toxicology, Baltimore, MD, May, 1999.

Jay I. Goodman. The policy and science of chloroform. Invited presentation in the Symposium entitled "Chloroform: EPA Policy or Science?" sponsored by the International Society of Regulatory Toxicology and Pharmacology, Washington, DC, June, 1999.

Jay I. Goodman. Altered DNA methylation: An epigenetic mechanism underlying aberrant gene expression in carcinogenesis. Invited presentation, Phase-I Molecular Toxicology, Inc., Santa Fe, NM, June, 1999.

Jay I. Goodman. Chair of a meeting of the Council of the Society of Toxicology, Baltimore, MD, July, 1999.

Jay I. Goodman. Altered DNA methylation: An epigenetic, secondary mechanism involved in carcinogenesis. Seminar presentation, Pathology and Toxicology seminar series, Parke-Davis Pharmaceutical Research, Ann Arbor, MI, September, 1999.

Jay I. Goodman. Participant in a meeting of the Expert Panel of the Flavor and Extract Manufacturers' Association, New York City, NY, September, 1999.

Jay I. Goodman. Chair of a meeting of the Council of the Society of Toxicology, Baltimore, MD, September, 1999.

Jay I. Goodman. Altered DNA methylation: An epigenetic, secondary mechanism involved in carcinogenesis. Invited presentation, International Conference on "Epigenetic Toxicant-induced Signal Transduction and Altered Cell-Cell Communication, University of Michigan, Ann Arbor, MI, October, 1999.

Jay I. Goodman. Science-based chloroform risk assessment. Presentation to the Science Advisory Board, U.S. Environmental Protection Agency, Washington, DC, October, 1999.

Jay I. Goodman. The Society of Toxicology's commitment to enhance the scientific basis for risk assessment. Invited presentation in the workshop entitled "Harmonization of Cancer and Non-Cancer Risk Assessment", sponsored by the Society of Toxicology and the U.S. Environmental Protection Agency, Arlington, VA, November, 1999.

Jay I. Goodman. Chair of a meeting of the Council of the Society of Toxicology, Baltimore, MD, November, 1999.

Jay I. Goodman. The Society of Toxicology's initiatives to enhance the scientific basis of risk assessment. Invited presentation, National Capitol Area Chapter, Society of Toxicology, National Library of Medicine, Bethesda, MD, November, 1999.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Participant in a meeting of the Expert Panel of the Flavor and Extract Manufacturers' Association, San Juan, Puerto Rico, January, 2000.

Jay I. Goodman. Chair of a meeting of the Council of the Society of Toxicology, and Chair of a Long-Range Planning Meeting, Society of Toxicology, Dallas, TX, January, 2000.

Jay I. Goodman. Altered DNA methylation and carcinogenesis: Implications for safety assessment. Seminar presentation, AstraZeneca, Ltd., Central Research Laboratory, Manchester, United Kingdom, February, 2000.

Jay I. Goodman. Epigenetic carcinogenesis: Implications for safety assessment. Seminar presentation, Pfizer, Inc., Central Research Division, Drug Safety Department, Groton, CT, March, 2000.

Jay I. Goodman. Altered DNA methylation and carcinogenesis: Implications for cancer etiology, chemotherapy and prevention. Invited presentation, Clinical Oncology Conference, Michigan State University, East Lansing, MI, March, 2000.

Jay I. Goodman. Chloroform: Viewpoints on human cancer risk assessment. Invited presentation in the workshop entitled: “Rodent Toxicity and Nongenotoxic Carcinogenesis: Knowledge-based Human Risk Assessment from Molecular Mechanisms”, Society of Toxicology Meeting, Philadelphia, PA, March, 2000.

Jay I. Goodman. Participant in a meeting of the Nonclinical Studies Subcommittee, Advisory Committee on Pharmaceutical Science, U.S. Food and Drug Administration, Rockville, MD, March, 2000.

Jay I. Goodman. Invited presentation in support of the FY2001 budget for the National Institutes of Health, National Institute of Environmental Health Sciences, Congress of the United States, House of Representatives, Committee on Appropriations, Subcommittee on Labor, Health and Human Services, Washington, DC, March, 2000.

Jay I. Goodman. Chaired a meeting of the Executive Council, Society of Toxicology, Philadelphia, PA, March, 2000.

Jay I. Goodman. Interaction of p-alkoxyallylbenzene derivatives with DNA: Review of genotoxicity studies. Invited presentation, International Workshop on p-Alkoxyallylbenzene Derivatives: Methyleugenol and Estragole, Tyson’s Corner, VA, May, 2000.

Jay I. Goodman. Altered DNA methylation: An epigenetic, secondary mechanism involved in carcinogenesis. Seminar presentation, Department of Biochemistry and Molecular Biology, University of Minnesota Medical School, Duluth, MN, May, 2000.

Jay I. Goodman. The Society of Toxicology’s initiatives to promote science-based risk assessment, and evaluation of the carcinogenic potential of chloroform. Invited presentation, Annual Meeting of the Northland Chapter of the Society of Toxicology, Duluth, MN, May, 2000.

Jay I. Goodman. Invited participant, National Institutes of Health, National Institute of Environmental Health Sciences, Leadership Retreat, Warrenton, VA, May, 2000.

Jay I. Goodman. Threshold-exhibiting events in carcinogenesis: Epigenetics and secondary mechanisms. Invited presentation, Annual summer meeting of the Toxicology Forum, Aspen, CO, July, 2000.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. U.S. EPA's chloroform drinking water standard: An update. Invited presentation, Annual summer meeting of the Toxicology Forum, Aspen, CO, July, 2000.

Jay I. Goodman. Invited panel member, session entitled "Application of Genomics to Toxicology." Annual summer meeting of the Toxicology Forum, Aspen, CO, July, 2000.

Jay I. Goodman. Participant in a meeting of the Alternatives to Carcinogenicity Testing Committee, International Life Sciences Institute, Health ands Environmental sciences Institute, Washington, DC, July, 2000.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Baltimore, MD, July, 2000.

Jay I. Goodman. Participant in a meeting of the Global Environmental Advisory Council, Dow AgroSciences, Indianapolis, IN, September, 2000.

Jay I. Goodman. Chaired a meeting of the working group "Support of Science-Based Decisions Concerning the Evaluation of the Toxicology of Mixtures". Society of Toxicology, National Institutes of Environmental Health Sciences, U.S. Environmental Protection Agency and the Chlorine Chemistry Council/American Chemistry Council, Herndon, VA, September, 2000.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Baltimore, MD, September, 2000.

Jay I. Goodman. DNA methylation, epigenetics and secondary mechanisms in carcinogenesis. Seminar presentation, Department of Pharmacology, The University of Michigan, Ann Arbor, MI, October, 2000.

Jay I. Goodman. Altered DNA methylation and carcinogenesis: Implications for risk assessment. Seminar presentation, Chemical Industry Institute of Toxicology, Research Triangle Park, NC, October, 2000.

Jay I. Goodman. A perspective on the use of alternating models for carcinogenicity testing. Invited speaker, Workshop on the Evaluation of Alternative Methods for Carcinogenicity Testing, International Life Sciences Institute, Health and Environmental Sciences Institute, Leesburg, VA, November, 2000.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Baltimore, MD, November, 2000.

Jay I. Goodman. Invited participant, Planning meeting of the International Program on Chemical Safety. Sponsored by the World Health Organization and the International Life Sciences Institute, London, United Kingdom, November, 2000.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, Wye River, MD, January, 2001.

Jay I. Goodman. Co-Chairperson of the session entitled "Alternatives to Carcinogenicity Testing: Why Bother." Annual meeting of the International Life Sciences Institute, Montego Bay, Jamaica, WI, January, 2001.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Participant in a meeting of the Expert Panel, Flavor and Extract Manufacturer's Association, Miami, FL, January, 2001.

Jay I. Goodman. Participant in a meeting of the Council of the Society of Toxicology, San Francisco, CA, March, 2001.

Jay I. Goodman. Invited speaker, Roundtable Discussion entitled "Are Alternative Models for Carcinogenicity Testing Ready for Integration into Cancer Risk Assessment?" Annual meeting of the Society of Toxicology, San Francisco, CA, March, 2001.

Jay I. Goodman. Participant in a meeting of the Science Advisory Board, R.J. Reynolds Tobacco Co., San Francisco, CA, March, 2001.

Jay I. Goodman. Mechanisms of toxicity. Invited presentation, Meeting on Agricultural Chemical Safety Assessment, International Life Sciences Institute, Health and Environmental Sciences Institute, Washington, DC, April, 2001.

Jay I. Goodman. Participant in a meeting of the Nonclinical Studies Subcommittee of the Advisory Committee on Pharmaceutical Sciences, U.S. Food and Drug Administration, Rockville, MD, May, 2001.

Jay I. Goodman. Participant in a meeting of the Expert Panel of the Flavor and Extract Manufacturer's Association, Cambridge, United Kingdom, May, 2001.

Jay I. Goodman. Participant in a meeting of the Siloxane Science Advisory Board, Dow Corning Corp., Midland, MI, May, 2001.

Jay I. Goodman. Delegate, representing the Society of Toxicology, Meeting of the International Union of Toxicology, IUTOX 9, Brisbane, Australia, July, 2001.

Jay I. Goodman. Participant in a meeting of the Board of Trustees, International Life Sciences Institute, Health and Environmental Sciences Institute, Long-Range Planning meeting, Washington, DC, August, 2001.

Jay I. Goodman. Chairperson, meeting of the Nominating Committee, Society of Toxicology, Reston, VA, September, 2001.

Jay I. Goodman. Participant in a meeting of the Alumni Steering Committee, The University of Michigan, Department of Pharmacology, Ann Arbor, MI, September, 2001.

Jay I. Goodman. Participant in a meeting of the Expert Panel of the Flavor and Extract Manufacturer's Association, Baltimore, MD, October, 2001.

Jay I. Goodman. "Toxicogenomics: Making progress by maintaining a focus on the fundamentals of toxicology." Invited presentation, Toxicogenomics International Forum 2001, National Institute of Health Sciences, Tokyo, Japan, October, 2001.

Jay I. Goodman. "Epigenetics, DNA methylation, and carcinogenesis." Seminar, National Food Safety and Toxicology Program, Michigan State University, East Lansing, MI, October, 2001.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Toxicogenomics: Making progress by focusing on the fundamentals of toxicology. Invited presentation, Symposium on "Genomics and Toxicology," Annual Meeting of the Society of Toxicology of Canada, Montreal, Quebec, Canada, December, 2001.

Jay I. Goodman. Participant in a meeting of the Alternatives to Carcinogenicity Testing Committee, International Life Sciences Institute, Health and Environmental Sciences Institute, Washington, DC, January, 2002.

Jay I. Goodman. The chloroform saga: Science trumps ideology. Invited presentation, meeting of the Expert Panel of the Flavor and Extract Manufacturer's Association, Key Biscayne, FL, February, 2002.

Jay I. Goodman. Altered DNA methylation: A secondary mechanism involved in carcinogenesis. Seminar presentation, Johns Hopkins University, Baltimore, MD, March, 2002.

Jay I. Goodman. Invited participant, Session on Toxicogenomics, Annual Summer Meeting of the Toxicology Forum, Aspen, CO, July, 2002.

Jay I. Goodman. Participant in a meeting of the Board of Scientific Counselors, National Toxicology Program, National Institute of Environmental Health Sciences. Review of the National Center for Toxicogenomics, Research Triangle Park, NC, September 2002.

Jay I. Goodman. Chairperson, workshop entitled "Risk Assessment of Mixtures: Development of Testable Hypotheses." Sponsored by the Society of Toxicology, Chlorine Chemistry Council, National Institute of Environmental Health Sciences and U.S. Environmental Protection Agency, Atlanta, GA, September, 2002.

Jay I. Goodman. Invited plenary lecture entitled "Results of the Society of Toxicology's Expert Panel Workshop, Risk Assessment of Mixtures Development of Testable Hypotheses as Science Input into Policy Decisions." Sponsored by the Agency for Toxic Substances and Disease Registry, Atlanta, GA, September, 2002.

Jay I. Goodman. Chairperson of the session entitled "Epigenetics, non-genotoxic mechanisms underlying carcinogenesis and the importance of species differences: Implications for safety assessment," American Cancer Society, Shilling Conference 2002, "From the Cancer Cell to a Tumor: Tumors as Outlaw Organs," Santa Cruz, CA, September, 2002.

Jay I. Goodman. Altered DNA methylation: A secondary mechanism involved in carcinogenesis. Invited presentation, American Cancer Society, Shilling Conference 2002, "From the Cancer Cell to a Tumor: Tumors as Outlaw Organs," Santa Cruz, CA, September, 2002.

Jay I. Goodman. Participant in a meeting of the Science Advisory Board, R.J. Reynolds Tobacco Company, Chicago, IL, October, 2002.

Jay I. Goodman. Participant in a meeting of the Expert Panel, Flavor and Extract Manufacturer's Association, Washington, DC, October, 2002.

Jay I. Goodman. Participant in a meeting of the Siloxane Science Advisory Board, Dow Corning Corporation, Midland, MI, November, 2002.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Participant in a meeting of the Global Environmental Advisory Committee, Dow AgroSciences, Indianapolis, IN, November, 2002.

Jay I. Goodman. Chairperson, Meeting of the Board of Trustees, International Life Sciences Insti-tute, Health and Environmental Sciences Institute, Cancun, Mexico, January, 2003.

Jay I. Goodman. Participant in a meeting of the Agricultural Chemical Safety Assessment Committee, Subcommittee on Systemic Toxicity, International Life Sciences Institute, Health and Environmental Sciences Institute, London, UK, February, 2003.

Jay I. Goodman. Use of alternative models for carcinogen risk assessment: Areas of agreement and disagreement in the United States, Europe and Japan. Invited presentation, International Life Sciences Institute, Health and Environmental Science Institute Workshop on Alternatives for Carcinogen Testing, Washington, DC, February, 2003.

Jay I. Goodman. Co-Chairperson, Continuing Education course entitled "Epigenetics of Cancer," Annual Meeting of the Society of Toxicology, Salt Lake City, UT, March, 2003.

Jay I. Goodman. Altered DNA methylation: A secondary mechanism involved in carcinogenesis. Presentation in the Continuing Education course entitled "Epigenetics of Cancer," Annual Meeting of the Society of Toxicology, Salt Lake City, UT, March, 2003.

Jay I. Goodman. "Will transgenic models 'knock out' the traditional mouse bioassay?" Presentation and panel discussant , meeting of the Society of Toxicology's Safety and Regulatory Evaluation Specialty Section, Salt Lake City, March, 2003.

Jay I. Goodman. Participant in a meeting of the Expert Panel, Flavor and Extract Manufacturer's Association, Baltimore, MD, October, 2002.

Jay I. Goodman. Participant in a meeting of the ILSI Health and Environmental Sciences Insti-tute, Technical Committee on Agricultural Chemical Safety Assessment (ACSA), Systemic Toxicity task Force, Sophia-Antoplis, France, May, 2003.

Jay I. Goodman. Invited speaker "Dose-response relationships: Chloroform carcinogenicity," Conference on Non-linear Dose Response Relationships in Biology, University of Massachusetts, Amherst, MA, May, 2003.

Jay I. Goodman. Ad Hoc Reviewer of Research Proposals, Liver Foundation of Canada, May, 2003.

Jay I. Goodman. Participant in a meeting of the Pharmacology and Toxicology Subcommittee, Pharmaceutical Science Advisory Committee, U.S. Food and Drug Administration, Rockville, MD, June, 2003.

Jay I. Goodman. Chairperson of the session entitled "The Toxicology, Risk Assessment and Risk Management of Siloxane D_4," Annual Summer Meeting of the Toxicology Forum, Given Institute, Aspen, CO, July, 2003.

Jay I. Goodman. Chairperson, mid-year Meeting of the Board of Trustees, International Life Sciences Institute, Health and Environmental Sciences Institute, Washington, DC, July, 2003.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. DNA methylation and tumor promotion. Seminar presentation, Institut de Recherches Internationales Servier, Gidy, France, August, 2003.

Jay I. Goodman. Participant in a meeting of the ILSI Health and Environmental Sciences Institute, Technical Committee on Agricultural Chemical Safety Assessment (ACSA), Systemic Toxicity Task Force, Brussels, Belgium, August, 2003.

Jay I. Goodman. Participant in a meeting of the Nominating Committee, Society of Toxicology, Reston, VA, September, 2003.

Jay I. Goodman. Participant in a meeting of the Expert Panel, Flavor and Extract Manufacturer's Association, Florence, Italy, September, 2003.

Jay I. Goodman. Participant in a meeting of the ILSI Health and Environmental Sciences Institute, Technical Committee on Agricultural Chemical Safety Assessment (ACSA), Systemic Toxicity Task Force, Washington, DC, November, 2003.

Jay I. Goodman. Participant in a meeting of the Board of Trustees, International Life Sciences Institute, Washington, DC, January, 2004.

Jay I. Goodman. Chairperson, Meeting of the Board of Trustees, International Life Sciences Institute, Health and Environmental Sciences Institute, Washington, DC, January, 2004.

Jay I. Goodman. Altered DNA methylation: A component of multistep carcinogenesis. Seminar presentation, Institut de Recherches Internationales Servier, Courbevoie, France, February, 2004.

Jay I. Goodman. Participant in a meeting of the Expert Panel, Flavor and Extract Manufacturer's Association, Sarasota, FL, February, 2004.

Jay I. Goodman. Research should be judged based upon scientific merit, not the source of funding. Invited presentation, Issues Session, Annual Meeting of the Society of Toxicology, Baltimore, MD, March, 2004.

Jay I. Goodman. Participant, scientific mapping/planning meeting. International Life Sciences Institute, Health and Environmental Institute, Orlando, FL, April, 2004.

Jay I. Goodman. Overview, synopsis and future directions. Invited presentation, meeting entitled "Biological Significance of DNA Adducts," sponsored by the International Life Sciences Institute, Health and Environmental Institute and U.S. Environmental Protection Agency, Washington, DC, April, 2004.

Jay I. Goodman. Invited participant, Workshop on the Significance of Rodent Liver Tumors, sponsored by the International Life Sciences Institute, Health and Environmental Institute, U.S. Environmental Protection Agency, and the National Institute of Environmental Health Sciences, Research Triangle Park, NC, May 2004.

Jay I. Goodman. Invited participant, session entitled "Biological Significance of Rodent Liver Tumors," Annual Summer Meeting of the Toxicology Forum, Aspen, CO, July, 2004.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. DNA adducts, biological consequences and application to risk assessment. ILSI Health and Environmental Sciences Institute Workshop update. Annual Summer Meeting of the Toxicology Forum, Aspen, CO, July, 2004.

Jay I. Goodman. Participant in a meeting of the Expert Panel, Flavor and Extract Manufacturer's Association, Aspen, CO, July, 2004.

Jay I. Goodman. Altered DNA methylation: A biomarker for cancer diagnosis and prognosis. Fifth Annual Molecular Imaging Workshop: The Potential of Molecular Imaging in Drug Discovery, Michigan State University, Department of Radiology and General Electric Medical Systems, East Lansing, MI, July, 2004.

Jay I. Goodman. Participant in the mid-year meeting of the Board of Trustees, International Life Sciences Institute, Health and Environmental Sciences Institute, Washington, DC, August, 2004.

Jay I. Goodman. Seminar presentation "Epigenetics, Altered DNA Methylation and Carcinogenesis: Implications for Safety Assessment," Millenium Pharmaceuticals, Boston, MA, September, 2004.

Jay I. Goodman. Participant in a meeting of the Expert Panel, Flavor and Extract Manufacturer's Association, Lisbon, Portugal, October, 2004.

Jay I. Goodman. Altered DNA methylation: An epigenetic, secondary mechanism involved in carcinogenesis. Invited presentation, Annual Meeting of the Genetic and Environmental Mutagenesis Society, "DNA Methylation and Its Toxicological Consequences," Chapel Hill, NC, November, 2004.

Jay I. Goodman. Participant in a meeting of the Board of Trustees, International Life Sciences Institute, San Juan, PR, January, 2005.

Jay I. Goodman. Participant in a meeting of the Expert Panel, Flavor and Extract Manufacturer's Association, Miami, FL, February, 2005.

Jay I. Goodman. Plenary Lecture, Epigenetics, DNA Methylation and Carcinogenesis: Implications for Safety Assessment. The John Barnes Prize Lecture, Annual Meeting of the British Toxicology Society, The University of Warwick, England, March, 2005.

Jay I. Goodman. Mode of action-based framework for risk assessment. Invited presentation, Roundtable Discussion on Large Granular Lymphocyte Leukemia in F344 Rats: Relevance for Human Cancer Risk Assessment, University of Pennsylvania Medical Center, Hershey, PA, June, 2005.

Jay I. Goodman. Participant in the mid-year meeting of the Board of Trustees, International Life Sciences Institute, Health and Environmental Sciences Institute, Washington, DC, August, 2005.

Jay I. Goodman. Participant in a meeting of the Advisory Committee to the Director, Center for Disease Control and Prevention, Atlanta, GA, August 2005.

Jay I. Goodman. Participant in a meeting of the Expert Panel, Flavor and Extract Manufacturer's Association, Boston, MA, September, 2005.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Invited participant, Workshop on Framework Approaches to Risk Assessment: DNA Adducts in Risk Assessment, International Life Sciences Institute, Health and Environmental Sciences Institute, EuroForum, Nice, France, November, 2005.

Jay I. Goodman. Invited participant, Workshop on Framework Approaches to Risk Assessment: Rodent Liver Tumors as a Predictor of Human Cancer Risk? International Life Sciences Institute, Health and Environmental Sciences Institute, EuroForum, Nice, France, November, 2005.

Jay I. Goodman. Invited speaker, "Current Trends to Streamline the Safety Assessment of Pharmaceuticals," Institute de Recherches Internationales Servier, Paris, France, November, 2005.

Jay I. Goodman. Participant in a meeting of the Board of Trustees, International Life Sciences Institute, San Juan, PR, January, 2006.

Jay I. Goodman. Participant in a meeting of the Board of Trustees, International Life Sciences Institute, Health and Environmental Sciences Institute, San Juan, PR, January, 2006.

Jay I. Goodman. Participant in a meeting of the Advisory Committee to the Director, Centers for Disease Control and Prevention (CDC), Atlanta, GA, February, 2006.

Jay I. Goodman. Chairperson, Platform Session entitled "Regulation of Gene Expression in Carcinogenesis," Annual Meeting of the Society of Toxicology, San Diego, CA, March, 2006.

Jay I. Goodman. Participant in a meeting of the Cancer Hazard Identification Strategies Committee, International Life Sciences Institute, Health and Environmental Sciences Institute, Washington, DC, March, 2006.

Jay I. Goodman. Invited presentation, "Assessment of DNA Methylation, and the Agouti Mouse Model," in the workshop entitled "Impact of Epigenetics on Risk Assessment." Syngenta Central Toxicology Laboratory, Alderley Park, Macclesfield, United Kingdom, May, 2006.

Jay I. Goodman. Seminar presentation, "Identification of Regions of Altered DNA Methylation Which May Lead to Carcinogenesis: Implications for Safety Assessment." Syngenta Central Toxicology Laboratory, Alderley Park, Macclesfield, United Kingdom, May, 2006.

Jay I. Goodman. Invited participant, workshop entitled "Relevance and Follow-Up of Positive Results in *In Vitro* Genetic Toxicology Testing." International Life Sciences Institute, Health and Environmental Sciences Institute, Washington, DC, June, 2006.

Jay I. Goodman. Invited presentation, "Mechanistic Lessons from Human Leukemia." Review of large granular lymphocytic leukemia in F344 rats, Center for Environmental Health, Indiana University, Indianapolis, IN, July, 2006.

Jay I. Goodman. Participant in a meeting of the Board of Trustees, International Life Sciences Institute, Health and Environmental Sciences Institute, Washington, DC, July, 2006.

Jay I. Goodman. Invited presentation, Altered DNA Methylation: An Epigenetic Mechanism Underlying Carcinogenesis. Symposium on Epigenetic Mechanisms in Toxicology, EUROTOX Meeting, Cavtat, Croatia, September, 2006.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Invited presentation entitled "Epigenetics and transgenerational effects: Implications for safety assessment," CEFIC (European Chemistry Industry Council) Long-Range Workshop, Brussels, Belgium, November, 2006.

Jay I. Goodman. Invited participant, Risk Assessment Methodologies Workshop on Approaches to Weight-of-Evidence Evaluation in Risk Assessment, ILSI Health and Environmental Sciences Institute, Baltimore, MD, December, 2006.

Jay I. Goodman. Participant in a meeting of the Board of Trustees, International Life Sciences Institute, San Juan, PR, January, 2007.

Jay I. Goodman. Participant in a meeting of the Board of Trustees, International Life Sciences Institute, Health and Environmental Sciences Institute, San Juan, PR, January, 2007.

Jay I. Goodman. Invited presentation entitled "Epigenetics and Carcinogenesis: The Role of Altered DNA Methylation." Symposium entitled "Epigenetic Regulation in Development, Reproduction and Disease. Annual Meeting of the Society of Toxicology, Charlotte, NC, March 25-29, 2007.

Jay I. Goodman. Invited participant, Roundtable Discussion entitled "Relevance and Follow-up of Positive In Vitro Genetic Toxicology Testing: Strategies to Integrate Results into Risk Assessment, Annual Meeting of the Society of Toxicology, Charlotte, NC, March, 2007.

Jay I. Goodman. Invited seminar presentation entitled "A Novel Approach to Identify Genes Involved in Carcinogenesis Due to Altered DNA Methylation." Merck Research Laboratories, West Point, PA, April, 2007.

Jay I. Goodman. Invited presentation "Altered DNA Methylation: An Epigenetic Mechanism Underlying Carcinogenesis," Gordon Conference on Toxicogenomics, Colby-Sawyer College, New Long, NH, June, 2007.

Jay I. Goodman. The George H. Scott Memorial Award Lecture "A Novel Approach to Identify Genes Involved in Carcinogenesis Due to Altered DNA Methylation," The Toxicology Forum, Aspen, CO, July 2007.

Jay I. Goodman. Invited presentation entitled "Review of the Carcinogenicity Data Concerning Hair Dyes: Is there Biologically Plausible Cancer risk?" The Toxicology Forum, Aspen, CO, July, 2007.

Jay I. Goodman, Invited presentation entitled "What We Need to Know Prior to Considering Incorporating An Epigenetic Evaluation Into Human Health Assessments," The Toxicology Forum, Aspen, CO, July, 2007.

Jay I. Goodman. Invited presentation entitled "A Novel Approach to Identify Genes Involved in Carinogenesis Due to Altered DNA Methylation," The Annual John Doull Symposium, Department of Pharmacology, Toxicology and Therapeutics, University of Kansas, Kansas City, KS, September, 2007.

Jay I. Goodman. Invited presentation entitled "What We Need to Know Prior to Considering Incorporating An Epigenetic Evaluation Into Safety Assessment," Workshop on Epigenetic Transgenerational Effects, Syngenta, Berkshire, United Kingdom, September, 2007.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Participant in a meeting of the leadership of the International Life Sciences Institute, Health and Environmental Sciences Institute (HESI), as a member of the Executive Committee of HESI's Board of Trustees with representative of the leadership of the NIH, National Institute of Environmental Health Sciences (NIEHS), including Dr. Samuel Wilson, acting Director of NIEHS, to discuss enhanced HESI-NIEHS cooperation with regard to advancing science-based safety assessment of chemicals. Research Triangle Park, NC, October, 2007.

Jay I. Goodman. Participant in a meeting of the leadership of the International Life Sciences Institute, Health and Environmental Sciences Institute (HESI), as a member of the Executive Committee of HESI's Board of Trustees with representative of the leadership of the U.S. Environmental Protection Agency (EPA), including Dr. George Gray, Assistant Administrator for Research and Development, to discuss enhanced HESI-EPA cooperation with regard to advancing science-based safety assessment of chemicals. Washington, DC, November, 2007.

Jay I. Goodman. Invited presentation entitled "Altered DNA Methylation: An Epigenetic Mechanism Underlying Carcinogenesis," Symposium entitled: "The Interface of Chemistry and Biology in the "Omics" Era: Environment and Health and Drug Discovery," The 6th Princess Chulabhorn International Science Congress, Bangkok, Thailand, November, 2007.

Jay I. Goodman. Invited presentation entitled "Genotoxicity and Carcinogenicity Testing: What are we Doing and What Should we be Doing?" The Toxicology Forum, Annual Winter Meeting, University of Delaware, Washington, DC, January, 2008.

Jay I. Goodman. Participant in a meeting of the Board of Trustees, International Life Sciences Institute, San Juan, PR, January, 2008.

Jay I. Goodman. Participant in a meeting of the Board of Trustees, International Life Sciences Institute, Health and Environmental Sciences Institute, San Juan, PR, January, 2008.

Jay I. Goodman. Invited presentation entitled "Transgenerational Epigenetics: What do we Need to Know Before Altering the Risk Assessment Paradigm?" Workshop on Transgenerational Epigenetics, sponsored by the United Kingdom Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment, Cheshire, United Kingdom, February, 2008.

Jay I. Goodman. Invited presentation entitled "Carcinogenicity Hazard Assessment of Hair Dyes: Is There a Biologically Plausible Cancer Risk?" Workshop entitled "To Dye or Not to Dye: Safety of Oxidative Hair Dyes," Annual Meeting of the Society of Toxicology, Seattle, WA, March, 2008.

Jay I. Goodman. Invited presentation entitled "Orphan Nuclear Receptor Constitutive Active/Androstane Receptor (CAR)-mediated Alterations in DNA Methylation During Phenobarbital (PB) Promotion of Liver Tumorigenesis," Symposium entitled "New Developments in Liver Tumor Biology," Annual Meeting of the Society of Toxicology, Seattle, WA, March, 2008.

Jay I. Goodman. Seminar presentation "What We Need to Know Prior to Considering Incorporating An Epigenetic Evaluation Into Human Health Assessments," Dow Chemical Company, Midland, Mi, April, 2008.

Jay I. Goodman. Invited participant, workshop on Alternative Approaches to Assessment of Systemic Toxicity Without the Use of Animals, sponsored by The European Partnership for Alternative Approaches for Animal Testing, Brussels, Belgium, April, 2008.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Seminar presentation entitled "Identification of Genes Involved in Phenobarbital-Induced Tumorigenesis Due to Altered DNA Methylation," U.S. Food and Drug Administration, National Center for Toxicological Research, Jefferson, AK, May, 2008.

Jay I. Goodman. Invited participant, Epigenomics of Environment and Disease, Gordon Conference on Mechanisms of Toxicity, Bates College, Lewiston, ME, July, 2008.

Jay I. Goodman. Invited presentation entitled "Genotoxicity and Carcinogenicity Testing: What are we Doing and What Should we be Doing?" Genetic Toxicology Association, Annual Meeting, University of Delaware, Newark, DE, September 2008.

Jay I. Goodman. Invited seminar presentation entitled "Identification of Genes Involved in Carcinogenesis Due to Altered DNA Methylation," Department of Pharmacology, East Carolina University, Greenville, NC, November, 2008.

Jay I. Goodman. Invited presentation entitled "Epigenetics and Carcinogenesis: Identification Of Genes Involved Due To Altered DNA Methylation," Annual Fall Meeting of the Michigan Chapter of the Society of Toxicology, Ann Arbor, MI, November, 2008.

Jay I. Goodman. Invited presentation entitled "Identification of Genes Involved in Phenobarbital-Induced Carcinogenesis: Emphasis on Altered DNA Methylation," Syngenta Epigenetics and RNA Conference, London, United Kingdom, December, 2008.

Jay I. Goodman. Participant in a meeting of the Board of Trustees, International Life Sciences Institute, Tucson, AZ, January, 2009.

Jay I. Goodman. Invited presentation entitled "Epigenetic Implications for Toxicology: An Introduction," Symposium entitled "Epigenetic Implications to Toxicology," Annual Meeting of the Society of Toxicology, Baltimore, MD, March, 2009.

Jay I. Goodman. Invited symposium presentation entitled "Identification of genes involved in phenobarbital-induced tumorigenesis: Emphasis on altered DNA methylation and Expression," Symposium entitled "Biological Factors that Impact Assessment of Human Relevance of Animal Neoplasia." Annual Meeting of the Society of Toxicologic Pathology, Washington, DC, June, 2009.

Jay I. Goodman. Plenary speaker: Identification of genes involved in phenobarbital-induced tumorigenesis: Emphasis on altered DNA methylation and Expression. Annual EUROTOX Meeting, Dresden, Germany, September 2009.

Jay I. Goodman. Invited speaker: Role of Epigenetic Changes in Carcinogenesis. Workshop on the State of the Science of Epigenetics. National Institute of Environmental Health Sciences, Research triangle Park, NC, October, 2009.

Jay I. Goodman. Invited speaker: Biology of Carcinogenesis: Implications for Discerning Potential Modes of Action of Carcinogens. Workshop to Develop a Framework for Estimating Potential Human Cancer Risk from Intermediate and/or Short-Term Exposures. Washington, DC, December 2009.

Jay I. Goodman. Participant in a meeting of the Board of Trustees, International Life Sciences Institute, San Juan, PR, January, 2010.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Invited speaker: Driving CAR (Constitutive Active Androstane Receptor) to Cancer: Identification of Genes Involved in Phenobarbital-Induced Carcinogenesis: Emphasis on Altered DNA Methylation, Gene Expression and Pathways. 15th Annual Toxicology Symposium, Department of Environmental Health Sciences, University of Michigan, Ann Arbor, MI, February, 2010.

Jay I. Goodman. Invited speaker: Identification of Genes Involved in Phenobarbital-Induced Carcinogenesis: Emphasis on Altered DNA Methylation, Gene Expression and Pathways. Symposium entitled "Mechanisms of Chemical-Induced Liver Cancer: Putting the Pieces Together." Annual meeting of the Society of Toxicology, Salt Lake City, UT, March, 2010.

Jay I. Goodman. Seminar speaker: "Identification of Genes Involved in Phenobarbital-Induced Carcinogenesis: Emphasis on Altered DNA Methylation, Gene Expression and Pathways." Cellular and Molecular Pathology Branch, National Institute of Environmental Health Sciences, Research Triangle Park, NC, June 2010.

Jay I. Goodman. Invited speaker: "Phenobarbital drives CAR to tumorigenesis," workshop entitled "Dose-response approaches for nuclear receptor-mediated modes of action." National Institute of Environmental Health Sciences, Research Triangle Park, NC, September 2010.

Jay I. Goodman. Participant in a meeting of the Board of Trustees, International Life Sciences Institute, Orlando, FL, January, 2011.

Jay I. Goodman. Invited speaker: "Epigenetics Meets Toxicology: Implications for Carcinogenesis and Safety Assessment," 25th Annual Toxicology Symposium, University of Guelph, Ontario, Canada, March 2011.

Jay I. Goodman. Invited speaker: "What We Need to Know Prior to Incorporating an Epigenetic Evaluation Into Safety Assessments," Continuing Education Course entitled "Epigenetics in toxicology: Introduction, mechanistic understanding, and applications in safety assessment," Annual Meeting of the Society of Toxicology, Washington, DC, March 2011.

Jay I. Goodman. Invited speaker: "TOX21, ToxCast, NexGen & Risk21: Possibilities, Pitfalls and a Path Forward," Annual Summer meeting of the Toxicology Forum, Aspen, CO., July 2011

Jay I. Goodman. Member of the Steering Committee, Gordon Research Conference, Mechanisms of Toxicity, Proctor Academy, NH, August 2011.

Jay I. Goodman. Invited speaker: "Identification of genes involved in phenobarbital-induced carcinogenesis: Emphasis on altered DNA methylation, expression and pathways," Epigenetics session, Gordon research Conference, Mechanisms of Toxicity, Proctor Academy, NH, August 2011 – could not participate due to illness

Jay I. Goodman. Organizer of the symposium entitled "Evaluating Potential Adverse Epigenetic Effects of Chemicals: Possibilities and Pitfalls," EUROTOX-2011 meeting, Paris, France, August 28-31, 2011.

Jay I. Goodman. Symposium speaker "Epigenetics Meets Toxicology," symposium entitled "Evaluating Potential Adverse Epigenetic Effects of Chemicals: Possibilities and Pitfalls," EUROTOX-2011 meeting, Paris, France, August 28-31, 2011.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Invited speaker: "Epigenetics: An integrated view of the regulation of gene expression based on mechanisms superimposed on DNA base sequence," continuing education course entitled "Epigenetic Mechanisms in Regulation of Xenobiotics and Methodologies for Their Investigation," North American ISSX (International Society for the Study of Xenobiotics) Meeting, Atlanta GA, October 16-20, 2011.

Jay I. Goodman. "Epigenetics meets toxicology: Is it time to incorporate an epigenetic evaluation into risk assessment?" Workshop on Epigenetics and Chemical Safety, sponsored by the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC), Rome, Italy, December 2011.

Jay I. Goodman. Invited speaker: "Epigenetics Meets Toxicology: An Integrated View of Mechanisms Controling Transcription that are Superimposed on DNA Base Sequence," Symposium entitled "Toxicological considerations of Epigenetic Targets in Product Development." Annual Meeting of the Society of Toxicology, San Francisco, CA March 2012.

Jay I. Goodman. Invited speaker: "Phenobarbital-Induced Mouse Liver Tumorigenesis: Altered DNA Methylation, Changes in Gene Expression and Implications for Safety Assessment."
Molecular and Environmental Toxicology Seminar Series, University of Wisconsin, Madison, WE, April 2012.

Jay I. Goodman. Invited speaker: "Role of Epigenetics in Toxicological Safety Assessment," EUROTOX meeting, Stockholm, Sweden, June 2012.

Jay I. Goodman. Invited speaker: "Epigenetics Meets Toxicology: An Overview of Epigenetics with Emphasis on the Underlying Mechanisms and how they are Integrated," Annual Summer Meeting of the Toxicology Forum, Aspen, CO, July 2012.

Jay I. Goodman. Invited speaker: "Toxicology Meets Epigenetics." Symposium entitled "Epigenetics and Chemical Safety." Annual meeting of the European Environmental Mutagen Society (EEMS), Warsaw, Poland, September 2012.

Jay I. Goodman. Invited participant, workshop entitled "Future Tox: Building the Road for 21st Century Toxicology and Risk Assessment Practices," sponsored by the Society of Toxicology, Arlington, VA, October 2012.

Jay I. Goodman. Co-Chair, Toxicology Workshop, New developments and Cooperation of Modern Tools: Omics, Mass Spectroscopy and Imaging. Institut de Recherches Internationales Servier, Paris, France, November 2012.

Jay I. Goodman. Invited speaker, "Identification of Genes Involved in Phenobarbital-Induced Mouse Liver Carcinogenesis: Emphasis on Altered DNA Methylation, Expression and Pathways," workshop entitled "Human Relevance of Rodent Hepatocarcinogenicity," BASAF, Bad Durkheim, Germany, November 2012.

Jay I. Goodman. Participant, meeting of the Board of Trustees, International Life Sciences Institute (ILSI), Miami, FL, January 2013.

Jay I. Goodman. Participant, meeting of the Board of Trustees, International Life Sciences Institute (ILSI), Health and Environmental Sciences Institute (HESI), Miami, FL, January 2013.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Invited participant, workshop entitled "Weight of Evidence," International Life Sciences Institute (ILSI) North America Technical Committee on Food and Chemical Safety, Miami, FL, January 2013.

Jay I. Goodman. Invited speaker, "Driving CAR to Rodent Liver Tumors: Altered DNA Methylation, Gene expression and Implications for Safety Assessment." 20th EUROTOX Training and Discussion Session, Epigenetic Carcinogenicity in Risk Assessment, Dortmund, Germany, February 2013.

Jay I. Goodman. Participant, meeting of the Board of Trustees, International Life Sciences Institute (ILSI), Health and Environmental Sciences Institute (HESI), Alexandria, VA, June 2013.

Jay I. Goodman. Invited speaker: "Adverse v. Adaptive: A View from the Epigenetic Landscape," Session on Adverse Versus Adaptive Effects in Toxicology Studies: Application to Human Risk Assessment," Annual Summer Meeting of the Toxicology Forum, Aspen, CO, July 2013.

Jay I. Goodman. Invited speaker: "An Integrated View of Epigenetics: Epigenomics Impact on Drug Safety Sciences," Session on Epigenetics and Drug Safety, Annual Summer Meeting of the Toxicology Forum, Aspen, CO, July 2013.

Jay I. Goodman. Invited speaker, Gordon Research Seminar (for Graduate Students and Postdoctoral Fellows), Mechanisms of Toxicity, "An Integrated View of Epigenetic Regulation of Gene Expression: Implications for Safety Assessment," Andover, NH, August 2013.

Jay I. Goodman. Invited speaker, Gordon Research Conference, Mechanisms of Toxicity, "An Integrated View of Epigenetics: Implications for Safety Assessment," Andover, NH, August 2013.

Jay I. Goodman. Participant, meeting of the Board of Trustees, International Life Sciences Institute (ILSI), Bermuda, January 2014.

Jay I. Goodman. Participant, meeting of the Board of Trustees, International Life Sciences Institute (ILSI), Health and Environmental Sciences Institute (HESI), Bermuda, January 2014.

Jay I. Goodman. Invited speaker: "An Integrative View of Epigenetics: Implications for Safety Evaluation," Symposium entitled "Epigenetics: The state of the science for its use in safety evaluation and product development." Procter & Gamble, Cincinnati, OH, June 2014.

Jay I. Goodman. Participant, meeting of the Board of Trustees, International Life Sciences Institute (ILSI), Health and Environmental Sciences Institute (HESI), Washington, DC, June 2014.

Jay I. Goodman. Invited speaker: "A Systems Biology View of Epigenetics: Implications for Safety Assessment," Symposium entitled "Epigenetic Endpoints in Toxicologic Pathology and Relevance to Human Health," Society of Toxicologic Pathology Annual Symposium. Washington, D.C., June 2014.

Jay I. Goodman. Invited speaker: "A Systems Biology Approach to Epigenetics: Implications for Safety Assessment," Janssen Pharmaceuticals, Inc., Johnson & Johnson Research and Development. Raritan, NJ, August 2014.

PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

Jay I. Goodman. Invited speaker: "Driving CAR (Constitutive Androstane Receptor) to Carcinogenesis: Mechanistic and Practical Implications," Symposium entitled, "Receptors at the Interplay Between Endogenous and Xenobiotic Agonists." Annual Congress of the European Societies of Toxicology (EUROTOX) Edinburgh, Scotland, September 2014.

Jay I. Goodman. Invited speaker: "Regulation of chemicals based on an epigenetic liability: Are we there yet?." Symposium entitled "Environmental epigenetics, epigenotoxic assays and regulation." Environmental Mutagenesis and Genomics Society, Orlando, FL, September 2014.

Jay I. Goodman. Invited speaker. "Toxicity testing in the 21st century: Making progress by maintaining a focus on the fundamentals. Annual Summer meeting of The Toxicology Forum, Colorado Springs, CO, July 2015.

Jay I. Goodman. Invited speaker. "Toxicity education in the 21st century: Making progress by maintaining a focus on the fundamentals. Annual Summer meeting of The Toxicology Forum, Washington, DC, July 2016.

Jay I. Goodman. Member of the Organizing Committee and Invited participant, Toxicology Forum, Relevance of Rodent Liver Tumors Workshop, Arlington, VA, October 2016.

Jay I. Goodman. Member of the Organizing Committee and Invited participant, Toxicoepigenetics Meeting, a Society of Toxicology Current Concepts in Toxicology meeting, Tysons, VA, November 2016.

Jay I. Goodman. Invited speaker: "Epigenetics: Implications for safety assessment." Symposium entitled" Epigenetic mechanisms as drug targets: Toxicological considerations." Annual meeting of the American College of Toxicology, Palm Springs, CA, November 2017.

ABSTRACTS OF PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS

1. **Goodman, J.I.** and Tephly, T.R.: Peroxidative oxidation of methanol in rat and monkey liver: Role of microbody and soluble flavin enzymes. Fed. Proc. 26: 616, 1967.

2. **Goodman, J.I.** and Tephly, T.R.: Some properties of rat hepatic formaldehyde dehydrogenase. The Pharmacologist 10: 173, 1968.

3. Watkins, W.D., **Goodman, J.I.** and Tephly, T.R.: Effect of pyrazole on methanol and ethanol oxidation. Fed. proc. 28: 546, 1969.

4. **Goodman, J.I.** and Potter, V.R.: Early effects of 3'-methyl-4-dimethylaminoazobenzene (MeDAB) administration: Evidence of an increased turnover of hepatic DNA. Proceedings of the American Association for Cancer Research 12: 36, 1971.

5. **Goodman, J.I.**: The effect of 5-fluorodeoxyuridine on the synthesis of DNA pyrimidines in precancerous rat liver. Fed. Proc. 32: 735, 1973.

6. **Goodman, J.I.**: Multiple precursor pools for the synthesis of DNA-thymine in Novikoff hepatoma cells. Proceedings of the American Association for Cancer Research 14: 37, 1973.

7. Rothenberg, R.J. and **Goodman, J.I.**: DNA synthesis in regenerating rat liver *in vivo* and in slices *in vitro.* The Pharmacologist 15: 204, 1973.

8. **Goodman, J.I.**: Extent and duration of covalent binding of carcinogen residues to the nuclear DNA of different cell populations in precancerous liver. Proceedings of the American Association for Cancer Research 16: 4, 1975.

9. **Goodman, J.I.**: Identification of a reaction product formed *in vivo* between 2-acetylaminofluorene and DNA-guanine by high pressure liquid chromatography. Proceedings of the American Association for Cancer Research 17: 47, 1976.

10. **Goodman, J.I.** and Adams, M.P.: Alterations in template activity of the nuclear DNA of different cell populations in precancerous liver. Proceedings of the American Association for Cancer Research 18: 16, 1977.

11. Schwartz, E.L. and **Goodman, J.I.**: Effects of 2-acetylaminofluorene ingestion on hepatic chromatin structure. The Pharmacologist 19: 181, 1977.

12. Schwartz, E.L. and **Goodman, J.I.**: Preferential carcinogen modification of specific hepatic chromatin fractions. Proceedings of the American Association for Cancer Research 19: 34, 1978.

13. Schwartz, E.L. and **Goodman, J.I.**: Studies on carcinogen-chromatin interactions. Fed. Proc. 37: 749, 1978.

14. Schwartz, E.L. and **Goodman, J.I.**: 2-Acetylaminofluorene (AAF) ingestion and DNA damage. Proceedings of the American Association for Cancer Research 20: 125, 1979.

15. Doolittle, D.J., Warren, S.T., Trosko, J.E., Chang, C.C. and **Goodman, J.I.**: An *in vitro* mammalian assay system for the detection of toxic and mutagenic chemicals. The Pharmacologist 22: 172, 1980.

ABSTRACTS OF PRESENTATIONS AT NATIONAL/INTERNATIONAL MEETINGS (Continued)

16. Faustman, E.M. and **Goodman, J.I.**: Alkylation of DNA in specific hepatic chromatin fractions following exposure to methylnitrosourea (MNU). The Pharmacologist 22: 211, 1980.

17. Baranyi, B.L. and **Goodman, J.I.**: Rapid assessment of the covalent binding of carcinogen residues to hepatic DNA. The Pharmacologist 22: 264, 1980.

18. Doolittle, D.J., Kazanski, M.B. and **Goodman, J.I.**: Lack of a correlation between arylhydrocarbon hydroxylase (AHH) activity and capacity to generate toxic metabolites of benzo(a)pyrene (BP). The Toxicologist 1: 25, 1981.

19. Faustman-Watts, E.M. and **Goodman, J.I.**: DNA-purine methylation in hepatic chromatin following exposure to dimethylnitrosamine (DMN) or methylnitrosourea (MNU). The Pharmacologist 23: 115, 1981.

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Attachment B

Materials Considered List

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