May 20, 2005

C-4

Dear Dr. Siegel,

Since offering my views of risks from acrylamide September 26, 2003, noting uracil deamination likely, the question of deamination from glycidamide, previously answered through an unpublished report, was answered in 2004, with an adduct at cytidine deaminating to uridine.

Therefore, I continue to support the warning of consumers of the danger of acrylamide through the Right-to-know Law of California. Given its high risk from diets of particular foods, acrylamide's carcinogenicity should be public knowledge, particularly since regulation was replaced by Right-to-know law.

OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT
Received
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SACRAMENTO

Comparison to ethylene oxide, a known human carcinogen, should help establish acrylamide as a known human carcinogen. Recent epidemiology of ethylene oxide is linked to the adducts it causes which are similar, through deamination, to those of

glycidamide. The Carcinogenic Identification Committee should request to the I.A.R.C. the review of acrylamide danger from its epoxide glycidamide.

In a recent "Science Times" summary, benz pyrene was explained as a cause of dietary cancer. Yet, this kind of public information process is ineffective, from a psychological, behavioral change standpoint. Cigarette smoke and cancer rate change only occurred after labels on products were required. It would be likely best to avoid court conflicts like those of patients and tobacco interests. Perhaps this could be accomplished by labeling based on similarities of cancer onset with food products. The glycidamide adducts are common to tobacco smoke exposure and qualify this argument.

Since the April 2002 Swedish National Food Administration announcement of acrylamide content and popular diet, many have had the chance to follow the progress of research scientists to explain how acrylamide causes cancer. My contacting you regarding your October 17, 2003 meeting followed my suggestion that deamination was important to acrylamide carcinogenesis. I repeat my opinion that deamination presents a great danger, and is contributing significantly to the need to review acrylamide at IARC and provide warning through Right-to-Know law.

The mutation of P53 by glycidamide in human epithelial cells is of interest, it may be that the deamination is there, since there is a link to cyclic adducts of 4-HNE, and adducts of AFB, possibly these mutate P53. The resulting adducts of dietary exposure, the

mutations bear significance to the P53 mutation especially given the epithelial cell site, where many cancers, 90% occur. That P53 mutation occurs in 50% of cancers is of concern. The finding of 90% of prostate cancers including cytidine adducts is noteworthy.

With the application of a multistage carcinogenesis, several discoveries since 2002 are useful. First, GSTP1, as with prostate cancer, is ineffective in prevention. Second, APC gene, as with colon cancer, or HPRT gene, which deaminates in cancer, are mutated. Third, P53 mutation may cause tumor suppression to fail.

The reason for deamination is currently under study. The 2004 results (mentioned at the beginning of this letter) show that glycidamide causes deamination in vitro. Mammalian studies involving deamination of

cytidine adducts are reported, including results by Wang and Zhang. Since deamination is replicable recently even in UV exposure, by Pfeifer, Bockrath, perhaps the process should be a determinant in warning approval. At the American Chemical Society Meeting, San Diego, CA, 2004, Eisenbrand found human blood cells to have the HPRT gene. Explanations as these are great advances that have been helpful towards the understanding of this cause of cancer.

My appreciation is given herein to the Carcinogenic Identification Committee in its attempts to establish a danger and use the Right-to-Know law. I am hopeful that my letters may be of interest to committee members.

If possible, some bearing on this issue may be the study "Biases about Man-made Cancer among Researchers" Social Studies of Science, 31/5 (October 2001) by Mazur, Rothman, and Lichter. Their opinion is that it is not a matter of ascribing to natural causes, among scientists, away from man-made causes, cancer in the United States. Rather, it is that man-made causes are viewed as less dangerous, with identity factors of researchers suggesting bias. With references to Richard Doll Causes of Cancer and Bruce N. Ames "Ranking Possible Carcinogenic Factors," the authors, though not explaining a source of bias, present the views of scientists, through this bias, of high significance of industry and tobacco, and low significance of food. The question posed to objectivity should be understood whereby it cannot be expected that educators will provide a lead in providing

the public with substantial warning. Therefore, it is in the best interests of the public to have the warning developed by OEHHA in the case of acrylamide.

Sincerely,

Richard Segal

C-4a

From: <rich6412@localnet.com>
To: <sluong@oehha.ca.gov>
Date: 7/8/2005 5:00:15 PM
Subject: acrylamide label

Dear Ms. Luong,
Since Dr. Bea Singer has found that cyclic adducts will follow deamination, the question exists regarding acrylamide exposure, and glycidamide formation, concerning cyclic adduct presence in human tissue. For the following reasons there is a likelihood that cyclic adducts result from acrylamide exposure, whereupon a lobel warning consumers of acrylamide danger is needed. The finding of cyclic adducts from DNA exposed ao acrylonitrile is substantial to risk assessment, that chloro-acrylonitrile causes cyclic adducts and is comparable to the dguanosine kind is thus to lead to the question of whether cytidine adduct deamination coexists. The suggestion at NYU of this may find proof in adduct decoy, preferential repair, the order of adduct occurence and repair of mutation. That NYU has found cyclic adducts would like to study cytidine, and comments on the relevancy of base excision repair (of importance to acrylamide) futher suggests likelihood that the dguanosine cyclic adducts will coexist with deaminated cytidine adducts and uridine. The acrolein deamination may point to a repeated phenomena. Or, the P53 mutation by acrylamide could occur as the cytidine adducts do at P53. That one can see cyclic adducts from diet (hexenal) and that one can see the deamination process from ethylene oxide and its presence in endogenous adducts may point to future work. Certainly, the comments by Hecht '05 in relation to dietary study, whereby rather than prevention this second kind of adduct was studied, is important, likewise Lindahl's views of uracil repair- that there is no repair function improvement from outside sources once again emphasizes the matter is of preventing the carcinogenesis to begin with. If cyclic adducts are preventable through glutathione, then once again acrylamide's rejection of it is futher notable. The main objective of a label thgerefore is supported because of the lack of human preventability of acrylamide carcinogenesis. Wang's review in Mutation Research notes Ames, Sowers, and Wallace works of importance. R Segal