UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C., 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

May 29, 2014

MEMORANDUM

SUBJECT: Materials for Review by the Human Studies Review Board for its June 11, 2014 Meeting

TO: Jim Downing
Designated Federal Official
Human Studies Review Board
Office of Science Advisor (8105R)

FROM: William L. Jordan
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This memorandum describes the materials that the Environmental Protection Agency's (EPA's) Office of Pesticide Programs is providing for review by the Human Studies Review Board (HSRB or Board) at the meeting scheduled for June 11, 2014. At this meeting, EPA will ask the Board to address scientific and ethical issues surrounding the following three completed human toxicity studies with iodine that appear in the published literature. The Agency's regulation, 40 CFR §26.1602, requires EPA to seek HSRB review if EPA intends to rely on the results of pre-rule studies, like these, that identify or quantify a toxic effect.

1. Paul, T., Meyers, R.J., Witorsch, R.J., Pino, S., Chipkin, S.H., Ingbar, S.H., Braverman, L.E. The Effect of Small Increases in Dietary Iodine on Thyroid Function in Euthyroid Subjects. *Metabolism,* Vol. 37, No. 2 (February) 1988: pp. 121-124.

2. Gardner, D.F., Centor, R.M., Utiger, R.D. Effects of Low Dose Oral Supplementation of Thyroid Function in Normal Men. *Clinical Endocrinology,* Vol. 28 (1988): pp. 283-288.

3. LeMar., H.J, Georgitis, W.J. and McDermott, M.T. Thyroid Adaptation to Chronic Tetraglycine Hydroperiodide Water Purification Tablet Use. *Journal of Clinical Endocrinology and Metabolism,* Vol. 80 (1995): pp. 220-223.

The ethical standards from EPA's rule at 40 CFR part 26 subpart Q that apply to completed pre-rule studies are as follows:

> **§26.1703.** Except as provided in **§**26.1706, EPA must not rely on data from any research subject to this subpart involving intentional exposure of any human subject who is a pregnant woman (and therefore her fetus), a nursing woman, or a child.
>
> **§26.1704.** EPA must not rely on data from any research subject to this section if there is clear and convincing evidence that: (1) The conduct of the research was fundamentally unethical (e.g., the research was intended to seriously harm participants or failed to obtain informed consent); or (2) The conduct of the research was deficient relative to the ethical standards prevailing at the time the research was conducted in a way that placed participants at increased risk of harm (based on knowledge available at the time the study was conducted) or impaired their informed consent.

Background Materials:

The background information for each of these studies consists of three documents:

1. Copy of the published article
2. EPA data evaluation record (the EPA science review)
3. EPA ethics review

Charge Questions:

The charge questions for each of these studies are provided below.

Charge questions for Paul et al. (1988)

1. Is this study scientifically sound, providing reliable data?

2. If so, is this study relevant for quantitative use in support of an assessment of the oral risk of exposure to iodine?

3. Does the study meet the applicable requirements of 40 CFR part 26 subpart Q?

Charge questions for Gardner et al. (1988)

1. Is this study scientifically sound, providing reliable data?

2. If so, is this study relevant for quantitative use in support of an assessment of the oral risk of exposure to iodine?

3. Does the study meet the applicable requirements of 40 CFR part 26 subpart Q?

Charge questions for LeMar et al. (1995)

1. Is this study scientifically sound, providing reliable data?

2. If so, is this study relevant to establish the reversibility of high dose iodine exposure?

3. Also, is this study sufficient to establish that there are no sustained adverse effects from high dose iodine exposure?

4. Does the study meet the applicable requirements of 40 CFR part 26 subpart Q?