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

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

December 30, 2014

MEMORANDUM

SUBJECT: Materials for Review by the Human Studies Review Board for its January 14, 2015 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 January 14, 2015. At this meeting, EPA will ask the Board to address scientific and ethical issues surrounding the following three completed human toxicity studies that appear in the published literature. The Agency's regulation at 40 CFR §26.1604 requires EPA to seek HSRB review if EPA intends to rely on these studies in decisions under the Federal Insecticide Fungicide and Rodenticide Act (FIFRA) or Section 408 of the Federal Food Drug and Cosmetic Act.

1. Ezratty, Veronique et al. (2014) Repeated Nitrogen Dioxide Exposures and Eosinophilic airway Inflammation in Asthmatics: A Randomized Crossover Study. *Environmental Health Perspectives.* Volume 122, Number 8, August 2014. (MRID 49519201)

2. Spak, C.J. et al. (1989) Tissue Response of Gastric Mucosa after Ingestion of Fluoride. Karolinska Institute, Huddinge University Hospital, Huddinge, Sweden. *British Medical Journal. 298:1686-7.* (MRID 49489101)

3. Hansson, T. and Roos, B. (1987). The Effect of Fluoride and Calcium on Spinal Bone Mineral Content: A Controlled, Prospective (3 years) study. Sahlgren's Hospital, University of Gothenberg, Sweden. *Calcified Tissue International.* 40:315-317. (MRID 49489102)

The ethical standards from EPA's rule at 40 CFR part 26 subpart Q that apply to these 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
4. (For Ezratty only) – copies of protocol, consent form, and ethics review approval

Charge Questions:

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

Charge questions for *Ezratty et al. (2014)*

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

2. If so, is this study adequate for quantitative use in support of an inhalation risk assessment for the use of nitrogen dioxide as a medical equipment sterilant?

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

Charge questions for *Spak et al. (1989)*

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

2. If so, is this study adequate for quantitative use in support of an acute dietary risk assessment for fluoride?

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

Charge questions for *Hansson and Roos et al. (1987)*

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

2. If so, is this study adequate for qualitative use in support of an acute dietary risk assessment for fluoride?

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