UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF PREVENTION, PESTICIDES, AND TOXIC SUBSTANCES

MEMORANDUM

Sept.11, 2006

SUBJECT: Review of the Study: " Kinetics of the Reaction Between Chlorite Ion and Tomato Extract"

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Study ID#: PA-0105

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DP Barcode: n/a
MRID#: 46944202

Background:

The premise of the study is that food/ fruits and vegetables when treated (disinfected) with chlorine dioxide it converts to chlorite ion, and chlorite ion is not stable (degrades) in the matrix of fruits or vegetables like tomatoes. In addition, the study was also initiated to estimate the presence of residues of chlorite or any other possible degradation moiety. The rationale of the study was to help in the process of risk assessment for the chlorine dioxide and sodium chlorite RED and to show that the initial presence of chlorine dioxide and or chlorite pose no dietary concerns. The Agency has noted that the study was completed in September 2005 but was not submitted till the tail end of the RED process. The study, therefore , was submitted and received too late for consideration in the RED process. It is being reviewed now.

Study Methodology:

Fresh tomatoes were purchased, macerated and its extracts were prepared in three concentration ranges: 0.1%, 0.6%, and 1%. (extract solutions were made by diluting with water). Liquid portion of this solution was separated from the solid residues and it is this liquid which was used for the kinetic investigation. Similarly analytical grade sodium chlorite solutions were prepared with nominal chlorite ion concentrations of: 100 ppb, 150 ppb and 200 ppb.

Prior to the actual testing, total chlorite anion in sodium chlorite solution was determined by iodometric titration (Pilling & Associates' SOP #:Ana001.00)

a. ***Instrumentation:*** Dionex Ion Chromatograph Model # 500 DX was used for the chlorite detection.

AS50 Dionex Autosampler
Dionex AD25 Detector Absorbance Detector operated at 450 nm wavelength
Dionex GS50 Gradient Pump set at flow rate of 1.0 ml/min
IonPac AS9-HC 4 mm Anion Exchange column, attached to an IonPac AG9-HC 4 mm Guard column
Software: Dionex PeakNet 6 was to measure the chromatographic peak height/width.
Sample vial: Dionex 2 mL sample vials with split septum were used.

b. ***Analytical Method***: EPA's Method 317 was modified for this experiment

c. ***Calibration Curve***: A calibration curve was generated in the range of 10, 20, 99.8, 200, 299, 399, and 499 ppb nominal concentration of sodium chlorite.

d. ***Sample Frequency***: Each sample for the determination of the calibration curve was analyzed in duplicates. Average retention time for chlorite ion peaks were 4.44 minutes and a standard deviation of 0.015 min.

e. ***Calculations***: Calculations were carried out with the measurement of the average peak area of the chlorite ion. Peak areas of chlorite ion ,obtained from the IC Chromatograms of the calibaration curve, were estimated using a least square linear regression relation which had the general equation:
Peak Area = M x10^{-5} x (ppb chlorite) – N x 10^{-x} where x= -4, 0r -5
M and N varied with the concentrations of chlorite ions.

f. ***Results***: 1) Kinetics of the mixtures of tomato extract and chlorite were run and, reduction in the amounts of chlorite were determined using an Excel Spread sheet
2) Each reaction mixture was analyzed four times.
3) It was assumed that reaction kinetics between tomato extract and chlorite was first order for each chemical and an overall second kinetics.
4) First order rate constants for each component (tomato extract and chlorite) were estimated as also a second order rate constant were determined.
5) A first order half life for tomato extract and chlorite determined.
6) For a first order kinetics half life was determined by using the established equation: half life (t) = ln2/first order rate constant
7) Semi log plot of chlorite ion conc. Vs time yielded the rate constant k_1 = (slope of plot Ln(chlorite ion conc.) vs time).
8) At chlorite = 95.1 ppb concentration and tomato extract at 1%, the half life was 45 minutes at temperature 11 ° C; at temperature of 6 ° C, and chlorite concentration of 197.3 ppb, and tomato extract at 0.2%, the half life was 433 minutes (~7.2 hours).
9) The rate constants at 11 and 6 ° C respectively were: 0.006± 0.002 /min/% and 0.014 ± 0.003 /min/%.

g. ***Conclusions***: 1) Reactions proceed faster at higher concentrations of tomato extract and but lower chlorite conc. 2) The reaction between tomato extract and chlorite is second order overall. 3)When the rate constants are extrapolated to 100% tomato extract, half life of the reaction between tomato and sodium chlorite is about 1 minute (6 ° C) and 0.5 min (at 11 ° C).
4) Chlorite is likely to totally degrade when tomatoes are treated with chlorine dioxide and are kept for prolonged storage.

The **Agency** has noted the following **shortcomings** in the study:

1) Ion chromatograms (retention times, peaks) are not provided with the study. These data should be provided by the registrants.
2) Agency encourages industry to conduct analytical studies with triplicate samples. The present study was conducted only with duplicate samples.
3) The study was not conducted according to GLP.
4) The study should be submitted through Agency's front-end office so that it can be assigned an MRID# and it becomes part of the permanent records of the Agency.
5) The protocols for the study were not submitted to the Agency fro review. It is an established procedure of the Agency that for a non-guideline study, registrants generate or obtain working protocols for a study and get the approval from the Agency.
6) It is not clear from the study why temperature of 6 and 11 ° C were chosen for the kinetic runs.

Agency Conclusions:

a. It is the conclusion of the Agency that the kinetic data generated with tomato is very scattered and can not be unambiguously classified as a first order reaction. (Table 27 and the attached graphics). Tomato is a mixture of many naturally occurring constituents like: lycophene, beta carotene, vitamins C and E etc. As such any attempt to do a kinetic study with a mixture is bound to result in scattered and ambiguous results. With these and other constituents there may be: 1) competing and simultaneous reactions 2)consecutive reactions, or 3) both.
b. The study in the present format is **unacceptable .** However, registrants can resubmit the study after deleting the kinetic aspects with respect to the tomato extract, and use a format similar to the **Raspberry Extract Study**. A simple time line of degradation of chlorite from a study is sufficient. OR
c. If registrants have information that only one constituent in the tomato extract is reacting or other constituents are very small in quantities such that these will not impact the kinetics reactions, the Agency is willing to review such information.

Cc: RMBII file room (NShamim)

APPENDIX

Following attachments are part of this review.

Copies of the:

1. All calibration curves
2. Data Tables 16 through 27, including any graphics attached to these tables.