Ethylene Oxide
White Paper

What is Ethylene Oxide?

Ethylene Oxide (EtO) is the most significant tool available to the U.S. spice industry to prevent human microbial contaminants such as *Salmonella* and *E.coli* in spices.

EtO is a flammable, colorless gas at temperatures above 51.3 F (10.7 C). When used directly in the gaseous form or in nonexplosive gaseous mixtures with nitrogen or carbon dioxide, Eto serves as a disinfectant, fumigant, sterilizing agent, and insecticide.

On an annual basis, the spice industry uses approximately 800,000 pounds of EtO, or less than ten percent of all of the EtO used for sterilization purposes in the U.S. The majority of EtO is used for the sterilization of medical equipment.

The Importance of EtO to the Spice Industry

The primary purpose of treatment is to protect public health. Most spices originate in developing countries where sanitation and food handling practices are not at the levels expected in the U.S. Consequently, it is well recognized and acknowledged that raw spices may contain pathogens, including *Salmonella* and *E.coli*, which can cause severe illness. EtO is extremely effective eliminating these as well as reducing bacterial loads, yeast and mold, coliforms and other pathogens. Exact numbers are difficult to determine, however, ASTA estimates that between 40% and 85% of spices in the U.S. are treated with EtO each year.

EtO is also used to address plant or animal pests that may find their way into spice packaging material. Treatment is effective in protecting U.S. agricultural crops and native vegetation from the introduction or dissemination of these plant or animal pests into the U.S.

The main advantage of EtO is that its use on spice generally has no significant impact on the appearance or flavor of the spice. Appearance and taste are essential for spices, thus EtO treatment can resolve the potential public health issues without negatively effecting the marketability of the spice.

Regulatory Review and Reregistration

EtO has been registered by the Environmental Protection Agency (EPA) for use as an antimicrobial pesticide since 1948, thus it fell into the large group of pesticides that were required to be reregistered to ensure they meet modern safety standards. Amendments to the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) were passed in 1988 requiring all pesticides approved prior to November 1, 1984 to complete the reregistration process by 1997.

In August 1996, the Food Quality Protection Act (FQPA) was passed that amended both FIFRA and the Federal Food, Drug and Cosmetic Act (FFDCA). This Act required the EPA to review all existing tolerances for pesticides to ensure with "reasonable certainty that no harm will result from aggregate exposure" to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information.

FQPA also impacted the 1958 Delaney Clause, which had established a zero cancer risk standard for pesticide residues on some processed foods, so that it no longer affected pesticides. The zero cancer risk standard for pesticide residues in some processed foods was replaced with a single "safe" standard of a reasonable certainty of no harm to consumers for pesticide residues in raw and processed foods. The law also provided new protections for infants and children by requiring an additional safety factor of 10-fold to allow for uncertainty in data collected on children's diets.

These new changes once again resulted in delaying the final reregistration process for EtO and many other pesticides, which brings us to the status of EtO today. FIFRA requires that registered pesticides be reviewed periodically to determine whether they meet current standards for continued registration. The review leads to a Reregistration Eligibility Decision (RED). The final decision is based, in part, on the determination that the benefits of use outweigh the risks to individuals and the environment. The RED for EtO was issued in the Federal Register Notice of February 22, 2006 – 71 Fed. Reg. 9110-12 and the Reregistration Eligibility Decision was issued by the EPA on April 16, 2008.

As part of this process, the EPA issued a Tolerance Reassessment Decision Document (TRED) on August 9, 2006.

Dietary Exposure

The status of dietary exposure issues today requires a look back at some of the history involving EtO. In the 1980s carcinogenicity concerns were raised related to the possible presence of EtO residues in treated spices. The EPA also had problems with the incomplete data base for many pesticides, including ETO. Consequently, ASTA, over a ten year period, developed and submitted data to the EPA on EtO for use on spices.

In 1996, ASTA met with the EPA to discuss the initial ASTA residue study. The EPA announced that EtO was not a significant concern but that the agency wished to evaluate the relevance of ethylene chlorohydrin (ECH), a potential residue of EtO application in spices. ASTA either had to show that ECH was not carcinogenic or reduce ECH residues.

As the costs of studies related to carcinogenicity tend to be extremely high, ASTA opted to find a way to measure and reduce ECH residues.

Contributions were received from a number of companies in the spice industry, both ASTA members and non-members, to fund an extensive study to find ways to measure and reduce ECH residues. The study was completed and submitted to EPA on August 5, 2005, detailing a new treatment process that was found to substantially reduce residue levels of both EtO and ECH in treated spices. However, one concern remained for both ASTA and the EPA and that was the residue levels in basil which in both the 1994 and the 2005 studies was much higher than for any other treated spice.

aPAD and Basil

In determining acceptable residue levels, the Agency considers the acute dietary exposure as a percentage of the acute Population Adjusted Dose (aPAD). A dietary risk assessment of less than 100% of aPAD does not exceed the EPA's level of concern. This data is broken out over the population and particular attention is paid to the exposure levels of infants and children.

The first chart below shows the acute dietary exposure profile from ASTA's 1994 study using the treatment method typical at that time with the results clearly exceeding acceptable residue levels.

Traditional Treatment	**ECH**
General US Population	**230% of the aPAD**
Infants < 1 year old	**480% of the aPAD**
Children 1-2 years old	**650% of the aPAD**
Children 3-12 years old	**540% of the aPAD**
Youth 13-19 years old	**130% of the aPAD**
Adults 20-49 years old	**130% of the aPAD**
Females 13-49 years old	**160% of the aPAD**
Adults 50+ years old	**120% of the aPAD**

The next chart demonstrates the results using the improved treatment process that was developed by ASTA for submission in the 2005 study, and while the results are within acceptable limits for some areas of the population, the overall numbers are higher because of the calculated potential exposures in infants and children. Infants and children may consume spices such as basil through eating foods such as pizza and because of their much lower body weight, increased potential exposures may be calculated.

*Improved Process	ECH
General Population	**120% of the aPAD**
Infants < 1 year old	**160% of the aPAD**
Children 1-2 years old	**330% of the aPAD**
Children 3-12 years old	**250% of the aPAD**
Youth 13-19 years old	**140% of the aPAD**
Adults 20-49 years old	**80% of the aPAD**
Females 13-49 years old	**64% of the aPAD**
Adults 50+ years old	**36% of the aPAD**

* Based on second ASTA study

The residue limits in basil were focused on as the risk driver in the Agency's dietary risk analysis. As the numbers below demonstrate, if basil is excluded, the aPAD drops into an acceptable range for all remaining spices.

*Improved Process – W/out basil	ECH
General Population	**36% of the aPAD**
Infants < 1 year old	**61% of the aPAD**
Children 1-2 years old	**96% of the aPAD**
Children 3-5 years old	**63% of the aPAD**
Children 6-12 years old	**37% pf the aPAD**
Youth 13-19 years old	**31% of the aPAD**
Adults 20-49 years old	**25% of the aPAD**
Females 13-49 years old	**27% of the aPAD**
Adults 50+ years old	**20% of the aPAD**

* Based on second ASTA study

ASTA engaged in discussions with the EPA on the best way to proceed. The options were either to drop basil from the label and no longer allow EtO treatment for basil or

risk losing EtO for all spices. It was agreed that EtO was important enough for the spice industry that its usage on basil should be eliminated in an effort to preserve usage for other spices.

The EPA agreed with the request to allow EtO treatment of basil to continue through July 30, 2007. At that time, existing stocks could be used for up to 120 days before EtO use on basil was discontinued. Other treatment options are now required for basil. As part of these discussions with EPA it was agreed that if refinements can be made to the process to reduce residue levels in basil, ASTA could ask the EPA to reconsider EtO's use in the future.

Worker Exposure

Occupational concerns were first raised as an issue in 1978. Most recently in the RED concerns have been raised with both the spice industry and the medical device industry regarding long-term non-cancer risks as well as cancer risks. ASTA submitted study data related to workplace exposure to address the concerns raised by the Agency.

ASTA Activities

ASTA's position is that all reasonable efforts should be made to assure the continued availability of this important health protection tool with minimal, acceptable limitations and regulatory restraints.

For over ten years ASTA has worked with the EPA by submitting numerous comments, meeting with EPA staff, suggesting wording for labeling, and providing extensive scientific data, including the study that explains the new treatment method. A great deal of time and effort has gone into providing information and data and ensuring that the EPA understand the necessity of EtO to both the spice industry and as a health protection tool.

Additional comments were submitted in June 2006 related to the reregistration because EPA sought more information related to dietary exposure and occupational exposure.

Without ASTA's expertise, verbal and written input and new treatment method, it is very likely that EtO would not be available for the spice industry today.

Status

The EPA issued its Reregistration Eligibility Decision (RED) for ETO on April 16, 2008. It can be found under the Federal Register listings at http://www,epa.gov/fedrgstr.

ASTA supports the recent FQPA TRED as proposed by the EPA, including the tolerances specified for EtO of 7 ppm on spices and 7 ppm on dried vegetables, as well as the ECH tolerances of 940 ppm on spices and 940 ppm on dried vegetables.

ASTA proposed use directions for the EtO label that would assure consistency in residues from treatment and has asked the EPA to allow other treatment methods if they are able to demonstrate similar acceptable residue levels. The recommended use directions were accepted for the label and they take effect on August 1, 2008. ASTA's specific use directions are:

"Place spices in the treatment chamber. Assure that the mixture of ethylene oxide and air is compatible with the chamber design, then, introduce into the chamber a concentration of Ethylene Oxide not to exceed 500 mg/L, with a dwell time not to exceed 6 hours. Then evacuate the gas from the chamber using a sequence of not less than 21 steam washes (injections and evacuations) between 1.5 PSIA (27" Hg) and 5.0 PSIA (20" Hg) while maintaining a minimum chamber temperature of 115°F."

Effective August 1, 2008, any spices treated with ETO in the U.S. must be treated using the process detailed on the label. New treatment processes will be considered for approval by the Agency as long as the residues are below the tolerances.

If product is treated outside the U.S. the product being imported must meet the new tolerances for EtO of 7 ppm on spices and 7 ppm on dried vegetables, as well as the ECH tolerances of 940 ppm on spices and 940 ppm on dried vegetables. These tolerances must be met for all spices, even if they are to be added to a spice blend prior to shipping to the U.S.

While the RED has been issued, the EPA has indicated that the decision is contingent upon a new request for reproductive and developmental studies to be conducted to address data gaps on the toxicity of ECH residue. A waiver request was submitted citing data that was available through studies that have already been conducted. The Agency denied the waiver and decisions are pending on the next steps in developing the requested data. Additional data was submitted and the Agency agreed to the waiver request for the prenatal developmental toxicity study. The reproduction and fertility effects study is pending.

For more information on ASTA activities:
Recent comments submitted to the EPA
http://www.astaspice.org/members/regulatory/ETORevisedRiskAssessment.PDF

Useful Websites for Additional Information about EtO
Office of Pesticide Programs (OPP) at the EPA
http://www.epa.gov/oppad001/index.htm

Agency for Toxic Substances and Disease Registry (ATSDR)
ATSDR@CDC.gov

Occupational Safety and Health Administration (OSHA)
www.osha.gov/SLTC/ethyleneoxide/

U.S. Department of Health and Human Services, National Toxicology Program
http://ntp-server.niehs.nih.gov/