In the United States clothianidin was given a conditional registration by the EPA in 2003. Originally approved for use as a seed coating on corn and canola, it is now being approved for a growing list of other crops as well.

February 2003: EPA calls for lifecycle study prior to registration & for strong labeling language.

The memo of interest is buried in several others. Scroll down to page 6 to see the beginning. It is here that EFED scientists call for a life cycle study before registration, and strong label language should it be registered. Toward the end of the second paragraph the concerns about bees are listed and further down the field test is called for.

Memo #1: EPA Risk Assessment for clothianidin seed treatment (Poncho)

> "Considering the toxicitiy profile and reported incidents of other neonicotinoids (e.g. imidacloprid), the proposed seed treatment with clothianidin has the potential for toxic risk to honey bees, as well as other pollinators. As a result of this concern, EFED is asking for additional chronic testing on bee hive activity.
>
> The possibility of toxic exposure to nontarget pollinators through the translocation of clothianidin residues that result from seed treatment (corn and canola) has prompted EFED to require field testing that can evaluate the possible chronic exposure to honeybee larvae and the queen. In order to fully evaluate the possibility of this toxic effect, a complete worker bee life cycle study (about 63 days) must be conducted, as well as an evaluation of exposure to the queen."

April 2003: EPA reconsiders, allows conditional registration contingent upon the field study.

In the opening paragraph the concerns about bees are again emphasized and a strong label caution is recommended. I don't believe the label caution has ever been included. Then there is the "after further consideration", and EFED agrees to a conditional registration. The condition is the field study, what comes to be called the chronic life cycle study. It is to be completed by December of 2004, but clothianidin goes on the market in the spring of 2003.

Memo #2: EPA Addendum to Feb '03 risk assessment

> "Since this compound is persistent (field dissipation ½ life = 277 – 1,386 days), toxic to honeybees, and has the potential for expression in pollen and nectar of flowering crops, EFED also concluded that there was a potential for long term toxicity to these pollinators. The possibility of toxic chronic exposure to nontarget pollinators through the translocation of clothiandidin residues in nectar and pollen has prompted EFED to require field testing (141-5) that can help in evaluating this uncertainty. In order to fully evaluate the possibility of this long term toxic effect, a complete worker bee life cycle study must be conducted, as well as an evaluation of exposure to the queen. Because of this concern, EFED suggested that the following honeybee label statement be included:
>
> > *This compound is toxic to honey bees. The persistence of residues and the expression of clothianidin in nectar and pollen suggests the possibility of chronic toxic risk to honey bee larvae and the eventual stability of the hive.*
>
> **However, after further consideration, EFED would like to suggest that the registrant be given conditional registration that is contingent on their conducting the chronic honey bee study that evaluates the sublethal effects of clothianidin to the hive over time.** EFED will therefore defer the requirement for this bee labeling statement until after the chronic study has been reviewed. In order

to cover poignant endpoints and objectives, the honey bee study should evaluate the effects of clothianidin to the hive over time and should include but not necessarily be limited to the following criteria:

a) an evaluation of two complete life cycles (~130 days), including egg, larvae, adult stages, and mortality of the honey bee colony;

b) an evaluation of the exposure and effects to the queen during these life cycles;

c) provide clothianidin residue analysis of the stored nectar, honey, and pollen at the beginning of the study, at periodic time intervals during the study and at the end of the study; and

d) the study must include replicated data with statistical comparison to controls.

[To be completed by December 2004]

March, 2004: Bayer gets an extension, EPA agrees to study design changes.

Memo #3:

Bayer asks for an extension on the deadline and is granted until May of 2005. It is in this memo that corn is dismissed with a single sentence and the study is allowed to take place in Canada on canola. Earlier EFED scientists had said that any testing done should occur in the U.S. Corn pollen had been the vector in huge bee losses just a few years before during the years of damage from encapsulated parathion.

November, 2007: EPA finally reviews the field study, finds it "acceptable."

Memo #4: EPA's review of the field study. It was a year late after the deadline extension, completed August, 2007. The EPA did not review it for 15 months, then in the spring of 2008 stonewalled for several months and claimed not to have it. This is the study the NRDC ultimately sued for. Read down to page 5 Submission Purpose. The field study was a condition of registration.

Study issues:

- *Bees likely foraged on control & other non-treated forage crops ::* Treated and control fields were separated by at least 250m. Although potential forage crops were within 1 km of some fields, none were in bloom (p. 31). Bees forage distances between 2km – 10km.
- *Canola, not corn was studied :*: see release for explanation.
- *No over-wintering data ::* The subsequent over-wintering data were not sound & raw data were unavailable for scrutiny. "Data presented …were not collected in accordance with GLP requirements, and raw data were not submitted." (p.30)

November 2010: EPA downgrades the field study upon which the conditional registration was granted from "acceptable" to "supplemental." A new study is needed.

Memo #5: EPA Review of Bayer's registration request for Clothianidin uses on cotton & mustard

Canola & corn aren't at issue in this memo – of interest is the downgrading of the core field study from scientifically "acceptable" to "supplemental" because that study did not satisfy guideline requirements.

(p.2) **Clothianidin's major risk concern is to nontarget insects (that is, honey bees).** Clothianidin is a neonicotinoid insecticide that is both persistent and systemic. Acute toxicity studies to honey bees show that clothianidin is highly toxic on both a contact and an oral basis. Although EFED does not conduct RQ based risk assessments on non-target insects, information from standard tests and field studies, as well as incident reports involving other neonicotinoids insecticides (e.g., imidacloprid) suggest the potential for long term toxic risk to honey bees and other beneficial insects. An incident

in Germany already illustrated the toxicity of clothianidin to honeybees when allowed to drift off-site from treated seed during planting.

A previous field study (MRID 46907801/46907802) investigated the effects of clothianidin on whole hive parameters and was classified as acceptable. However, after another review of this field study in light of additional information, deficiencies were identified that render the study supplemental. It does not satisfy the guideline 850.3040, and another field study is needed to evaluate the effects of clothianidin on bees through contaminated pollen and nectar. Exposure through contaminated pollen and nectar and potential toxic effects therefore remain an uncertainty for pollinators.

EFED expects adverse effects to bees if clothianidin is allowed to drift from seed planting equipment. Because of this and the uncertainty surrounding the exposure and potential toxicity through contaminated pollen and nectar, EFED is recommending bee precautionary labeling.

(p. 16, under "Data Gaps and Uncertainties")
Honey Bee Toxicity of Residues on Foliage (850.3030): This study is required for chemicals that have outdoor terrestrial uses in which honeybees will be exposed and exhibit an LD50 < 11µg a.i./bee. The study that was submitted to satisfy this guideline is supplemental but does not satisfy the guideline requirement. This study is not required for this assessment due to the lack of exposure to residues on foliage from the seed treatments. This study is placed in reserve pending future new uses.