

031301

(2)

Memorandum of Conference

8/8/79

H. J. Vostral

Upjohn Co.

M. J. Nelson

HED/RCB

T. McLaughlin

"

The above representative from Upjohn met with RCB to discuss Botran metabolism. In particular, Upjohn has submitted a protocol for a repeat goat metabolism study and wants RCB to review and comment on its applicability to resolve certain deficiencies found in the initial study.

In our letter to Upjohn of 3/5/79, we stated that since 90% of the radiolabeled material transferred to goat milk in the initial study is unidentified, further work would be necessary, such as an attempt to release bound conjugates by enzyme, acid, or other hydrolytic methods. Possibly 90% unidentified portion could be categorized by the fraction that is ring-opened and the fraction that is bound by conjugates. Also, the presence of any azobenzene compound(s) was to be determined. Furthermore, we required the results of tissue analyses to determine secondary transfer of residues to meat.

Dr. Vostral, in presenting the protocol for a repeat goat metabolism study (see Botran study file), stated that radiolabeled Botran with a higher specific activity than originally employed had been prepared. This should facilitate the isolation and identification of the unidentified portion in goats milk. The protocol submitted was also designed to address the other deficiencies as stated above.

We agreed to review the protocol and respond in writing to Upjohn with our comments concerning the applicability of the protocol towards resolving the deficiencies outlined above.

T. McLaughlin, Ph.D.

TS-769:RCB:T.MCLAUGHLIN:sdb:X77484:RM810:CM#2:8/10/79
cc: Botran SF, Quick, McLaughlin, RF, PM-21
RDI:MJN:8/8/79:J.G.CUMMINGS:8/9/79

Upjohn Co
1023-36

Botran 75W

3F1365

2,6 - Dichloro-4-Nitroaniline

5/24/73

Use - Post-harvest decay by *Rhizopus* and *Monilia* rot

Apply only with fruit wax.

Use flat-fan or flood jet nozzles to uniformly

spray fruit during packing line operations.

Collect spray run-off in a drain tray and

Petition seeks to amend Reg. 1023-36 by

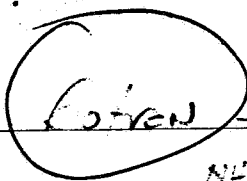
- ✓ 1) increasing tolerance of Botran from 1 ppm to 5 ppm
in order to allow post harvest as well as pre-harvest
treatment
- ✓ 2) and repeal the 15 ppm tolerance for *Monilia*
(no longer registered)

NAC 10/26/73 JWA

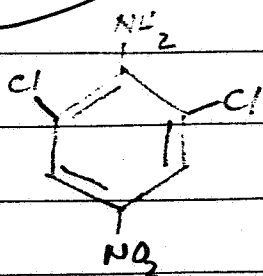
Res - Botran appears to be persistent and stable.

70-15 data will be needed when new field data is required

Akers - Should consider reproductive toxicity data
when proposed new data is



Cloren - Allisen, DCNA, dichloran, U-2000



molecular wt 207.0

Solubility - practically insoluble in water

Stability - stable to hydrolysis and
relatively stable to oxidation

Safety and Toxicological Studies - Synopsis & previous submitted data.

- 1) Rat - metabolism studies have shown Cloren to be
(1962) rapidly absorbed, metabolized and excreted in rats. Not stored in any body tissue.

Metabolized to three metabolites

90% 3,5-dichloro-4-amino phenylacetic acid
or 3,5-dichloro-4-aminophenylacetic
caproic acid.

5% 3,5-dichloro-4-aminophenol

5% 3,5-dichloro-4-aminophenyl
glucuronide

- 2) Rat - chronic (104 weeks)

Dietary adm 3000, 100, 20 ppm

No effects (with certainty) at 20 and 100 ppm.

3000 ppm red effects - result of ...

Conit Butran - Toxicology

3. Dog - chronic (104 weeks). (1964)

Adm 20, 100, 3000 ppm

No effects 20 and 100 except vascular hepatic

cell size in 2/6 at 100 ppm and of

gall bladder change in 1/6 at 20 ppm.

3000 ppm - liver changes, enlargement of vessels

4. Cat - subacute

20 and 80 ppm in diet 28-30 days

No adverse effect

No detectable levels of Conit Butran in

liver, kidney, muscle, fat or bone.

5. Dairy cow - range finding

Dosage levels = 100 and 50 mg/kg/day
for five days

100 mg/kg/day

mucoid secretion from vagina } death for each cow w/ 48 hr of
rectal bleeding, lacrimation, } the first dose.
polydipsia, polyuria

50 mg/kg/day

- all cows survived, but showed behavior

and extreme symptomatology

The effects on
cattle should
be more closely
examined when
new cases are proposed.
Jen