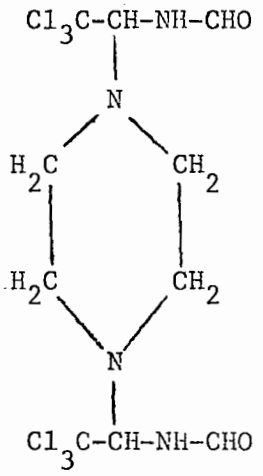
JASHAUGHNESSY:PH: 11-7-72

Preliminary Evaluation of New Chemical
Temp. Permit - FUNGINEX - Submitted by
EM Labs (Cela-Merck) 2-18-72, 3-1-72,
5-1-72, and 9-12-72 (later)

Identity Chemical name (per Loening of CA) is N,N'-[1,4-piperazinediylbis (2,2,2-trichloroethylidene)] bis [formamide]

Proposed common name is triforine
Other names are FUNGINEX, CA 70203, Cela W524



Background In our last letter (5-23-72) (OBJ) we asked for:

1. Mfg. process
2. Storage stability data
3. % comp. tech
4. Soil persistence data
5. Evidence that CA name is being used. We also stated that registration would require:

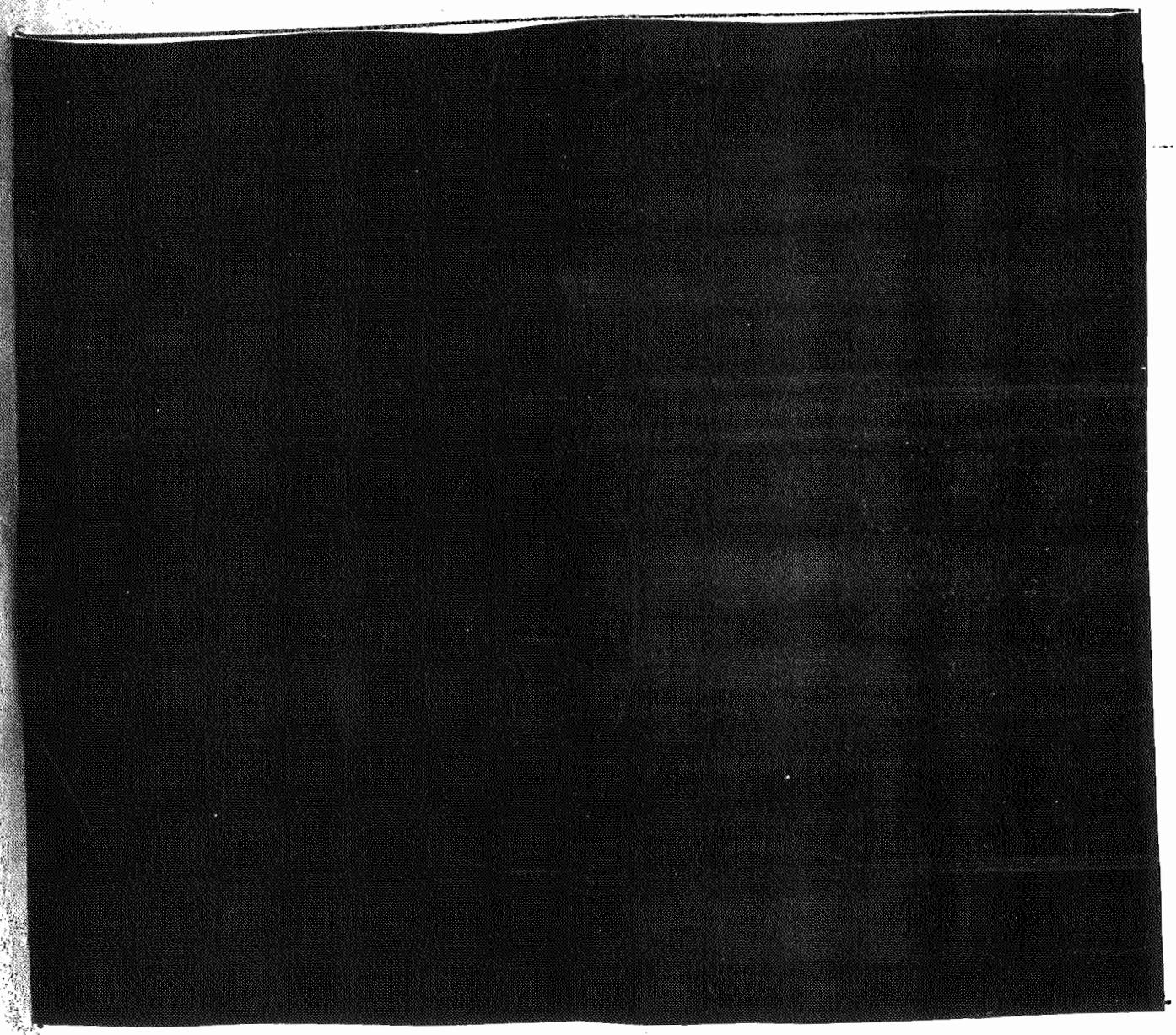
   (a) PR 70-15
   (b) Analytical methods for impurities & a.i.

   Note: My request for analytical standards and confidential formula were ignored - i.e., they were not sent out. See my previous evaluation.

Latest Submission (Label still calls for use on ROSES only)

1. Mfg. process

MANUFACTURING PROCESS INFORMATION IS NOT INCLUDE



2. Storage Stability Data

20 EC was stored for 1 year with these results:

Temp	% claim remaining
6°C	95%
22°C	86%
30°C	78%

This is NOT ACCEPTABLE for usual registration. We told the Cela-Merck this when they came in. They are working on the problem, but I think we can grant a temp permit.

3. % composition of tech chemical

They claim the tech chemical assays at 99 ± 2%. The only contaminants detected are:

[redacted]

Impurities information is not included.

This is not very good. They can do better.

4. Soil persistence data

Outdoor study in Germany --

Ingelheim sand, Schwabenheim loam, Alsenzloam

Plots: 1 sq. meter
Dose: 0.5 g act per sq. meter
Date of applic: June 16, 1971
Samples at 0 days, and 1,3,6,9,12,20 weeks later
Method of anal: GLC (really measures chloral hydrate)

Residues of a.1. (parent) decline from 2 ppm at 0 days to 0.2 ppm at 20 weeks.

Comments: Not a complete study. Not radiolabelled, no idea of degradation products, bound residues, etc. However, I think we can go ahead with a temp permit while telling them that registration will require the type of study outlined in our Guidelines.

5. CA name:

They submit a letter from Dr. Loening of CAS, giving the name as:

N,N'-[1,4-piperazinediylbis(2,2,2-trichloroethylidene)]bis[formamide]

For 70-15 data, they submit a leaching study, a study on FUNGINEX its influence on aerobic soil activity, and stability of aqueous solutions at different light conditions.

Leaching study

Laboratory; 3 soils: low organic loam, medium organic loam, and sand (high organic)

Columns: 5 cm dia X 30 cm

Soil Saturated:
dose: ⇨ 1 liter of 20% formulation per hectare

1st test

Added 39 ml of water over 2 days.

2nd test

Added 98 ml of water over 5 days.

GLC method for parent cpd.

Results: No toxicant went further than the 5-10 cm soil depth. None detected in the drainage water.

This study does not meet the Guidelines (no control column, only 3 soil types, no TLC, no work in degradation products, no field leaching studies). Also no radioactivity study as required by Guidelines.

Influence of FUNGINEX on aerobic activity in soil

Treated-untreated sandy soil (5.2% organic matter)

Manometric method - detn. of oxygen consumption over 3 hour period.
Results claimed: No influence on biological balance of aerobic activities. The O_2 consumption of untreated and treated soils was essentially the same.

This may be OK but they have not done the Anaerobic Metabolism Test in the Guidelines.

Stability of aqueous solutions

A 30 ppm solution was made up. One test in dark. One in diffuse light (no sun, no UV).
Stored for 28 days.
Measured a.l. by polarograph
Results: life is about 7-8 days both in light and in dark.

This does not meet the requirement of the Guidelines, but it indicates breakdown in water; and sunlight has no effect.

Conclusions

The applicant has submitted most of what we asked for. Their representatives have come in for a discussion of what was needed (after this submission). We gave them a copy of the Guidelines.

I think we can grant the temp. tolerance with the following RL comments:

1. C-70 (submit analyt. stds)
2. The storage stability data are not acceptable for full registration.

We understand that you are working on a new formulation and/or labelling restrictions against extended storage.

3. The statement of percentage composition of tech. chemical is not sufficiently complete. We need a discription of each ingredient present at more than 0.1%.

4. Registration of this proposed use will require the submission of all PR Notice 70-15 data, as outlined in our Guidelines. The data submitted thus far are not completely acceptable because:

1. Soil persistence study does not follow Guidelines in that it is not a radiolabel study, there is no mention of degradation products, and no discussion of bound residues.

2. The leaching study departs from the Guidelines in that it used no control column, only 3 soil types, no TLC, no study on degradation products, and no field work. Also no radio-label study.

3. The anaerobic study is acceptable but we also need the Anaerobic Metabolism Test as described in Guidelines.

4. The "stability of aqueous solutions" report does not fulfill all Guideline requirements. There is no definition of the light source, no mention of degradation products, etc.

Note: I removed one copy of data for our files. Method for Bontoyan.