FC-143 AND APME

TOXICOLOGY RELATED ISSUES FROM 1995 TO PRESENT

01/13/1997

Roger G. Perkins
APME TOXICOLOGY COMMITTEE

■ DUPONT - GERRY KENNEDY
■ ICI-UK - DAVID FARRAR
■ AUSIMONT - GIUSEPPE MALINVERNO
■ HOECHST AG - REINHARD JUNG
■ MITENI - MARIO MISTRORIGO
■ 3M as invited guest - ROGER PERKINS

01/13/1997

Roger G. Perkins
APME TOXICOLOGY COMMITTEE MEETINGS

- IN BALTIMORE, MD MARCH 1995
- IN GENEVA AND BRUSSELS IN JUNE & OCTOBER 1995
- IN ANAHEIM, CA MARCH 1996
- PROPOSED 1997 MEETING

01/13/1997 Roger G. Perkins
APME TOX. COMMITTEE
INTEREST IN FC-143

■ COMPILe TOXICITY DATA
FOR Scientific Committee for Food

■ LIST OF ADDITIVES FOR
PLASTICS AND COATINGS
  - INCLUDES AMMONIUM
    PERFLUOROOCTANOATE
  - INCLUDES SODIUM
    PERFLUOROOCTANOATE
  » LIST 8 FOR SCF = substances for which
    no or only scanty and inadequate data were available

01/13/1997          Roger G. Perkins
APME TOX. COMMITTEE
INTEREST IN FC-143

- OUTLINE OF 3M DATA PER PTSS
- IDENTIFICATION OF DATA NEEDED
- 3M SCD COMMITS TO DOING STUDIES
- STUDIES COMPLETED AND ADDED TO PTSS
- STUDY NEEDS APPLIED TO FC-1090

01/13/1997
Roger G. Perkins
APME TOX. COMMITTEE
INTEREST IN FC-143

SCF GUIDELINES RE TOXICITY TESTS

- IF 5 < M < 60 MG/KG "FULL DOSSIER"
  » 90-DAY ORAL
  » 3 MUTAGENICITY STUDIES
    ■ GENE MUTATION IN BACTERIA
    ■ CHROMOSOMAL ABERRATION
    ■ GENE MUTATION IN MAMMALIAN CELLS
  » STUDIES ON ABSORPTION, DISTRIBUTION, METABOLISM AND EXCRETION

01/13/1997
Roger G. Perkins
APME TOX. COMMITTEE
INTEREST IN FC-143

SCF GUIDELINES RE
TOXICITY TESTS

- IF 5 < M < 60 MG/KG
CONTINUED

» DATA FOR REPRODUCTION
» DATA FOR TERATOGENICITY
» DATA ON LONG-TERM
TOXICITY / CARCINOGENICITY

01/13/1997

Roger G. Perkins
APME TOX. COMMITTEE
INTEREST IN FC-143

■ SCF GUIDELINES RE TOXICITY TESTS
  – IF $0.05 < M < 5 \text{ MG/KG}$
    » REDUCED EXCLUDES LAST THREE

■ SCF GUIDELINES RE TOXICITY TESTS
  – IF $M < 0.05 \text{ MG/KG}$
    » THREE MUTAGENICITY TESTS LISTED FOR “FULL DOSSIER”

01/13/1997Roger G. Perkins
3M SCD ACTIONS

■ FURTHER MUTAGENICITY TESTING
  – MOUSE MICRONUCLEUS
    14 MAY 96 REPORT DATE
  – CHROMOSOMAL ABERRATION
    25 APR 96 REPORT DATE

■ MEETING ON SCF TECHNICAL DOSSIER
  – NEED FOR EXTRACTION DATA

01/13/1997               Roger G. Perkins
APME TOX. COMMITTEE
ISSUES RE LONG-TERM DATA

■ MEMBER TOXICOLOGISTS DISCUSS

– 3M TWO YEAR FEEDING STUDY RESULTS
– DuPont TWO YEAR FEEDING STUDY RESULTS

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APME TOX. COMMITTEE
ISSUES RE LONG-TERM DATA

IDENTIFY OPEN ISSUES ON MECHANISM OF TUMOR FORMATION

- CONSENSUS THAT LEYDIG CELL MECHANISM IS EXPLAINED
- CONSENSUS THAT LIVER TUMOR MECHANISM IS EXPLAINED
- CONCERN THAT ACINAR PANCREATIC TUMORS MECHANISM NOT CLEAR

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APME TOX. COMMITTEE
ISSUES RE LONG-TERM DATA

- PROPOSAL FROM ICI-ZENECA
  - PREPARE PROTOCOL
    » TO OUTLINE METHODS FOR RESEARCH ON PANCREAS ACINAR CELL TUMORS
    » CONDUCT STUDIES OF EFFECTS OF FC-143 IN ACINAR CELLS

- PROPOSAL PRESENTED MARCH 1996
  - NO CONSENSUS, REQUESTED REVIEW

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3M RESPONSE TO APME TOX. COM ISSUES RE LONG-TERM DATA

■ 3M SCD ASKED FOR MORE TIME
  – FALL 1996

■ DUPONT DRAFT ARTICLE ON WYETH
  – 3M TOX. SUGGESTS AS METHOD FOR STUDYING MECHANISM OF PANCREATIC TUMOR FORMATION

■ DUPONT PROPOSES MONKEY STUDY
  – DECEMBER 1996 MEETING WITH CHW

01/13/1997  Roger G. Perkins
R. JUNG QUESTIONS 17 JUNE 1996

- CAS NUMBERS ON 3M FC-143 MSDS
- ANALYTICAL METHOD FOR SUBSTANCE IN BLOOD
- REVIEW OF EU R-40 LABEL CRITERIA
- CHROMOSOMAL ABERRATION ASSAY IN HUMAN VERSUS ANIMAL CELLS

01/13/1997 Roger G. Perkins
Tuesday, August 20, 1996

1a. Discuss and resolve if the MSDSs for FC-143, 118, 1006, etc. should list cas numbers found in EINECS for the branched isomers.

1b. Determine which structures cas number 3825-26-1 includes.

1c. Which structures are listed on TSCA, EINECS, etc.

01/13/1997
Roger G. Perkins
Tuesday, August 20, 1996

2. Provide Reinhard Jung the analytical method for determining level of perfluorooctanoic acid in employee blood. They want to start monitoring of their employees; R. Jung would pass information to their physicians. Discussion between J. Mandel and their physicians is also desirable.

01/13/1997 Roger G. Perkins
3. Review the criteria for use of R-40 EU label statement and determine if FC-143 and related products need such warning for irreversible damage.
4. Get chromosomal aberration assay in human lymphocytes started for FC-1090 which is the sodium salt of perfluorooctanoic acid and also get okay for the same study for FX-1006.
3M ACTION ON R. JUNG QUESTIONS

AUGUST MEETING CALLED BY SCD ST. PAUL

- DECISION THAT CAS NUMBERS ARE COMPLETE
- SCD SEeks CONFIDENTIALITY AGREEMENT FOR BLOOD ANALYSIS METHODS
- REVIEW INDICATES R-40 "POSSIBLE RISK OF IRREVERSIBLE DAMAGE" IS NOT WARRANTED
- STUDY ON FC-1090 IN HUMAN LYMPHOCYTES DONE

01/13/1997 Roger G. Perkins
PENDING ISSUES RE FC-143

- APME RELATED
  - STUDY OF MECHANISM OF PANCREATIC TUMORS
  - COMPLETE TOXICITY SUMMARY
    STARTED JOINTLY BY 3M AND DUPONT
  - COMPLETION OF SCF DOSSIER

- 3M DUPONT RELATED
  - MONKEY STUDY
  - RISK ASSESSMENT

01/13/1997

Roger G. Perkins
DYNEON INTEREST IN APME

DYNEON PERSON NOW IN APME

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