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JAN 29 1976

APCI CHEM. GROUP

LAW DEPT.

January 26, 1976

TELEPHONE
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No. 14

TO: All Members of PVC/VCM Mailing Lists

Ladies and Gentlemen:

The purpose of this letter is to keep you up to date on the regulatory situation as regards the Food and Drug Administration (FDA), Environmental Protection Agency (EPA) and the Occupational Safety and Health Administration (OSHA).

FDA

In our last letter we advised that we would attempt to bring you information as promptly as we could regarding any further moves towards resolution of the jurisdictional question between FDA and EPA, particularly with reference to PVC pipe. Only after Letter No. 13 went out did we learn so that we can now report that a "first meeting" was held on January 7, 1976 between high level groups from FDA and EPA. Although a number of different subjects were explored, the question of jurisdictional responsibilities for drinking water and water distribution systems was referred to a task force to be headed by Dr. Robert Angelotti of the Food and Drug Administration and Mr. Victor Kimm of EPA.

We are enclosing copies of two different memoranda on this conference, one prepared by Alan Levin of EPA (Enclosure 1), and one prepared by Sam Fine of FDA (Enclosure 2). Although not reflected in either of the memoranda, it is our understanding that Mr. Kimm suggested EPA might be prepared to acquiesce in FDA responsibility for "food additives" that might enter the water supply in light of FDA's greater expertise in this area. This is somewhat disturbing news but all it really means at this stage is that additional exploratory work and discussion is required. Along this line, we are planning to try to follow up on the activities of the newly designated task force as they relate to the jurisdictional

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problem, hopefully so that our views can be more forcefully made known. In any case, we will keep you informed as to any developments.

Not directly related to VCM/PVC matters but nevertheless a matter of some concern, was the Notice published in the Federal Register on January 12, 1976 proposing to withdraw approval of all of the New Animal Drug Applications for diethylstilbestrol (DES). The reason for our concern is that we have been informed by our contacts at the Bureau of Foods that they are worried about the way the Commissioner of Food and Drugs has stated, in the enclosed proposal (Enclosure 3), that, with regard to the sensitivity of an analytical method for DES it "must be both practicable, in the sense that it must be adaptable for use as a regulatory tool, and it must be sufficiently sensitive." As you will see, the Commissioner concluded that any method approved in accordance with Section 512(d)(1)(H) must at least be capable of detecting residues at a level that has been shown to be safe within the meaning of the Act. Then, the Notice states that "Data are lacking to justify the approval of any other analytical method(s) for detection of DES residues because no currently available method is capable of detecting residues at levels that have been shown to be safe within the meaning of the Act." On this basis he has, in effect, concluded that DES must be banned as an animal drug.

The law with respect to new animal drugs is not the same as that with respect to food additives. Nevertheless, the Commissioner has here set as a requirement for an analytical sensitivity for the detection of a carcinogen an assurance that it would detect the substance at a level shown to be safe within the meaning of the Act. Since the Act has sometimes been interpreted to legislate that carcinogenic food additives have no safe level, the application of a similar standard could lead to the adoption of the HRG position, i.e. PVC is made from VCM so some must get in, no level has been proven safe, ergo no data is acceptable to preclude a ban on the basis of the "no migration" concept.

Since some Staffers in the Bureau of Foods have expressed concern about whether the DES action might have to

govern treatment of the polyvinyl chloride situation, we thought it would be advisable to bring this matter to your attention. At the same time, we urge you not to overreact on the basis of this information. The fact is that there are important distinctions between the two situations. Indeed, I so indicated last Friday in an informal talk I had with the Staff member most concerned. In so doing, the following distinguishing features were called to his attention:

1. I pointed out with some vigor that it should be more difficult for the Commissioner to go the DES route as regards polyvinyl chloride in light of the willingness of the Occupational Safety and Health Administration (OSHA) and the Environmental Protection Agency (EPA) to at least implicitly accede to the existence of a "safe level" by the adoption and proposal, respectively, of their Standards.
2. I reminded him that, while all New Animal Drugs have to be specifically approved to be legally marketed, a potential indirect food additive need not even be cleared if there is no reasonable expectation of migration and the burden of proving reasonable expectation of migration is on the Government.
3. I also reminded him that further toxicological work is being done and there is every reason to believe a no effect level will be shown at perhaps as high as 100 parts per million (As far as we are aware, Maltoni has had no problem with the rats he is feeding 3.3 mg/kg. of VCM), while DES has apparently been proven a carcinogen at a level as low as 6.5 parts per billion.

4. I further reminded the Staffer that the Commissioner has thus far recognized that there is a whole group of PVC applications where he has conceded the validity of a "no reasonable expectation of migration" posture and no data, or even language, has been filed to contest this view.

5. Finally, I pointed out that the animal drug regulations, like the pesticides provisions, speak in terms of a flat "no residue," rather than in the hard fought for "no reasonable expectation of migration" language of the Food Additives Amendment.

We hope the foregoing list of concepts advanced will have a helpful impact. The only other information I can pass along is that the Staff member involved told me that the Bureau now has a target date of "sometime next spring" for action on the PVC situation. I think I need not tell any of you that there is very little we can do to expedite the process--our having been advised that the data is still under scientific review. The fact that there will be some delay could conceivably be helpful since another Maltoni report is expected soon. This is not to gainsay the fact that we know many of you would like a prompt favorable decision so as to remove the cloud on PVC food contact products. We do have both points of view fully in mind but all we can really promise is that we will try to keep you informed about the shifting tides.

EPA

The VCM/PVC Producers Group met on January 23 and approved plans for an appearance at the Hearing scheduled for February 3, and for the preparation of Comments to be filed in connection with EPA's proposed rulemaking on vinyl chloride emissions. It has been determined that any statements at the

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Hearing should be general in nature. In addition to a discussion of specific points at issue, a recommendation for additional joint research programs sponsored by EPA, industry, and labor will be presented. With respect to the more detailed Comments which must be submitted by February 23, the various technical, legal, health and economic arguments are now being gathered for a timely, comprehensive written filing.

OSHA

In a previous letter we reported that OSHA was interpreting the definition of fabricated product so as to include resins with a residual vinyl chloride level low enough so that employee exposure at or above the action level without regard to the use of engineering controls could not occur. Another recent letter from the Department of Labor addressed to Mr. R. R. (sic) Wheeler, Jr., Union Carbide Corporation, repeats the same opinion, states that there are no plans to amend the vinyl chloride standard, and notes that a revised Program Directive is contemplated. Since the letter refers to other matters which could be of general interest we are, with the permission of Union Carbide Corporation, sending each of you a reproduction of the December 17, 1975 communication from the Department of Labor (Enclosure 4).

General

In previous correspondence we have also made reference to an article in Rolling Stone magazine. The B. F. Goodrich Company has now written to Rolling Stone to correct inaccuracies in the story. Again, as an item we think you will find worth having and reading, we are herewith transmitting a copy of what we feel is a very thorough analysis of major errors in the Rolling Stone story, the same having been sent to the publication by Thomas B. Nantz, Executive Vice President of the B. F. Goodrich Company (Enclosure 5).

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We are somewhat at a loss to know exactly how to characterize the news release issued by the American Chemical Society in connection with a paper published in the January,

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1975 issue of Analytical Chemistry. The paper by D. Hoffman, C. Patrianakos, and K. D. Brunnemann reports that vinyl chloride has been found in tobacco smoke. A copy of the ACS news release and Table II from the paper itself is attached (Enclosure 6).

The fact that ACS issued a general news release about this article and that it was picked up rather widely by the lay press is indicative of the public interest the Society sees in the entire vinyl chloride situation.

* * *

To end on one bright note, we are pleased to report that the California Assembly's Ways and Means Committee, at its hearings last Friday, January 23, on Assemblyman Carpenter's bill that would have permitted state regulation of PVC food packaging materials, voted 10 to 4 against the bill. In short, the defeat in Committee of this measure, the details of which were described in our last letter (No. 13), brings to an abrupt end another piece of threatening anti-PVC legislation; credit in this instance goes to the whole SPI Public Affairs Committee team, and especially to all those on the scene in California.

* * *

We shall continue to keep you as fully informed as possible on all these matters.

Cordially yours,



Enclosures

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

ENCLOSURE 1

SUBJECT: EPA - FDA Meeting Held on January 7, 1976

DATE: 12 JAN 1976

FROM: Alan Levin *Alan Levin*
Special Assistant for Water Supply & Pesticides

TO: Memorandum of Record

Participants

FDA

Sam D. Fine	Associate Comm. for Compliance
Sherwin Gardner	Deputy Commissioner
Terry Coleman	Associate Chief Counsel for Food
Robert Angelotti	Associate Dir. Compliance, Bur. Foods
Howard R. Roberts	Acting Director, Bureau of Foods
Robert M. Schaffner	Assoc. Director for Technology, Bur. Foods
Bob Lake	Reg. Coord. Staff Bureau of Foods
Gerard L. McCowin	Division of Food and Color Additives
Richard J. Ronk	Director, Div. of Food and Color Additives
John R. Wessel	Scientific Coordinator, Office of the Associate Commissioner for Compliance

EPA

William M. Upholt	Senior Science Advisor, Office of Water and Hazardous Materials
Alan Levin	Special Assistant for Water Supply and Pesticides
Andrew Breidenbach	Assistant Administrator for Water and Hazardous Materials
Christopher Little	Assistant General Counsel
Victor J. Kimm	Deputy Assistant Administrator for Water Supply

1. The purpose of the meeting was a get acquainted session for Commissioner Schmidt and Dr. Breidenbach and to explore areas of mutual interest to our two agencies. Commissioner Schmidt was unable to attend and Deputy Commissioner Gardner substituted for him.
2. Dr. Breidenbach made an opening statement indicating a number of areas where EPA and FDA regulatory responsibilities may overlap. Among these are:

- a. Pesticides that may contaminate food or feed.
- b. Pesticides which may also be drugs.
- c. Toxic Substances
- d. Domestic Water Supplies.

Dr. Breidenbach pointed out that relations between our two agencies have generally been good and have resulted in a number of interagency agreements, particularly in the area of pesticides. He indicated that he preferred to limit the discussion at this meeting to water supply.

- 3. Deputy Commissioner Gardner responded that he endorses the idea of an interagency agreement on water supply matters.
- 4. Mr. Kimm outlined the principal problems involving drinking water as they relate to FDA:
 - a. Enforcement of interstate carrier watering points;
 - b. Regulation by product or food additives (such as pipe);
 - c. Water supplies not covered by the Safe Drinking Water Act;
 - d. Bottled water
- 5. It was agreed that Mr. Kimm and Dr. Angelotti would take the lead to form a task force consisting of representatives of EPA and FDA to identify issues requiring top level decision in the area of water supply, with item 4b. above receiving the highest priority.
- 6. Additional task forces on other problems such as pesticides and toxic substances would be formed as needed.
- 7. There was mention made of the need for further consultation on regulatory philosophies. EPA indicated their increasing use of risk/benefit evaluation as a basis for regulation and expressed a need for a degree of understanding, if not agreement, between the regulatory agencies, especially FDA and EPA but eventually probably OSHA and CPSC as well. FDA indicated a willingness to discuss it further at a later date.

cc: Participants

January 7, 1976

MEMORANDUM OF CONFERENCE

ENCLOSURE 2

Present : EPA Participants:

Dr. Andrew W. Breidenbach, Assistant Administrator for
Water and Hazardous Materials
Dr. William M. Upholt, Senior Science Advisor, Office of
Water and Hazardous Materials
Alan Levin, Special Assistant for Water Supply and Pesticides
Christopher Little, Assistant General Counsel
Victor J. Kimm, Deputy Asst. Administrator for Water Supply

FDA Participants:

Sherwin Gardner, Deputy Commissioner
Sam D. Fine, Associate Commissioner for Compliance
John R. Wessel, Scientific Coordinator, Office of the
Associate Commissioner for Compliance
Terry Coleman, Associate Chief Counsel for Food
Dr. Robert Angelotti, Associate Director for Compliance,
Bureau of Foods
Dr. Howard R. Roberts, Acting Director, Bureau of Foods
Dr. Robert M. Schaffner, Associate Director for Technology,
Bureau of Foods
Bob Lake, Regulations Coordination Staff, Bureau of Foods
Richard J. Ronk, Director, Division of Food and Color
Additives, Bureau of Foods
Gerad L. McCowin, Division of Food and Color Additives,
Bureau of Foods

Dr. Breidenbach and his associates met with Deputy Commissioner Sherwin Gardner and members of the staff of the Food and Drug Administration in the Commissioner's Conference Room in FB-8 on January 7, 1976, as a follow-up to Dr. Breidenbach's letter of November 7, 1975, to Dr. Alexander M. Schmidt, Commissioner of Food and Drugs.

Dr. Breidenbach explained that he had just recently been appointed Assistant Administrator for Water and Hazardous Materials, and that he realized there were several areas of concern which require a close working relationship between EPA and FDA. He listed the following areas:

1. Water Supply - Interstate Carrier Program
2. Pesticides
 - a. Contamination of food and animal feed - setting of tolerances and action levels.
 - b. Pesticides as drugs for both man and other animals.

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3. Toxic Substances

Dr. Breidenbach referred to the current problem with PCB's and the new legislation now in the Congress on toxic substances. He said he was aware of the cooperation there has been in the past between Glen Sweitzer, Coordinator, Office of Toxic Substances, EPA and Mr. Wessel on problems dealing with toxic substances.

4. Philosophy of regulation

Dr. Breidenbach made reference to the generation of data on which regulations are based. He also called attention to EPA's publication in the Federal Register of December 24, 1975, under the new Safe Drinking Water Act, of National Interim Primary Drinking Water Regulations. He stated that Mr. Train was sending to FDA through Secretary Mathews an official communication on the work required by FDA on bottled drinking water as a result of the new EPA regulations. (Later during the meeting Dr. Upholt said that he meant, under term "philosophy of regulation," the kind of philosophy FDA follows due to the Delaney Clause of the Food Additives Amendment).

5. NCTR

Dr. Breidenbach referred to the cooperative program of the two agencies at Pine Bluff, Arkansas.

It was Dr. Breidenbach's view that the main concern at the moment for both agencies is the problem of water supply. He asked Victor Kimm to discuss the interface between the two agencies on this problem.

Mr. Kimm referred to the interchange of information required because of overlapping jurisdiction under the various laws administered by the two agencies. He noted the difficult judgments required on the problem of contaminants, such as chloroform in the water supply of New Orleans, Louisiana. He pointed out the impact of FDA's publication of its proposed regulation on PVC, which included the problem of migration of vinyl chloride from PVC pipe to water. The need for the public and the regulated industries to know who does what on the Interstate Carrier Program was emphasized by Mr. Kimm. He also referred to what he identified as "products problems."

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At Mr. Gardner's request, Dr. Angelotti reviewed for the EPA visitors FDA's concerns with water problems under both the Food, Drug and Cosmetic Act and the Public Health Service Act. Reference was made to the problems that arise when EPA applies the term "Use Prohibited" to water supplies, when there are administrative deficiencies or there is no standard. It was pointed out that in some instances where EPA has applied this designation, FDA has made a determination that the water is safe, and thus FDA allows it to go on interstate carriers, and further allows it to be used for manufacturing foods. Reference was made to the meeting held by Messrs. Fine, Angelotti, Nacewicz and McNamara with Mr. Kimm and other EPA staff members in June of 1975, where there was a discussion of the new authority granted to EPA under the Safe Drinking Water Act on control of water on interstate carriers. It was pointed out that under the old Public Health Service, where FDA had not been involved, there had been no concern with food additives in water (Mr. Kimm's "products problems"). The problem with PVC caused FDA to look at vinyl chloride migration to water; this logically could lead to FDA looking at liners for reservoirs, etc.

After Dr. Angelotti's review there was a general discussion, with a consensus being reached that there should be additional formal agreements between the two agencies to deal with problems caused by overlapping jurisdiction. It was agreed that the problems in the pesticide area would be handled by Mr. Wessel with the current EPA staff members that he has been working with. Mr. Wessel gave a brief review of the status of the agreements with EPA on pesticides. It was agreed that a task force would be set up, headed by Dr. Angelotti and Mr. Kimm, to deal with the water supply -- interstate carrier problems. It was agreed that at intervals of 2 to 4 months on an as-needed-basis, Dr. Breidenbach would telephone Mr. Fine to arrange for discussions at the Commissioner/Assistant Administrator level.


Sam D. Fine

cc: HF-1 HF-2 HFC-1 HFC-2 HFC-13(Wessel) GCF-1 GCF-1(Coleman)
HFF-300 HFF-1 HFF-400 HFF-302 HFF-330 HFF-330(McCowan)

SDFine:br:eh 1/9/76

AP00053914

**DEPARTMENT OF HEALTH,
EDUCATION, AND WELFARE**

Food and Drug Administration

[Docket No. 75P-0308]

MONSANTO CO.

Filing of Petition for Food Additive
Correction

In FR Doc. 75-30109, appearing at page 52427, in the issue for Monday, November 10, 1975, change the seventh line of the second paragraph to read as follows: "sidered in a draft environmental impact".

[Docket No. 75N-0003]

ELANCO PRODUCTS CO. ET AL

Diethylstilbestrol: Notice of Opportunity for Hearing on Proposal To Withdraw Approval of New Animal Drug Applications

The Food and Drug Administration (FDA) is proposing to withdraw approval of all outstanding new animal drug applications for use of diethylstilbestrol in animals used for food for human consumption on the ground that use of the drug results in residues that have not been shown to be safe within the meaning of the act and that render continued approval of the drug unlawful under the Delaney anticancer clause of the Federal Food, Drug, and Cosmetic Act. Holders of approved applications have until February 11, 1976 to submit requests for hearing in accordance with § 514.200 (21 CFR 514.200). Such requests should be identified with the Hearing Clerk docket number found in brackets in the heading of this notice.

BACKGROUND

Diethylstilbestrol (DES), a synthetic estrogen used by feeders of cattle and sheep as a growth promotant, has been shown to cause a statistically significant increase of cancer in female C₃H mice at the lowest levels at which it was tested, i.e., 6.25 parts per billion (ppb). In humans, a statistically significant relationship has been identified between the administration of DES to pregnant women and the appearance in daughters born of these pregnancies of a rare type of cancer—adenocarcinoma of the vagina.

Since 1938, any new drug for use in animals, just as any new drug for human use, has been required to be shown to be safe for its intended uses. Even before the enactment of the Food Additives Amendment of 1958 (sec. 409, Pub. L. 85-929, September 8, 1958, 72 Stat. 1785-1788 (21 U.S.C. 348)), FDA had interpreted this basic safety requirement as demanding proof that drugs intended for use in animals used for human food would not cause harm if ingested by humans.

DES was first approved for use in cattle feed in November 1954. A new drug application (NDA) for the drug was permitted to become effective on the basis of data demonstrating that, using the so-called mouse-uterine assay test, no residues could be detected in edible tissue

48 hours after withdrawal of DES. NDA's for DES implants in cattle became effective in December 1955, again on the basis of mouse-uterine assay data demonstrating "no residue" under the permitted conditions of use. Applications became effective for DES in feed for sheep and as implants for sheep in 1957 and 1959.

The current standards for approval of new animal drugs, set forth in section 512 of the act as added by Pub. L. 90-399, July 13, 1968, 82 Stat. 343-351 (21 U.S.C. 360b), include several criteria. In addition to requiring substantial evidence of efficacy, section 512(d) makes very clear that the sponsor of any animal drug has the burden of demonstrating that the drug is safe for humans if encountered in food produced from the animal, and causes no adverse effect to the animal. Section 512(d)(1)(H) imposes additional restrictions on the approval of animal drugs that have been shown to cause cancer. That provision requires that FDA shall refuse to approve a drug if the Commissioner finds that "such drug induces cancer when ingested by man or animal or, after tests which are appropriate for the evaluation of the safety of such drug, induces cancer in man or animal" This language is the codification in section 512 of the Delaney anticancer clause that was added to the act by the Food Additives Amendment of 1958.

In 1962, Congress enacted an exception to the anticancer clause. The focus of Congress at that time was so clearly on DES that this exception has ever since been known as the "DES clause." This exception, now also part of section 512(d)(1)(H) of the act, permits approval of the use of a carcinogen as a drug in animals only if the Secretary (by delegation under § 2.120 (21 CFR 2.120), the Commissioner of Food and Drugs) finds that:

... under the conditions of use specified in proposed labeling and reasonably certain to be followed in practice (i) such drug will not adversely affect the animals for which it is intended, and (ii) no residue of such drug will be found (by methods of examination prescribed or approved by the Secretary by regulations, which regulations shall not be subject to subsections (c), (d), and (h)) (of this section), in any edible portion of such animals after slaughter or in any food yielded by or derived from the living animals.

In accordance with the foregoing provision, FDA in 1963 approved methods for the measurement and identification of DES residues: the mouse-uterine method, which measures total estrogenic activity at 2 ppb, and the so-called "paper chromatography" method, which is incapable of differentiating DES from other estrogens at levels below 10 ppb. Originally codified under §§ 135g.26 (b) and (c) and 121.241 (e) and (f) (21 CFR 135g.26 (b), (c) and 121.241 (e), (f)), the approved methods published in Part 135 were recodified under Part 556 without substantive change by a regula-

tion published in the Federal Register of March 27, 1975 (40 FR 13802). These methods have remained in effect since 1963, although significant improvements in sensitivity and reliability of other analytical methods have occurred in the intervening years.

Since publication of the detection methods in 1963, numerous new animal drug applications (NADA's) for the use of DES have been approved by FDA. In each instance, the agency concluded that if, when used in accordance with the conditions of use prescribed in the labeling, DES residues could not be detected in edible tissue by the approved methods, the requirements of the law were satisfied. Experience with the use of DES and advances in detection methodology have demonstrated that this conclusion is no longer supportable.

Since their original approval, no data have been submitted by the holders of approved NADA's for DES that cast doubt on the finding that the drug causes cancer in test animals. Furthermore, radioactive tracer research studies using ¹⁴C-labeled DES, conducted by the United States Department of Agriculture (USDA), have shown that radioactive residues attributable to the use of DES can result even when the prescribed conditions of use are strictly followed, i.e., withdrawal 7 days prior to slaughter for DES in feed or implantation of DES 120 days prior of slaughter. See T. S. Rumsey et al., "Depletion Patterns of Radioactivity and Tissue Residues in Beef Cattle after the Withdrawal of Oral ¹⁴C-Diethylstilbestrol," *Journal of Animal Science*, 40(3): 539-549, 1975, and T. S. Rumsey et al., "Fate of Radioactive Carbon in Beef Steers Implanted With ¹⁴C-Diethylstilbestrol," *Journal of Animal Science*, 40(3): 550-560, 1975 (available for public examination at the office of the Hearing Clerk, Food and Drug Administration). These radioactive residues were at levels that are below the sensitivity of the previously approved methods and that have not been shown to be safe within the meaning of the act.

In 1972 and 1973, the FDA, acting on these reports (then unpublished) of residues discovered by the USDA in radioactive tracer studies, withdrew all approvals of DES for use in animals used for human food. These actions were challenged by sponsors of NADA's for DES and ultimately vacated by the United States Court of Appeals for the District of Columbia Circuit in *Hess & Clark v. Food and Drug Administration*, 495 F. 2d 975 (1974), and *Chemetron v. Department of Health, Education, and Welfare*, 495 F. 2d 995 (1974) on the ground that the notice of withdrawal of approval issued by FDA had not afforded the sponsors adequate opportunity to demonstrate the need for a hearing, as required by 21 U.S.C. 360b(e)(1).

Since the resumption of the use of DES following the Court of Appeals' reinstatement of the NADA's, residues have been found in samples of edible tissues (livers) taken from cattle presented for

slaughter. In a USDA objective sampling program of cattle slaughtered throughout the country, 11 residues were detected in 3,854 samples in 1974 using gas liquid chromatographic (GLC) methods. During the first 3 quarters of 1975, 35 residues were detected in 1,717 samples, indicating an increase in the percentage of samples containing DES residues from 0.41 percent to 1.45 percent. Two additional residues detected by USDA during the fourth quarter of 1975 in edible tissues of beef cattle are not included in the percentage calculation because the fourth quarter sample size is not yet known.

These calculations likewise do not include 17 additional DES residues found during 1974 and the first 3 quarters of 1975 in the USDA selective sampling program. This program samples on a non-random basis both animals presented for slaughter by raisers who have previously presented residue-carrying animals as well as animals that are suspected, on some other basis, of containing DES residues. In the selective sampling program, as would be expected, the incidence of residues is considerably higher.

Only 1 of the 35 residues detected in the USDA objective sampling program was at a level (greater than 10 ppb) that could have been both detected and identified as DES if the currently approved mouse-uterine and paper chromatography methods had been used. Furthermore, although FDA investigation of the causes of these residues indicates that several may have resulted from DES contamination of withdrawal feed or failure to follow the prescribed conditions of use of DES, a substantial number of the residues cannot be attributed to misuse.

In the face of these findings, it is clear that the central assumption underlying the previous approvals by FDA of DES for use in animals used for human food, i.e., that no residues would be detected when the drug was used in accordance with the currently approved conditions of use, is no longer valid. The currently approved methods for DES have been shown to be inadequate to detect significant residues. Residues being detected by other methods have not been shown to be safe within the meaning of the act. This showing was not previously required of the applicants since a common premise of all previous DES approvals was that no residues would occur. Moreover, since no level of DES residues has been proven to be safe within the meaning of the act, the Commissioner concludes that no new method for the detection of DES can now be approved pursuant to the 1962 exception to the anticancer clause.

INADEQUACY OF APPROVED METHODS

The Commissioner issued, in the Federal Register of March 27, 1974 (39 FR 11299), a proposal to revoke the approved methods for identification and measurement of residues of DES, and invited interested persons to comment within 30 days (extended 10 days to the close of business of May 6, 1974 by a

notice published in the Federal Register of April 25, 1974 (39 FR 14611)).

Sixteen comments were received on the proposal within the extended comment period: Six from manufacturers of DES, four from individuals, two from cattle industry organizations, two from cattle feeders, and one each from a citizens' association, and a scientific society. Eight additional comments were received after the comment period closed. Several comments supported the proposed revocation of the detection methods and urged the Commissioner to act to terminate the use of DES in food-producing animals, while other comments objected to the Commissioner's proposed action. None of the comments received supplied data or studies adequate to support the approval of any new analytical method(s), much less data or studies to demonstrate that the methods previously approved are adequate to detect residues of DES now known to occur.

All the comments may be seen at the office of the Hearing Clerk, Food and Drug Administration.

The comments received and the Commissioner's responses are discussed below.

1. Nine comments suggested that the official methodology might be an issue for a hearing rather than the subject of a revocation before a hearing.

The Commissioner notes that the designation of officially approved methodology does not independently require a hearing under the act. However, opportunity for hearing is required on the proposal to withdraw approval of the NADA's for DES, and any hearing held could include the issue of whether a practicable analytical method exists that is adequate to detect DES residues.

2. Eight comments stated that the use of DES was important to the revenue of cattle raisers and to the reduction of the cost of cattle production. Two comments stated that the revocation of DES approvals could affect consumer prices for beef.

The Commissioner notes that the economic importance of diethylstilbestrol to a particular industry or even its effect on consumer beef prices is not relevant to or determinative of the acceptability of detection methods offered to justify exception of the drug from the anticancer clause, nor is it relevant to the safety of residues resulting from the use of the drug.

3. Two comments stated that the present approved test methods for DES are adequately sensitive. One of these comments limited its claim of adequacy to the use of the drug in implant form. The other stated that the sensitivity of the present methods is sufficient because the radioactive tracer studies that showed residues below the limits of the mouse-uterine test were discredited in court proceedings arising out of the agency's previous efforts to withdraw approval of these NADA's.

The Commissioner concludes that neither the scientific data cited in the proposal nor any information provided by this comment establishes any difference

between feed and implant uses of DES with respect to the adequacy of detection methodology. The Commissioner further observes that, whatever the deficiencies of other detection methods, there has been no showing that the approved methods are adequate to justify continued approval of DES. Neither comment submitted or referred to data that show that levels of DES below the sensitivity of the approved methods are safe within the meaning of the act.

4. Two comments stated that final action on the revocation of methods proposal should await resolution of the proposal on sensitivity of the method published in the Federal Register of July 19, 1973 (38 FR 19225).

The Commissioner notes that despite continuing efforts of FDA since that proposal to determine appropriate criteria for levels of sensitivity, the complexity and scope of the scientific and legal issues have combined to prevent completion of a final regulation to resolve the issues of methodology. No final regulation based on the Mantel-Bryan procedure is anticipated within the next 6 months. The Commissioner has concluded that the public and FDA should no longer await final action on that proposal before resolving the status of DES.

5. One comment contended that the GLC method, coupled with mass spectrometry identification, was superior to the present procedures, but the comment did not state that these procedures would be adequate to detect DES residues or provide data to support their adequacy. Another comment, while opposing any action to revoke existing methodologies, urged that if present methods were revoked they should be replaced with the GLC method as the official method and claimed that this method is sensitive to 0.5 ppb. This comment did not provide any information or data to demonstrate that levels of DES below 0.5 ppb are safe within the meaning of the act. Another comment stated that the GLC method reliably detects residues of DES as low as 1 ppb and noted that information describing this method had previously been submitted with an NADA. This comment, too, failed to provide data showing that a sensitivity of 1 ppb is sufficient to meet the requirements of the act or to show that residues of DES below 1 ppb are safe within the meaning of the act.

The Commissioner acknowledges that the results of USDA's GLC sampling program supply part of the basis on which he is proposing to withdraw approval of outstanding NADA's for DES. These results clearly demonstrate that the currently approved methods for DES, i.e., the mouse-uterine method and the paper chromatography method, are inadequate. The Commissioner concludes, however, that no showing has been made that the GLC method, whether used alone or in conjunction with mass spectrometry, may be approved in their place.

6. One comment stated that the burden of proof to demonstrate the safety of

DES should rest with those who wish to market the drug.

The Commissioner concurs with this comment and notes that Congress has placed the burden on the applicant to demonstrate the safety of any animal drug (21 U.S.C. 360b).

7. Three comments referred specifically to the Gass study cited in the proposal to revoke the methods for DES: Gass, Coats, and Graham, "Carcinogenic Dose-Response Curve to Oral Diethylstilbestrol," *Journal of the National Cancer Institute*, 33:971-977, 1964 (available for public examination at the office of the Hearing Clerk, Food and Drug Administration). The Gass study found that 8.33 ppb DES caused cancer in test animals (C₃H mice). Two of these comments claimed that this finding was a "false positive," one of them suggesting that another test animal should have been used instead of the mice that were used. Neither of these two comments provided data to demonstrate that DES does not cause cancer at levels of 8.33 ppb. The third comment questioned whether the Gass study was statistically sound and quoted two scientists who drew from that study widely divergent conclusions as to the lowest levels of DES capable of causing cancer. This comment concluded that this disparity of scientific opinion means that the present data are inadequate to determine safe levels and supports a request for additional funds to conduct more studies.

The Commissioner is of the opinion that, in the absence of convincing scientific evidence that the Gass study was in error or that there is some level at which DES is not carcinogenic, the determination that DES is carcinogenic in C₃H mice at 8.33 ppb cannot be ignored. The Commissioner agrees that data are not adequate to establish the lowest level at which DES causes cancer in test animals. The Commissioner is aware of no evidence that a level of DES that does not cause cancer in test animals can necessarily be assumed otherwise to be safe within the meaning of the act. On the basis of data currently available, the Commissioner questions whether any of the available analytical methods for the detection of DES residues affords adequate assurance that residues below the level of detection are safe within the meaning of the act.

8. One comment stated that one possible solution to the method suitability issue that should be explored would be to discard the livers of animals treated with DES.

The Commissioner is of the opinion that whether or not specific edible tissues may be discarded is not material to determining the adequacy of a method to detect DES residues in those or other edible tissues. It has not been demonstrated, for example, that DES residues in the liver may not serve as an indicator of residues present, albeit at lower levels, in other edible tissues.

9. Two comments suggested that the basic question of whether DES repre-

sented a public health threat as a carcinogen remained unanswered.

The Commissioner notes that the carcinogenicity of DES has long been recognized by scientists, and concludes that FDA need not await demonstration of a danger to public health before enforcing the act's requirements that animal drugs be shown to be safe and that any cancer-causing drug be demonstrated to leave no detectable residues.

10. Other comments, which opposed the administration of DES to cattle or its presence in any foods, pointed out that the Canadian Government had excluded United States beef failing to bear USDA certification that the animal had never received DES, and expressed hope that FDA would move expeditiously to remove DES from the food supply.

Although these comments are not directly relevant to the adequacy of the previously approved DES detection methods, they do support the agency's issuing of this notice of opportunity for hearing on the withdrawal of approval of NADA's for DES.

11. One comment suggested that in enacting section 512(d)(1)(H), Congress intended that carcinogens could be used in food animals and obliged the Secretary of Health, Education, and Welfare to establish some method of analysis.

The Commissioner disagrees. Section 512(d)(1)(H) of the act prohibits the use of any carcinogenic animal drug unless the Secretary makes certain affirmative findings, including a finding that no residue of the drug will be found in edible tissue by officially designated methods. Congress did not intend the Secretary to designate a method when no adequate method was available. Rather, the act requires that an animal drug not be approved unless an adequate detection method can be designated. To be approvable a detection method must be both practicable, in the sense that it must be adaptable for use as a regulatory tool, and it must be sufficiently sensitive. The Commissioner concludes that any method approved in accordance with section 512(d)(1)(H) must at least be capable of detecting residues at a level that has been shown to be safe within the meaning of the act. Because no such showing has been made with respect to residues of DES well below the combined sensitivity of the currently approved methods, the Commissioner maintains that those methods can no longer serve as the basis for approval of the use of DES in animals used for human food.

The Commissioner intends to revoke these methods at the time of final action based upon this notice of opportunity for hearing. If no hearing on the proposal to withdraw approvals for the use of DES is required, either because FDA receives no request(s) for hearing or because any request(s) for hearing fails to demonstrate a genuine and substantial issue of fact requiring a hearing, the approved methods will be revoked simultaneously with the announcement

of that fact. If a hearing is held, the currently approved method will be revoked, and any replacement method(s) demonstrated to be adequate will be designated at the time the Commissioner issues a final order based upon the hearing record and the decision of the Administrative Law Judge.

PROPOSED ACTION

On the basis of the comments received in response to the proposal to revoke the detection methods for DES, the data cited in the March 1974 proposal, and evidence that DES residues continue to be found in edible tissues of animals slaughtered for human food, the Commissioner concludes that:

1. DES has been shown to cause cancer in test animals and has been associated with the occurrence of cancer in humans.

2. Residues of DES have been and are being detected in the edible tissue of animals at levels that have not been shown to be safe within the meaning of the act.

3. The authority conferred by section 512(d)(1)(H) of the act to approve methods of examination allows, but does not require, the Commissioner to designate a method.

4. Any method designated by the Commissioner pursuant to section 512(d)(1)(H) must be practicable and capable of detecting drug residues regardless of the route of administration used for a drug.

5. The approved methods for detection of DES residues in edible tissue are not adequate to demonstrate that, within the meaning of the act, no residues will be found when the drug is used according to the approved conditions of use.

6. Data are lacking to justify the approval of any other analytical method(s) for detection of DES residues because no currently available method is capable of detecting residues at levels that have been shown to be safe within the meaning of the act.

Therefore, under the Federal Food, Drug, and Cosmetic Act (sec. 512(e)(1), 21 U.S.C. 360b(e)(1)), the Commissioner proposes to withdraw approval of all existing NADA's providing for the use of DES in animals used for human food on the following grounds:

1. Information and data available since these applications were approved, together with earlier data reevaluated in the light of current scientific knowledge, demonstrate that DES is not shown to be safe for use as approved.

2. The anticancer clause in section 512(d)(1)(H) of the act is applicable.

This notice applies to all outstanding NADA's for the use of diethylstilbestrol in animals used for food for human consumption. All such applications now known to FDA are listed below by NADA number and by each applicant's name and last known address in FDA records. Copies of this notice are being forwarded by registered or certified mail to each of these known applicants. Notice to other applicants or holders of such NADA's whose identity is not known to FDA is given by this publication.



DES should rest with those who wish to market the drug.

The Commissioner concurs with this comment and notes that Congress has placed the burden on the applicant to demonstrate the safety of any animal drug (21 U.S.C. 360b).

7. Three comments referred specifically to the Gass study cited in the proposal to revoke the methods for DES: Gass, Coats, and Graham, "Carcinogenic Dose-Response Curve to Oral Diethylstilbestrol," *Journal of the National Cancer Institute*, 33:971-977, 1964 (available for public examination at the office of the Hearing Clerk, Food and Drug Administration). The Gass study found that 6.35 ppb DES caused cancer in test animals (C3H mice). Two of these comments claimed that this finding was a "false positive," one of them suggesting that another test animal should have been used instead of the mice that were used. Neither of these two comments provided data to demonstrate that DES does not cause cancer at levels of 6.25 ppb. The third comment questioned whether the Gass study was statistically sound and quoted two scientists who drew from that study widely divergent conclusions as to the lowest levels of DES capable of causing cancer. This comment concluded that this disparity of scientific opinion means that the present data are inadequate to determine safe levels and supports a request for additional funds to conduct more studies.

The Commissioner is of the opinion that, in the absence of convincing scientific evidence that the Gass study was in error or that there is some level at which DES is not carcinogenic, the determination that DES is carcinogenic in C3H mice at 6.25 ppb cannot be ignored. The Commissioner agrees that data are not adequate to establish the lowest level at which DES causes cancer in test animals. The Commissioner is aware of no evidence that a level of DES that does not cause cancer in test animals can necessarily be assumed otherwise to be safe within the meaning of the act. On the basis of data currently available, the Commissioner questions whether any of the available analytical methods for the detection of DES residues affords adequate assurance that residues below the level of detection are safe within the meaning of the act.

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The Commissioner is of the opinion that whether or not specific edible tissues may be discarded is not material to determining the adequacy of a method to detect DES residues in those or other edible tissues. It has not been demonstrated, for example, that DES residues in the liver may not serve as an indicator of residues present, albeit at lower levels, in other edible tissues.

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The Commissioner notes that the carcinogenicity of DES has long been recognized by scientists, and concludes that FDA need not await demonstration of a danger to public health before enforcing the act's requirements that animal drugs be shown to be safe and that any cancer-causing drug be demonstrated to leave no detectable residues.

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The Commissioner disagrees. Section 512(d)(1)(H) of the act prohibits the use of any carcinogenic animal drug unless the Secretary makes certain affirmative findings, including a finding that no residue of the drug will be found in edible tissue by officially designated methods. Congress did not intend the Secretary to designate a method when no adequate method was available. Rather, the act requires that an animal drug not be approved unless an adequate detection method can be designated. To be approvable a detection method must be both practicable, in the sense that it must be adaptable for use as a regulatory tool, and it must be sufficiently sensitive. The Commissioner concludes that any method approved in accordance with section 512(d)(1)(H) must at least be capable of detecting residues at a level that has been shown to be safe within the meaning of the act. Because no such showing has been made with respect to residues of DES well below the combined sensitivity of the currently approved methods, the Commissioner maintains that those methods can no longer serve as the basis for approval of the use of DES in animals used for human food.

The Commissioner intends to revoke these methods at the time of final action based upon this notice of opportunity for hearing. If no hearing on the proposal to withdraw approvals for the use of DES is required, either because FDA receives no request(s) for hearing or because any request(s) for hearing fails to demonstrate a genuine and substantial issue of fact requiring a hearing, the approved methods will be revoked simultaneously with the announcement

of that fact. If a hearing is held, the currently approved method will be revoked, and any replacement method(s) demonstrated to be adequate will be designated at the time the Commissioner issues a final order based upon the hearing record and the decision of the Administrative Law Judge.

Proposed Action

On the basis of the comments received in response to the proposal to revoke the detection methods for DES, the data cited in the March 1974 proposal, and evidence that DES residues continue to be found in edible tissues of animals slaughtered for human food, the Commissioner concludes that:

1. DES has been shown to cause cancer in test animals and has been associated with the occurrence of cancer in humans.

2. Residues of DES have been and are being detected in the edible tissue of animals at levels that have not been shown to be safe within the meaning of the act.

3. The authority conferred by section 512(d)(1)(H) of the act to approve methods of examination allows, but does not require, the Commissioner to designate a method.

4. Any method designated by the Commissioner pursuant to section 512(d)(1)(H) must be practicable and capable of detecting drug residues regardless of the route of administration used for a drug.

5. The approved methods for detection of DES residues in edible tissue are not adequate to demonstrate that, within the meaning of the act, no residues will be found when the drug is used according to the approved conditions of use.

6. Data are lacking to justify the approval of any other analytical method(s) for detection of DES residues because no currently available method is capable of detecting residues at levels that have been shown to be safe within the meaning of the act.

Therefore, under the Federal Food, Drug, and Cosmetic Act (sec. 512(e)(1), 21 U.S.C. 360b(e)(1)), the Commissioner proposes to withdraw approval of all existing NADA's providing for the use of DES in animals used for human food on the following grounds:

1. Information and data available since these applications were approved, together with earlier data reevaluated in the light of current scientific knowledge, demonstrate that DES is not shown to be safe for use as approved.

2. The anticancer clause in section 512(d)(1)(H) of the act is applicable.

This notice applies to all outstanding NADA's for the use of diethylstilbestrol in animals used for food for human consumption. All such applications now known to FDA are listed below by NADA number and by each applicant's name and last known address in FDA records. Copies of this notice are being forwarded by registered or certified mail to each of these known applicants. Notice to other applicants or holders of such NADA's whose identity is not known to FDA is given by this publication.

ENCLOSURE 4

U.S. DEPARTMENT OF LABOR
Occupational Safety and Health Administration
WASHINGTON, D.C. 20210

DEC 17 1975



KIM:LU
JAN 02 1975

R N WHEELER JR.

Mr. R. R. Wheeler, Jr.
Vinyl Chloride Resins Manager
Union Carbido Corporation
270 Park Avenue
New York, New York 10017

Dear Mr. Wheeler:

This is in response to your joint letter with Mr. John Whittlesey dated June 17, 1975, petitioning for modifications of the Exposure to Vinyl Chloride Standard, 29 CFR 1910.1017 (formerly 1910.93 recodified May 28, 1975).

There are no plans presently to amend the Vinyl Chloride Standard. A revised program directive is contemplated, although we are not certain as to the date it will be available. Please be assured that your comments and suggestions are greatly appreciated and they will be considered fully in the revision of the program directive. In the meantime, the following administrative decisions have been made:

1. 29 CFR 1910.1017(a) and (b)(6) Scope and application (2), (3) and (b) Definitions (6)

The standard defines a fabricated product as being one which is "made wholly or partly from polyvinyl chloride, and which does not require further processing at temperatures, and for times, sufficient to cause mass melting of the polyvinyl chloride resulting in the release of vinyl chloride."

"Release of vinyl chloride" means the release of an amount of vinyl chloride which would likely result in employee exposure at or above the action level without regard to the use of engineering controls. Products which can be classified as fabricated products are exempt from the provisions of the vinyl chloride standard. All other products are subject to the requirements of the standard. If the employer uses or manufactures a product which is not a fabricated product, he must initiate monitoring procedures. If the monitoring reveals that the employees are not exposed to vinyl chloride at or above the action level, the employer's operations will be exempt from the

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2.

provisions of the standard. However, if the monitoring reveals exposure at or above the action level, the employer must implement the procedures specified in the standard.

2. 29 CFR 1910.1017(b) Definitions (5).

The petition requests that the definition of "emergency" be revised to include specific examples, such as fire and explosion. We agree that the definition might well be expanded to include examples. Again, this matter will be addressed in a program directive and not as an amendment to the standard.

The definition of a "massive release" as being "greater than 100 parts per million (ppm)" found in the current Program Directive #200-35, will also be addressed in a revised directive. We agree that the 100 ppm should be changed.

3. 29 CFR 1910.1017(d) Monitoring (4) -

The intent of paragraph (d)(4) is that the employer shall be 95% confident that his monitoring result is within 25%, 35% or 50% of the actual value depending on the concentration. Therefore, an employer using a method which has proven vinyl chloride detection accuracy of 25% or less need take only one measurement regardless of the actual vinyl chloride monomer concentration. In concentration ranges where accuracies of 35% or 50% are required, the employer need take only one measurement if the method accuracy is less than the specified accuracy. With methods of unknown accuracy or having errors greater than the specified accuracy requirements, repeated measurements are necessary. In these cases, one may use the coefficient of variation (CV) as a parameter to judge whether or not a sampling procedure is adequate to meet the standard. The CV in percentage units is defined as the standard deviation of the method, times 100, divided by permissible exposure limit. The required CV of the procedure is obtained by dividing the required accuracy by 1.96 (Z value for 95% confidence). Thus, for accuracies of 25%, 35% and 50%, method CV values should be less than 12.8%, 17.9%, and 25.5% respectively.

3.

To repeat, there are no plans presently to amend the standard but your comments on monitoring will be considered in the program directive revision and also in future rulemaking where monitoring is a requirement.

4. 29 CFR 1910.1017(j) Training.

The standard does not specify a level of exposure to trigger training activities. Section 6(b)(7) of the Occupational Safety and Health Act of 1970 provides that employees shall be apprised of the nature of the hazardous substances with which they come in contact.

The evidence we have compiled on vinyl chloride has indicated that it is sufficiently hazardous to warrant training for all personnel who have any possibility of coming in contact with vinyl chloride. There is always the opportunity for accidents to occur and employees should be aware of the possible consequences. There has also been some indication that storage containers may yield high concentrations of vinyl chloride when opened after transporting.

Therefore, it is not likely that the training provisions will be amended. For those operations covered by the standard, training is a requirement.

5. 29 CFR 1910.1017(e), Signs and labels (4)

If there are situations where the blended polyvinyl chloride must be labeled yet contains less than 0.5 ppm residual vinyl chloride monomer, the following wording may be used:

BLENDDED POLYVINYL CHLORIDE (PVC)

CONTAINS TRACE AMOUNTS (0.5 ppm)

OF VINYL CHLORIDE.

VINYL CHLORIDE IS A CANCER-SUSPECT AGENT.

We hope that the above clarifications will satisfy your petition for modification and amendment of the vinyl chloride standard. As previously stated, there are no plans presently to formally amend the standard. There will be an addendum or modification of the Program Directive #200-35. Should you wish to discuss any matter further do not hesitate to contact me or members of my staff.

Sincerely,



Barry J. White
Associate Assistant Secretary
for Regional Programs

The B. F. Goodrich Company

500 SOUTH MAIN STREET • AKRON, OHIO 44318 • PHONE 218-378-2388

THOMAS B. NANTZ
EXECUTIVE VICE PRESIDENT

January 16, 1976

Mr. Jann S. Wenner
Editor
ROLLING STONE
625 Third Street
San Francisco, California 94107

Dear Mr. Wenner:

We have read with considerable interest the article, "The Plastic Coffin of Charlie Arthur", in your January 15 issue. Because of the seriousness of this subject, we believe your readers are entitled to know the facts in regard to several inaccuracies in this story.

The article contains errors of fact and omissions but, more importantly, it accuses B.F. Goodrich officials of trying to cover up a critical problem. The fact is, Goodrich moved swiftly and openly to solve this problem. The following corrections of some of the more important inaccuracies indicate the flaws in your article.

ITEM: "Maltoni was working for a group of European chemical manufacturers who wanted his findings kept secret. The American companies were all too happy to agree -- so for the year before the Goodrich announcement the companies covered up Maltoni's findings that vinyl chloride caused cancer." (Page 44, Col. 4)

FACT: In late 1972 companies in the Manufacturing Chemists Association were planning research studies to evaluate previous findings that rats subjected to massive exposures to vinyl chloride in air (30,000 parts per million), had developed tumors. It was learned that European manufacturers were sponsoring similar studies in Italy. Representatives of American companies visited Dr. Cesare Maltoni in Bologna in January, 1973, to learn about his program. At that time Maltoni told them that preliminary results had found cancer in some test rats. Maltoni's work at that time was not complete enough to reach firm conclusions.

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Mr. Jann S. Wenner
San Francisco, California
January 16, 1976

U.S. government scientists knew of Maltoni's preliminary results early in 1973 but considered them to be as preliminary as did U.S. industry. Umberto Saffiotti, associate director of carcinogenesis at the U.S. National Cancer Institute, attended a symposium at Bologna, Italy, April 9 to 12, at which Dr. Maltoni showed a table giving preliminary results linking vinyl chloride with cancer in rats.

On April 17, 1973, members of the Manufacturing Chemists Association asked the European sponsors of Maltoni's work to make joint presentations to U.S. and European governments. The U.S. National Institute of Occupational Safety and Health (NIOSH) set up a meeting for July 17. One European and four U.S. industry representatives presented NIOSH information that malignant tumors had been found in animals exposed to vinyl chloride. At that time no human cancer cases had been reported, Maltoni's studies had not been completed and he had not issued a full report.

ITEM: The story reports that Dr. Peter Infante, then of the Ohio Department of Health, had found that three Northern Ohio communities with polyvinyl chloride plants had higher than average birth defects. (Page 45, Col. 2)

FACT: Dr. Infante, in his report to the New York Academy of Science, stated that there is not sufficient evidence to link vinyl chloride to birth defects.

The Center for Disease Control of the U.S. Public Health Service, in its weekly Mortality and Morbidity report for July 19, 1975, reports its own study of this subject. The report states that the study "could not establish any relationship between cases (birth defects) and vinyl chloride exposure."

ITEM: The story quotes a worker, only identified as "Harry", who charged that a supervisor had "pulled the plug" on a Goodrich plant monitoring system, so that work could continue during periods of higher exposure. The story correctly states that the company denied these charges. (Page 46, Col. 3)

FACT: First, Goodrich PVC plants have two monitoring systems -- a computerized area monitoring system, and personal monitoring systems. One backs up the other. OSHA requires that all records must be kept and made available to both federal inspectors and employees. It would have been very easy to verify Harry's allegation. A recent check of these records shows no gap.

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Mr. Jann S. Wenner
San Francisco, California
January 16, 1976

ITEM: The story quotes "other workers" as saying that when government inspectors visited our Ohio PVC plant, the company shut down most of the vinyl chloride lines, claiming that maintenance work was being done on them. (Page 46, Col. 3)

FACT: Under the OSHA inspection system, inspectors visit plants without prior notice, and therefore could arrive when maintenance operations are occurring. Since it takes some time to shut down and restart PVC reactions, this rumor is not only untrue, it just doesn't make sense.

ITEM: The ROLLING STONE story quotes a WALL STREET JOURNAL story of October 29, 1975 which reported that nine PVC workers at the Shawinigan plant of BFG Canada had died from angiosarcoma, "but the company had chosen not to make an official announcement." (Page 47, Col. 3)

FACT: The WALL STREET JOURNAL story, which itself resulted from a company announcement, states: Goodrich Canada announced in a news release last December that four cases of liver angiosarcoma had been uncovered from death records of former Shawinigan workers.... The U.S. parent company said in its annual report last spring that the Shawinigan angiosarcoma toll had climbed to eight deaths."

Only one of these men ever worked at the Shawinigan plant after it was purchased by Goodrich Canada. None of the rest were Goodrich workers, although the article said they were.

The WALL STREET JOURNAL also reported, correctly, that we had reported all these cases to the U.S. National Institute of Occupational Safety and Health. The cases also were reported to Quebec authorities and to all PVC employees in Canada. The Shawinigan release was carried in the U.S. by the Associated Press.

Since Joe Klein, your reporter, apparently had the WALL STREET JOURNAL story, we cannot understand his allegation that the company "chose not to make an official announcement."

ITEM: The report states that "...hearings were called on a proposed permanent standard of 1 ppm", and goes on to say that at the public hearings, the chemical manufacturers threatened that the whole industry would be forced to shut down if the standard was implemented. (Page 46, Col. 1)

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Mr. Jann S. Wenner
San Francisco, California
January 16, 1976

FACT: The proposed standard called for "no detectable" level of vinyl chloride in the work atmosphere, not 1 part per million on a time-weighted average as in the final standard. This may seem like a minute difference, but it is important in correctly reporting the industry's objection to the proposed standard. The proposed "no detectable" provision was ambiguous. If it had been interpreted as "no detectable" by any test method -- in other words, zero -- it would indeed have shut down the industry. Klein was at a Goodrich press briefing on December 4 when the industry position was explained in detail but he chose to ignore the explanation.

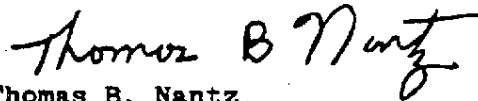
Just as important as these individual inaccuracies, however, is the overall impression created by the ROLLING STONE article. The article clearly implies that B.F. Goodrich executives, managers, and foremen conspired to suppress information relating to employees' health and then to prevent implementation of safeguards to resolve this most serious situation. This implication is unfounded.

Omitted from Klein's story are such facts as: Goodrich freely and voluntarily publicized its findings of the first angiosarcoma cases when they were discovered. The company supplied detailed information to employees, state and Federal officials and the industry. Goodrich has conducted the largest research program in its history, and is spending an estimated \$42,000,000 to prevent exposure to vinyl chloride in plants, in the environment and in products. The company has stated that it can operate within all present and expected regulations.

Klein sat in the front row at the press briefing where all these programs were explained in detail, and all questions fully answered, and he was given all supporting material to substantiate the open manner in which Goodrich has handled the entire matter. The fact that he did not choose to use any of this positive information is a clear indication of his lack of objectivity.

Yours very truly,

THE B.F. GOODRICH COMPANY


Thomas B. Nantz,
Executive Vice President

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NEWS SERVICE
1155 SIXTEENTH ST., N.W.
WASHINGTON, D.C. 20036
TEL. (202) 872-4460

FOR IMMEDIATE RELEASE

The first report of vinyl chloride, known to produce cancer in test animals and in humans, in mainstream cigarette smoke is detailed in the current (JANUARY) issue of Analytical Chemistry, a monthly publication of the American Chemical Society. In minute amounts, the vinyl chloride is formed during combustion and the amount is correlated with the inorganic chloride in the tobacco.

Revealing a new class of carcinogens in cigarette smoke and the first environmental appearance of vinyl chloride unrelated to its deliberate manufacture or use, this report raises the possibility that vinyl chloride and related substances, possibly cancer-causing, may be formed not only in burning cigarettes but also in other burning plant materials.

Drs. Dietrich Hoffmann of the American Health Foundation (AHF), Valhalla, N.Y. and Gio B. Gori of the National Cancer Institute, Bethesda, Md. are authors of the report, with AHF's Constantin Patrianakos and Klaus D. Brunnemann.

Charcoal filters were particularly effective in abstracting much of the vinyl chloride from the mainstream smoke of cigarettes, they say.

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The highest vinyl chloride concentration measured in the study was about 30 parts per billion in the smoke of a standard nonfilter cigarette or a "little cigar." This amount per cigarette is difficult to relate to the 50 parts per million (more than 1000 times more) that has been found to produce tumors via inhalation in test animals (number and length of exposures not specified). However, the significance, if any, of any added burden of the vinyl chloride to the already known load in smoke of polynuclear aromatic hydrocarbons, such as cancer-causing benz[a]pyrene, is not clear.

Although Dr. Hoffmann pointed out in a telephone interview that the amount of vinyl chloride measured in cigarette smoke is probably too minor to be a significant contributor to the known carcinogenicity of tobacco smoke, he acknowledged that vinyl chloride from burning tobacco does contribute to public exposure to the substance and that it conceivably could interact with other carcinogens in the environment to increase cancer-causing potency.

"Based on human data and results from animal studies, it appears to us that these minute amounts of vinyl chloride will not contribute to a measurable degree to the carcinogenic activity of tobacco," the authors write.

Vinyl chloride is widely used in manufacture of polyvinyl chloride plastics and has been labelled the cause of a high incidence of liver angiosarcoma in those who work with it.

The vinyl chloride content of the tested commercial cigarettes and cigars varied considerably, they report. Smoke from ordinary cigarettes contained from 5.6 to 15.8 nanograms (billionths of a gram) per cigarette, with an average of 11.7 nanograms. Ordinary filters had little effect on vinyl chloride content of smoke, but charcoal filters cut the gas by about two thirds.

-more-

A charcoal filter brand received the lowest score with 1.3 nanograms per cigarette. Smoke from the same brand without the filter contained 4 nanograms per "smoke," according to the report.

Marijuana cigarettes tested relatively low at 5.4 nanograms.

Since vinyl chloride has not been found in nature previously, the authors conclude that the vinyl chloride in cigarette smoke is not due to contamination of the tobacco itself, but forms through interaction of hydrocarbons and chlorine, a normal plant constituent, at the 800 or more degrees Celsius (1500 Fahrenheit) of the cigarette cone.

"It should be realized, however," they write, "that we have directed our analysis only toward the identification and quantitative determination of vinyl chloride and that tobacco smoke may also contain other unsaturated chlorinated hydrocarbons with carcinogenic activity. This may include the suspected human carcinogen 2-chlorobutadiene (chloroprene) as well as chlorinated products of unsaturated isoprene, the major unsaturated hydrocarbon in tobacco smoke."

Possibly a more serious problem than the presence of such small amounts of vinyl chloride in cigarette smoke, Dr. Hoffmann said, is the indication that chlorinated hydrocarbons may form when other plant materials are burned.

He cited burning of trash, especially trash enclosed in polyvinyl plastic bags, as an example of a practice that ought to be examined in light of the new findings.

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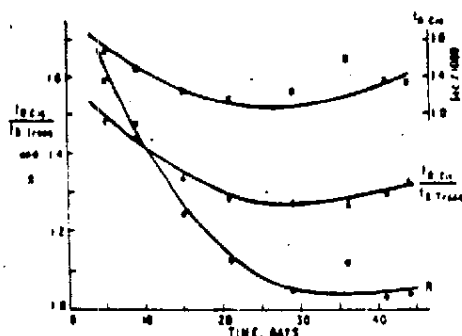


Figure 5. GC retention and resolution data for a mixture of *cis*- and *trans*-9-octadecenes on a 12.5% EGS polyester on silanized silver sulfobenzyl Porasil C column using 99.9999% helium carrier at a flow of 30 cm³/min. Column temperature, 180 °C

ence of H₂ in the carrier gas. Zero Gas grade helium contains about 1 ppm of H₂ (12) which reduced the Ag⁺ to Ag⁰ in 10 days of operation at 180 °C under the conditions of chromatography. The packing was removed from the column, extracted with CH₂Cl₂ and Ag⁰ removed with 5 N HNO₃. About 70% of initial capacity of the ionogenic groups remained. In order to determine the effects of H₂ in the carrier, Airco No. 6 grade helium was utilized. Each day for 44 days, over a total period of 10 weeks, two samples of a mixture of the *cis*- and *trans*-9-octadecenes were injected into the column. Figure 5 summarizes the experiment and depicts an initial decrease in retention time, relative retention, and resolution although an adequate separation was achieved throughout the course of the study. When the column was operated above 180 °C, alkene retention times decreased, but bleeding of the EGS polyester increased rapidly with temperature and loss of resolution was accelerated. When this loss of resolution becomes excessive, the column packing may be removed and regenerated as the Ag⁺ form.

The extent of interaction of solutes with the surface of the supposedly inert support in GLC is often debated. On

the basis of this study, there can be no doubt that the surface does interact — is evidenced by the effect of HMDS upon retention. In addition, the difference in interaction of AgSP with respect to the hydrogen-form support indicates that solutes penetrate the liquid coating and approach near to the surface. The surprising extent of coating penetration was apparent when *cis*- and *trans*-9-octadecenes were separated in 30 min at 188 °C with *R* = 1.45 on HMDS-treated AgSP at 15% loading of EGS. When a column with 20% EGS was used, a resolution of 0.57 at 180 °C was obtained. Thus, the approach described here has utility for analytical separations, provides a probe for the study of the migration of a solute through a liquid phase, and may be used to measure interactions of volatile solutes with surface-bonded groups.

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Chromatographic Determination of Vinyl Chloride in Tobacco Smoke

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A chemical-analytical method has been developed for the quantitative determination of vinyl chloride (VC) in tobacco smoke. VC from the mainstream smoke is trapped on charcoal, extracted, and subsequently converted to 1,2-dibromo-1-chloroethane (DB-VC). The latter is enriched by column chromatography and determined by gas liquid chromatography using an electron capture detector with a high sensitivity for DB-VC. From the mainstream smoke of a popular 85-mm cigarette without filter tip, we isolated 12.2 ng of VC per cigarette. The VC content in the smoke of

some domestic and foreign cigarettes and little cigars ranged from 5 to 27 ng, and that of a marijuana cigarette was 5.4 ng. The analytical data suggest that the total inorganic chloride in tobacco is a determining factor for the amount of VC in the smoke. VC may also be released into our respiratory environment during the burning of other chlorine-containing organic matter.

Vinyl chloride (VC) is causally associated with angiosarcoma of the liver in VC workers (1, 2). Exposure of mice,

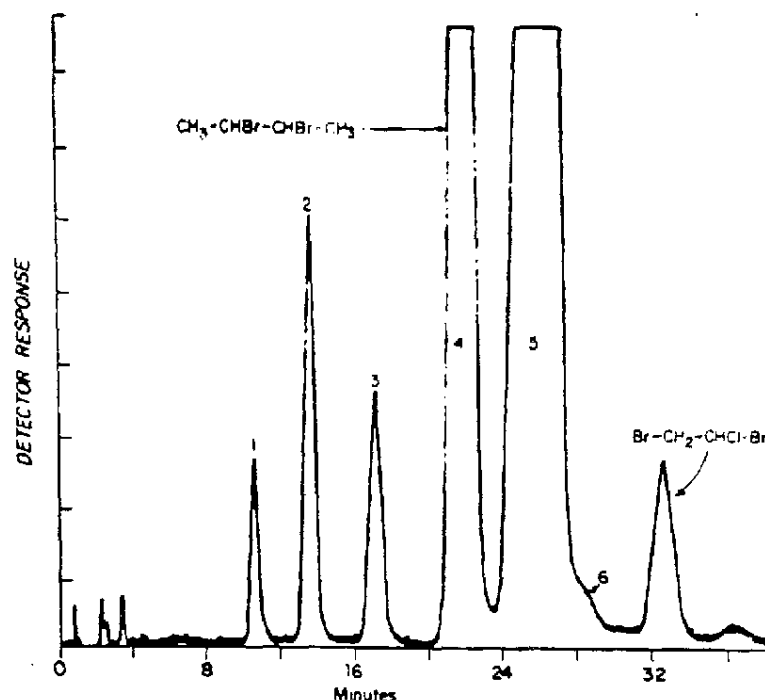


Figure 1. Gas chromatogram of a concentrate of vinyl chloride as 1,2-dibromo-1-chloroethane (DB-VC) from cigarette smoke

Peak 1 = a dibromopropane; 2 = a dibromopropane; 3 = a dibromobutane; 4 = 2,3-dibromo-*n*-butane; 5 = a dibromobutane and a dibromobutene; 6 (shoulder) = a dibromobutene; 7 (last peak) = 1,2-dibromo-1-chloroethane (DB-VC)

rats, and Syrian golden hamsters to VC in concentrations as low as 50 ppm leads to the induction of various types of tumors, including angiosarcoma of the liver (1-3). Until now, VC has been identified only in environments and materials related to vinyl chloride and poly(vinyl chloride) (1, 2).

The relatively high reactivity of VC, as well as its presumably low concentration in non-occupational respiratory environments, requires special analytical methods and sensitive detection techniques. This study reports a quantitative method for the determination of nanogram amounts of vinyl chloride in tobacco smoke.

EXPERIMENTAL

Apparatus. A Hewlett-Packard gas chromatograph Model 7260A with ^{63}Ni -ECD was used for the analysis. Cigarettes were smoked individually with a 30-port, automatic smoker (Heinrich Borgwaldt, Hamburg, Germany). Mass spectra were determined on a Hitachi/Perkin-Elmer RMU-8D instrument by the Mass Spectroscopy Laboratory of the Massachusetts Institute of Technology and on a Hewlett-Packard 5710-5980A GC/MS instrument. Conditions during analysis were: ion source, 185 °C; interface, 60 °C. NMR spectra were obtained with a Hitachi/Perkin-Elmer Model R-24 instrument. The elemental chlorine analysis was carried out by Galbraith Laboratories, Knoxville, Tenn.

Reagents. *n*-Hexane (spectrograde) was freshly distilled over Na_2SO_4 (anhydrous) prior to use. Bromine was extracted with concentrated H_2SO_4 . Activated charcoal was obtained from the Pittsburgh Activated Carbon Co. (PCC) - 12 S 30, silica gel (mesh 10-140) from J. T. Baker Chemical Co., OV-17 on Gas Chrom Q (mesh 80-100) from Applied Science Laboratories, pure vinyl chloride gas from Matheson Gas Products, and vinyl chloride mixture (49.5 ppm in air) from Scott Research Laboratories (Philmontville, Pa.). [All experiments with VC references were performed under well ventilated hoods].

Cigarettes. Domestic and foreign cigarettes were purchased on the open market in New York City and Westchester County, N.Y.,

during 1974-75. The cigarettes were selected by weight (± 20 mg of average weight of 200 cigarettes) and by draw resistance ($\pm 5\%$ of average value of 50 weight selected cigarettes). Before smoking, the cigarettes were stored at 22 ± 2 °C for at least 24 hr in a chamber with a relative humidity of $60 \pm 3\%$.

1-Chloro-1,2-Dibromoethane (reference compound). Twenty ml of bromine were dissolved in 100 ml of *n*-hexane. Under magnetic stirring at -5 °C, pure vinyl chloride gas was bubbled slowly through the solution until the color disappeared. Most of the solvent was distilled at atmospheric pressure, and the remainder under reduced pressure. 1-Chloro-1,2-dibromoethane (dibromovinyl chloride, DB-VC) was distilled at 52 °C under 12 mm Hg pressure. It was sealed under dry nitrogen, covered with dark paper, and stored at 0 °C. Under these conditions, DB-VC remains unchanged for up to two weeks. The known DB-VC was characterized by NMR: 4.0 ppm, d, 2H; 5.6 ppm, t, 1H; and by MS (m/z, rel. int.): 145 (25), 143, (100), 141 (50), 105, 107; 79, 81 [The parent peaks (220, 222, 224, 226) of DB-VC are not observed under our conditions; see Figure 2]; the ratios of the major fragments are consistent with the natural abundance of Br and Cl isotopes. The purity of the compound was ascertained by gas chromatography.

Gas Chromatography. The most satisfactory separation of DB-VC from a cigarette smoke concentrate was obtained at 60 °C on a 12-ft by 2-mm i.d. glass column filled with 10% OV-17 on Gas Chrom Q (mesh 80-100). 5% Methane in argon was used as the carrier and purge gas with a flow rate of 22 ml/min. The retention time for DB-VC was 32.5 min. Using a ^{63}Ni -ECD at 200 °C, the detection limit was 15 μg (10 μg) per injection. The detector response was linear in the range of 50-300 μg .

Model Studies. In model tests, it could be demonstrated that 1.0 g of activated charcoal packed in a 12 cm $\times$ 6 mm i.d. glass tube tends, closed with glass wool, retains VC quantitatively, at least up to 200 μg of VC from a stream of air (20 ml/sec) containing 19.5 ppm of VC. VC remains unchanged on charcoal for at least 6 hr.

The separation method was developed by blowing an air stream (flow rate 20 ml/sec) of 4 L containing 200 μg of VC through a Cambridge filter (CM-113A) loaded with tar of 30 cigarettes (~ 800 mg), and through 1.0 g of charcoal with the gas phase deposits from the cigarettes. After loading with VC, the charcoal was

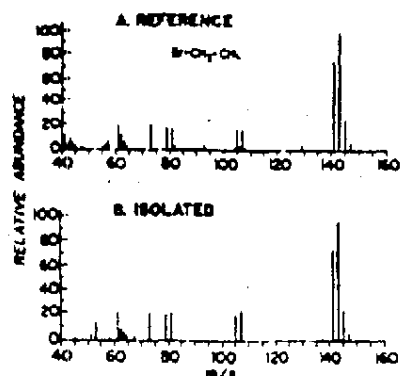


Figure 2. Mass spectra of 1,2-dibromo-1-chloroethane (DB-VC) (parent ions 220, 222, 224, 226 are unstable and not detected)

poured into a flask which was kept at -30°C and which contained 0.5 ml of bromine and 11 ml of *n*-hexane. The determination of DB-VC by GLC from the solution after column chromatography gave recovery rates of more than 95%. Two control runs (as outlined under Procedure), one involving extraction with *n*-hexane of charcoal with smoke gas-phase deposits (no bromination) and the other involving bromination of charcoal without smoke (blank test), produced no signals at the retention time of DB-VC. (All equipment used was the same as under Procedure).

Procedure: Isolation of Vinyl Chloride. An amount of the concentrate from cigarette smoke sufficient ($\approx 20\text{ }\mu\text{g}$) for mass spectral identification of the 1,2-dibromo derivative of VC was collected by several runs following the procedure for quantitative analysis of VC (see below). Each successive run was quantitatively and qualitatively monitored by gas chromatography.

Quantitative Analysis. Thirty cigarettes (selected by weight and draw resistance) were smoked with a 30-port automatic smoking machine at a rate of one puff of 2-sec duration per min, a puff volume of 35 ml, to a butt length of 23 mm. The mainstream smoke was drawn through a Cambridge filter (CM-113A; 92-mm diameter) and subsequently through a glass tube (12-cm $\times$ 6-mm i.d.) containing 1.0 g of activated charcoal (glass wool at both ends of the tube). Immediately after smoking, the contents of two such tubes were poured into a flask (Reacti-flask with screw cap and Teflon-faced disk (Pierce Chemical Co.) which was kept at -30°C and contained 0.5 ml of bromine in 11 ml of *n*-hexane. The flask was sealed and covered with dark paper, and the contents were magnetically stirred for 7 min. An aliquot of the reaction mixture was chromatographed with *n*-hexane on silica gel (mesh 50-80) 1.0 $\times$ 60-cm at a column temperature of 0°C . Fractions (average 7.3 ml) were collected every 2 min. Fractions 13-15 were combined and concentrated slowly under nitrogen at 45°C to a 7-ml volume.

This solution was rechromatographed with *n*-hexane on silica gel mesh 60-80 (column 1.3 $\times$ 75-cm) at room temperature; 7.3-ml fractions were collected every 1.25 min. An aliquot of fraction 24 was analyzed by gas chromatography. (To ensure maximal recovery, neighboring fractions were also analyzed for DB-VC and, if needed, combined with fraction 24).

Quantitative Analysis of Inorganic Chloride in Tobacco. The technique employed was the Caldwell and Moyer modification of the Volhard method (4), with the further change of filtering the sample solution with Norite prior to titration. Cl^{-} was extracted from tobacco samples according to Yamazaki and Yamazaki (5).

RESULTS AND DISCUSSION

A gas chromatogram of a vinyl chloride (VC) concentrate from cigarette smoke as 1,2-dibromo derivative (DB-VC) is shown in Figure 1. The column effluent, which by retention time corresponded with DB-VC, was identified by its mass spectrum (Figure 2). The main peaks in the gas chromatogram (Figure 1) with retention times lower than that of DB-VC were identified by mass spectrometry as dibromopropanes and dibromobutanes; however, because of a lack of reference compounds, we were unable to assign structures with the exception of one case. Five analyses of 60

Table I. Vinyl Chloride in Cigarette Smoke, ng/cig.^a

No. of analysis	Vinyl chloride isolated ^b
1	12.6
2	11.4
3	12.9
4	10.8
5	13.1
Average	12.2
Std dev	0.90
Dev coefficient	7.4 %

^a Commercial, 85-mm, nonfilter cigarette. ^b Not corrected for losses.

Table II. Vinyl Chloride in Cigarette Smoke

Product ^a	Length, mm	Butt length, mm	Vinyl chloride, ng/cig.
Reference cigarette IRI			
Cigarette A NF	85	23	12.4
Commercial cigarettes			
Cigarette A F	85	23	5.6
Cigarette B F	85	23	14.1
Cigarette C F	85	23	11.4
Cigarette D NF	70	23	11.9
Cigarette E NF	70	23	15.8
Cigarette G F	85	23	0.9
Cigarette H NF	85	23	2.2
Commercial little cigar:			
Little cigar A F	85	23	14.4
Little cigar B F	85	23	27.3
Charcoal filter cigarettes ^b			
Cigarette A with F	85	35	5.1
Cigarette A with F cut off	60	10	15.3
Cigarette B with F	85	35	1.3
Cigarette B with F cut off	60	10	4.0
Marijuana cigarette	85	23	5.4

^a F: Filter; NF: nonfilter. ^b Cigarette column smoked: 50 mm.

cigarettes each yielded an average of 12.2 ng VC isolated as DB-VC from the mainstream smoke of an 85-mm U.S. blended cigarette without filter tip (Table I). The recovery rate was found to be at least 85%. The minimum recovery rate was calculated by directing known amounts of VC in air through charcoal which was earlier loaded with the gaseous phase of the mainstream smoke of 10, 20, or 30 standard cigarettes, respectively. After completing the analysis, we calculated the recovery rate.

In addition to the standard nonfilter cigarettes, we analyzed the mainstream smoke of some domestic and foreign cigarettes, of two little cigars, and a marijuana cigarette. The results are summarized in Table II and indicate significant differences in the concentration of VC in the mainstream smoke of commercial cigarettes. As expected, the smoke of cigarettes with charcoal filter tips contains significantly lower amounts of VC than does the smoke of cigarettes without this type of filter tip.

CH radicals are long known to be generated during the burning of tobacco products (6). Since many tobacco constituents give rise to CH radicals, a search for possible specific precursors for the C_2H_3 moiety of VC appears rather futile. On the other hand, tobacco contains traces of residues of chlorinated pesticides (7), some unknown, chlorinated organic compounds (6, 8), and up to 3% of inorganic chloride (9). It is, therefore, reasonable to assume that the inorganic chloride in tobacco contributes significantly to the concentration of VC in the smoke. This hypothesis is supported by the observation that the amount of inorganic chloride in cigarette smoke is determined by the concentration

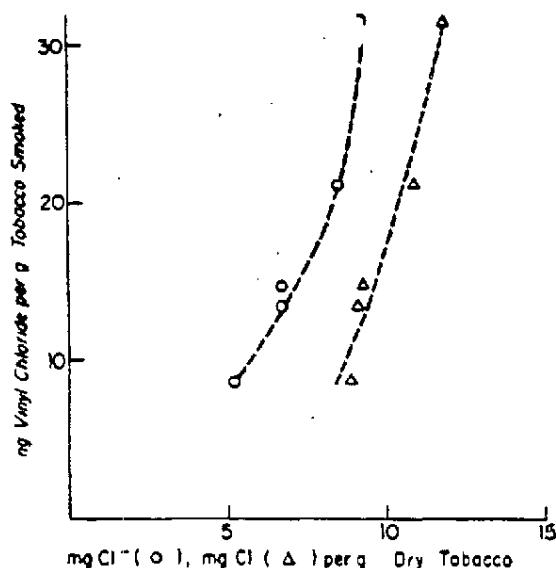


Figure 3. Correlation between inorganic chloride and total chlorine in tobacco and vinyl chloride in cigarette smoke

tion of inorganic chloride in tobacco (10). Figure 3 indicates that water soluble chloride, as well as total chlorine, in tobacco may contribute to the concentration of VC in the smoke. We realize that detailed studies are needed to ensure the nature of the major precursors in tobacco for the chlorine of VC in the smoke. Nevertheless, we should not disregard the possibility that also during the burning of other plant materials, and in fact of all organic matter which contains chlorine, vinyl chloride can be generated and can be released into our respiratory environment, as demonstrated for marijuana smoke.

This study has shown that smoke contains up to 16 ng of vinyl chloride per cigarette, and 27 ng of VC per little cigar. This amount corresponds to a concentration of about 30 ppb. Based on human data and results from animal studies, it appears to us that these minute amounts of VC will not contribute to a measurable degree to the carcinogenic activity of tobacco smoke. It should be realized, however, that we have directed our analysis only toward the identification and quantitative determination of vinyl chloride and

that tobacco smoke may also contain other unsaturated, chlorinated hydrocarbons with carcinogenic activity. This may include the suspected human carcinogen 2-chlorobutadiene (chloroprene; 11, 12) as well as chlorinated products of isoprene, the major unsaturated hydrocarbon in tobacco smoke.

NOTE ADDED IN PROOF. This study was presented at the 29th Tobacco Chemists' Research Conference (College Park, Md., Oct. 8-10, 1975). Two questions arose: 1) How much VC is in ambient air? Using the above method, at different times we passed 20 l. of ambient laboratory air through charcoal. The extract of the charcoal was each time free of VC. 2) Is VC artificially formed from the ethylene of the smoke (trapped on charcoal) and the trace amounts of chlorine possibly present in the bromine? To answer this question, we led 400 ml of ethylene (CP-Matheson Gas Products) through charcoal and, using the same bromine, we processed it in the usual way. We did not observe a signal in the glc at the retention time of DBVC using the ECD at twice the usual sensitivity.

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Thin Layer Chromatography/Densitometry with Transferable Calibration Factors

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The principle of a transferable calibration technique is discussed and introduced with examples of dihydroergotamine. The quantitation of spots is carried out with direct UV reflectance spectrometric measurements of methylergobasine on different series of chromatoplates. The applicability of this same calibration transfer model to *in situ* fluorescence measurements which require a derivatizing reac-

tion after separation is demonstrated with samples of digoxin. The reproducibility of the results obtained is comparable to individual calibration carried out for each plate (rel. std. dev. about 2%). With the use of transferable calibration, 5 analyses can be carried out on one 20 × 20 cm plate which represents an increase in capacity of 60% compared to a previously discussed method.

Vinyl Chloride Found In Cigarette Smoke

Associated Press

Vinyl chloride, a cancer-causing chemical, has been found for the first time in cigarette smoke, possibly indicating similar chemicals form when other plant material is burned, scientists say.

The researchers said yesterday the amount of vinyl chloride measured in cigarette smoke is probably too small to be a major factor in cigarettes causing cancer.

But one of the scientists said vinyl chloride from tobacco smoke contributes to public exposure to the chemical, and conceivably could interact with other cancer-causing agents in the environment to increase cancer risk.

The study, published in the American Chemical Society's journal *Analytical Chemistry*, was conducted by Drs. Dietrich Hoffman,

Constantin Patrinoakes and Klaus D. Brunnemann of the American Health Foundation, Valhalla, N.Y. Dr. Gio B. Gori of the National Cancer Institute, Bethesda, Md., coauthored the report.

Vinyl chloride is widely used in making plastics and has been linked to a higher incidence of liver cancer in those who work with it. Exposure also has produced various types of cancers in test animals.

The new study marks the first environmental appearance of vinyl chloride unrelated to its deliberate manufacture or use.

The highest vinyl chloride concentration measure was 30 parts per billion in the smoke of a nonfiltered cigarette. This amount per cigarette is 1,000 times smaller than found to produce tumors in animals inhaling the chemical.