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DEC 22 1976

December 16, 1976

No. 30

TO: All Members of SPI-VCM/PVC Mailing Lists

Letter Highlights

1. A meeting with the Food and Drug Administration is being arranged to bring the Bureau of Foods up to date regarding current industry capabilities with regard to the reduction of residual monomer levels in rigid and semi-rigid PVC food packaging materials. We are enclosing a current FDA analytical procedure for detecting vinyl chloride in food-simulating solvents and an interim report on a vinyl chloride feeding study; both are discussed in detail in this letter.

2. The status of the EPA standard on vinyl chloride emissions is somewhat clouded because of an EPA reevaluation of its position in light of a suit by an environmental group to have the standard set aside. The VCM/PVC Producers Group has moved to intervene in the suit to protect industry interests.

Ladies and Gentlemen:

Once more we are writing to bring you up to date regarding the status of pending matters that concern both the Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA) relative to polyvinyl chloride food contact surfaces and vinyl chloride emissions, respectively.

FDA

With respect to the situation at the Food and Drug Administration, in various meetings of the VCM/PVC Producers Group, the Plastic Bottle Institute, and the Food, Drug and Cosmetic Packaging Materials Committee, we have in the past two weeks reported that Mr. Richard J. Ronk had recommended that we meet with the Food and Drug Administration Staff to report on the current "state of the art" vis-a-vis the industry's ability to minimize residual monomer in food contact articles. Actually, Mr. Ronk recommended that we ask for a meeting with Acting Commissioner Sherwin Gardner so I placed a call on Friday, December 3 to try to set a date for such a session after having been provided with the names of persons who could constitute a representative delegation from the industry for such a session. Thereafter, the Acting Commissioner's office and Mr. Ronk advised that the meeting should be held at the Bureau of Foods level, instead of with the Acting Commissioner and his Staff present.

As matters stand, we are awaiting the setting of a date for such a session having received Mr. Ronk's promise that he would try to make arrangements and advise us about the date. We are expecting that the meeting will be held early in January. In the meantime, we have requested that the following attend a preliminary session with us on December 21 so that we can make plans for an effective presentation: Messrs. Abramowitz (Hooker Chemical), Ackart (Union Carbide), Haefner (Ethyl), Lees (Ethyl), Malone (B. F. Goodrich), Paradis (Diamond Shamrock) and Saggese (Tenneco). It will be our objective to give the Bureau of Foods sufficient information so that, hopefully, it will be aided in drafting a so-called "options paper" to be given to the Acting Commissioner so that he, in turn, can instruct the Staff on what sort of final PVC Regulations should be acceptable to him, especially with respect to the parameters to be used to govern the use of PVC for food contact surfaces like blister pack and bottles.

Many of you may recall our informing you that FDA had developed an analytical procedure for vinyl chloride in food-simulating solvents that was sensitive to a level

reported to be in the range of 1-2 parts per billion (ppb). We have obtained a copy of the procedure, actually in the form of a preprint of a paper scheduled for publication in May, 1977 in the Journal of the Association of Official Analytical Chemists. A copy of the preprint is enclosed for your consideration.

The procedure has a claimed detection limit in the range of 0.1-0.5 ppb and a quantitation level in the range of 1-2 ppb. This means that the FDA scientists believe that if vinyl chloride were present in the test solvent in the range of 0.1-1 ppb, its presence might be suspected; but if it were present at a level of 1 ppb or above, they would conclude that VCM was definitely present. This analytical procedure provides an FDA confirmation of the quantitative sensitivity limit for vinyl chloride analyses that have been achieved in water analysis in the recent past, and its extension to other solvents. It also provides a framework against which industry reductions of residual VCM in packaging should be measured.

Further with regard to the FDA sitution, albeit a somewhat collateral matter, word was received from Europe a couple of weeks ago about a Central Instituut Voor Voedingsonderzoek/TNO (CIVO-TNO) Report. We were told that the report would be given to the Dutch and German Governments shortly after December 1 and were also informed that we could then supply it to the Food and Drug Administration. The material we have received is by no means sufficiently descriptive of the results of the CIVO-TNO study but it is all we have so copies of it and our transmittal letter to the Food and Drug Administration are enclosed for your information. We might note in passing that we have been told informally that the European sponsors of the project, and probably some of the government officials who have received it, seem to have questions about the way in which the work was done. If and when we receive more information in this connection, you will be advised.

As an aid to you in interpreting the CIVO-TNO report, it may be helpful to note that a feeding level of 1 mg/kg can be considered very roughly equivalent to a level of

40 ppm in the whole diet of an adult human; 3 mg/kg would be equivalent to 120 ppm. Thus, if a sample of food were analyzed for vinyl chloride and showed none detected with the attached method (sensitive to 1 ppb), this would assure the absence of vinyl chloride in the sample at a level of 1/40,000 of the lowest whole diet level used in the CIVO-TNO study.

We still have no reason to believe that there will be rapid Food and Drug Administration action on the long awaited PVC Regulations. We do remain optimistic that FDA will ultimately become convinced that there is no need to ban any polyvinyl chloride food contact surface. All of our efforts are being directed towards this objective and we will continue to keep you informed of our progress.

EPA

The vinyl chloride emissions regulations which had been promulgated by the EPA have, as you know, been challenged by the Environmental Defense Fund, Inc. (EDF) in a Petition to Review the Standard filed in the United States Court of Appeals for the District of Columbia Circuit. The EDF contentions are that EPA should not have relied on the "best available technology" but should have set an absolute number as the emissions limitation (presumably zero, although this is not stated explicitly) and, furthermore, even if "best available technology" were a suitable basis for this regulation, EPA erred by not requiring the use of a technology EDF deems to be better.

As a result, EPA is reviewing the Standard to decide on the position it will take. To the best of our knowledge, EPA has not decided whether or how to oppose the EDF action. In connection with its internal review, we have been informed that EPA has undertaken a formal risk-benefit assessment of VCM/PVC. Finally, there is a good deal of uncertainty in the upper echelons of EPA because of the change in the Administration and the anticipated appointment of a new Administrator, General Counsel and others.

In order to protect the industry's interests against possible adverse agreements between EPA and EDF, the VCM/PVC Producers Group decided that intervention in the EDF suit would be desirable; accordingly, a Motion to Intervene was filed with the Court on December 9, 1976.

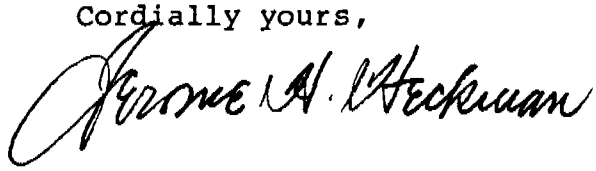
In addition, consideration is now being given to petitioning the Court of Appeals to stay the Standard because of the uncertainties generated by the EDF suit. The uncertainties flow from the fact that the standard requires the producers to make major contractual commitments within a tight time-frame in order to bring their plants into compliance with the Standard. If the Standard should be changed in any significant way, these contracts, the equipment sought to be purchased and installed, and the structural and procedural changes contemplated might be rendered useless or inadequate. Of course, if this uncertainty takes too long to resolve, the problem reverses and becomes one of whether the producers can comply with the Standard on time.

In any event, our associate counsel, Beveridge, Fairbanks and Diamond, is preparing a Motion for a Stay so that such a document will be ready to file, if necessary. Whether or not such a pleading is filed will ultimately depend on the posture EPA decides to take--a matter that should become clearer reasonably soon.

* * *

We shall, of course, continue to follow these and related matters concerning VC/PVC interests and will keep you as fully and promptly informed as we can.

Cordially yours,



Enclosures

PREPRINT
(Accepted for May 1977 issue of JAOAC)

Gas-Liquid Chromatographic Headspace Procedure for Determination of Vinyl Chloride in Vegetable Oil and Three Food Simulating Solvents.

By Gregory W. Diachenko, Charles V. Breder, Margaret Brown, and J. Lawrence Dennison

Division of Chemical Technology, Bureau of Foods, Food and Drug Administration, 200 "C" Street, S.W., Washington, D.C. 20204

ABSTRACT

A gas chromatographic (GLC) headspace procedure for the determination of vinyl chloride (VC) in corn oil, 50% ethanol, 3% acetic acid, and heptane is described. These food simulating solvents are placed in septum sealed bottles, heated to 90°C, and aliquots of headspace vapor are injected into a GLC equipped with a flame ionization detector. VC may be quantitated at concentrations of 1 ppb or less. This technique was used to measure the migration of VC into corn oil and 50% ethanol from two unplasticized PVC sheets containing 0.28 and 0.44 ppm residual monomer.

In early 1973, alcoholic liquors packaged in polyvinyl chloride (PVC) bottles were found to be contaminated with vinyl chloride (VC) migrating from the plastic (1). These findings, coupled with the demonstrated carcinogenicity of VC by inhalation (2), led to a great deal of concern about the possible migration of VC into foods. Several investigators subsequently detected VC in other foods such as vegetable oils, edible fats, and vinegars packaged in PVC bottles (2,3,4). These findings have increased significance in view of research by Maltoni et.al. (2), indicating the possibility that VC is also carcinogenic by ingestion.

PVC producers and converters have recently improved their manufacturing technology resulting in lower amounts of residual VC monomer in PVC resins and products. Several manufacturers have used new stripping technology to produce resin and finished rigid PVC articles with residual VC levels in the low ppm to low ppb range. Direct solution injection gas chromatographic (GLC) techniques generally do not have sufficient sensitivity to detect the small quantities of VC migrating from these materials. In view of this, it is desirable to have a more sensitive analytical procedure to detect and measure low levels of VC which may migrate from PVC into foods or food simulating solvents. Building on other GLC-headspace techniques (3,4,5) and the procedure of Breder et.al. (6), our laboratory has refined and developed procedures which permit the quantitative determination of VC at the 1 ppb level in food simulating solvents such as 50% ethanol, 3% acetic acid, n-heptane, and vegetable oil.

Experimental

Reagents

(a) Vinyl chloride.-3 lb cylinder (99.9% pure), Matheson, or equivalent.

(b) n-Heptane.-J.T. Baker, Baker grade, or equivalent. Using 3-ball Snyder column between pot and condenser, slowly distill off and discard first 40% of heptane, and use remainder.

(c) Vegetable oil.-Corn oil from glass or polyethylene bottles.

(d) Vinyl chloride gas standard.-1.00 ppm (2.6 ng ^{VC}/ml Nitrogen)MG Scientific, or equivalent.

Apparatus

(a) Sample vials.-Two ml. Hewlett-Packard No. 5080-8712 or equivalent. Vial caps-With Teflon-lined septa. Hewlett-Packard No. 5080-8713, or equivalent. Handcapper for vials.-Hewlett-Packard No. 8710-0979, or equivalent.

(b) Screw-cap bottles.-1 oz. narrow mouth. Ace Scientific Supply Co. No. 10-4256, or equivalent (35 $\pm$ 0.5 ml). Caps-With Teflon-lined septa. Alltech Associates No. 9522, or equivalent.

(c) Gas syringe, 2,5 and 10 ml.-Precision Sampling, Pressure-Lok, series A-2, or equivalent.

(d) Gas Chromatograph.-Hewlett-Packard Model 7620A, or equivalent, equipped with temperature programmer and flame ionization detector. Operating conditions: temperatures (°C)-detector 260, injection port 200; flows (ml/min)-hydrogen 70, oxygen 480; electrometer setting, 1 or $2X10^{-12}$ amps full scale. Detector sensitivity: 0.7 ng VC gave 50% full scale deflection at retention time of 2.5 min and electrometer setting of $1X10^{-12}$ amps full scale.

(e) Chromatographic column.-Coiled stainless steel column 5'X2 mm id, packed with 60-80 mesh Chromosorb 104; temperature programmed (°C), 95 for 5 min, 95-250 at 30/min, hold for 6 min; helium carrier flow adjusted to give VC retention time of 2.0-3.5 min (ca 50 ml/min).

Preparation of Standards

Prepare stock VC solutions of ca 1 and 5 ppm concentrations in each of desired food simulating solvents as previously described (6). Check VC concentration by injecting solution into gas chromatograph and comparing area response with that obtained from equivalent amount of 1.00 ppm VC standard gas. Area measurements should agree within ±5%. Prepare headspace standards by injecting calculated volumes of VC stock solution into 35 ml (1 oz) septum sealed bottles containing measured volumes of food simulating solvents. Volumes of sample and standard 35 ml septum sealed bottles should be matched within ±0.5 ml.

Preparation of Sample and Analysis:

Invert solutions to be analyzed for VC several times to insure solution homogenity. Analyze as described below.

Ethanol (50%) and acetic acid (3%)-Thoroughly purge 35 ml bottle with Nitrogen and seal with septum and cap. Using a 10 ml gas

syringe, withdraw 20 ml (2 X 10 ml) of Nitrogen to reduce pressure buildup. With 10 ml gas syringe, transfer 20.0 ml liquid sample to bottle and heat 30 min. in oven or constant temperature water bath at 90±2°C. Take 3.0 ml sample of headspace vapor with hot (90°C) 5.0 ml gas syringe using valve lock to seal in sample until injection onto chromatographic column.

Vegetable oils and heptane-Treat sample bottles with Nitrogen as above. With 10 ml gas syringe transfer 10.0 ml liquid sample to septum sealed bottle, and heat 30 min in oven or water bath at 90±2°C. Take 4.0 ml sample of headspace vapor with hot (90°C) 5.0 ml gas syringe using valve lock to seal in sample until injection onto chromatographic column.

Quantitate VC levels in samples by comparison of peak heights or peak areas with calibration curve constructed from blank food simulating solvent spiked with appropriate amounts of VC stock solution and treated identically to samples. Confirm VC identity by GLC-mass spectrometry (MS) using previously described GLC column and observing the 3:1 m/e 62 to 64 ratio.

Discussion and Results

The high vapor pressure of VC (B.P.-14°C) makes it ideally suited for determination by a headspace technique. The favorable partitioning of VC into the headspace over a sample and the relatively clean matrix in the headspace enables GLC injections of larger percentages of the total VC in samples than could be obtained by direct solution injection. Detection levels by this headspace technique ranged from approximately 0.1 ppb (^{ng} VC/ml) in 50% ethanol to 0.5 ppb in corn oil. These detection levels are 10 to 50 times lower than those obtainable using a direct solution injection technique for food simulating solvents (6).

Equilibration of the headspace/solvent system at 90°C is rapid. This was shown by the vinyl chloride concentration in the headspace remaining constant when analyzed at periods from 30 min to 2 hr. The experimentally determined concentrations of VC in the headspace over spiked solutions were used to calculate partition coefficients. By dividing the ^{ng} VC/ml of headspace by the ^{ng} VC/ml remaining in solution (obtained by difference), the following partition coefficients at 90° were calculated; 0.5 for 50% ethanol, 1 for 3% acetic acid, 0.09 for heptane, and 0.09 for corn oil.

Food simulating solvents spiked at concentrations ranging from 0.1 to 100 ppb with VC stock solutions in the same solvent gave linear calibration curves. The reproducibility in preparing and checking VC standards by this headspace technique was determined for corn oil and 50% ethanol. Three sets of standards, each consisting of 3 or 4 units, were prepared in each solvent , and quantitated using previously prepared

calibration curves. The essentially complete recoveries obtained are shown in Table 1. The standard deviations of 7.3 and 6.9 for the percent recovery of VC from corn oil and 50% ethanol respectively are also shown in Table 1, and compare favorably to the standard deviation obtained using a direct solution injection technique (6).

Example GLC chromatograms of headspace from over VC standard solutions are shown in Figs. 1 to 4. Unidentified GLC peaks eluting just prior to VC were observed in all cases. The PVC migration solutions chromatograms (Figs. 5-7) also contained extraneous peaks. The levels of these extraneous compounds varied, but normally did not interfere with the reproducible quantitation of VC. Pretesting of blank food simulating solvents should be performed to insure the absence of extraneous chromatographable compounds eluting at the VC retention time.

A VC migration study was conducted on two lots of "food grade" unplasticized PVC sheets. PVC lots 1 and 2 contained 0.28 and 0.44 ppm residual VC respectively, as determined by a solution technique (6). Duplicate sheets of each lot, measuring approximately 2"X 7/8", weighing approximately 0.6 g, and 15 and 12 mils in thickness for lots 1 and 2 respectively, were individually placed in 1 oz., septum sealed bottles containing 33.0 ml of 50% ethanol or corn oil. Four 1 ppb VC standard solutions were prepared in each solvent and treated identically to the PVC migration sample solutions. The corn oil and 50% ethanol solvents were in contact with PVC sheets for 54 and 19 days respectively at 120°F. At the end of these time periods, single 20 ml aliquots of the 50% ethanol solutions and duplicate 10 ml aliquots of the corn oil solutions

were analyzed as previously described. Previous work in our laboratory showed that equilibrium was reached for similar PVC materials within these two time periods. Results of the headspace analyses of these solutions, shown in Table 2, gave average concentrations of 1.6 and 2.4 ppb VC in 50% ethanol and 2.5 and 4.8 ppb in corn oil for lots 1 and 2 respectively. These concentrations represent total migrations of approximately one third and one half of the residual VC from the PVC sheets into 50% ethanol and corn oil respectively.

Consistent losses of VC were obtained for the four 1 ppb standard solutions in each solvent subjected to the same conditions as the sample migration solutions. Average losses of VC were 64% (60, 63, 63, 68) from 50% ethanol standards and 37% (35, 35, 37, 41) from corn oil standards. These losses are suspected to be due to diffusion of VC through the Teflon lined septa used to seal the migration bottles. If one assumes that similar losses occurred from the PVC migration solutions, then the migration of much larger amounts of VC actually took place. The measured values might therefore be corrected for losses by applying correction factors derived from the standard solutions. These loss-corrected values would give percentages of maximum VC migration into corn oil and 50% ethanol ranging from about 2/3 to near complete migration. Although the GLC chromatograms of these solutions, shown in Figs. 5 and 6, are less than ideal, the data in Table 2 indicate they were adequate for reasonably reproducible quantitation. The chromatogram in Fig. 7, obtained in a previous VC migration study in our laboratory, illustrates the type of chromatogram obtained for migration solutions containing higher concentrations of VC and smaller amounts of extraneous chromatographable compounds. The presence and approximate amounts of VC in the 50% ethanol migration solutions were confirmed by GLC-MS.

In summary, a headspace technique has been presented which permits the quantitative determination of vinyl chloride in food simulating solvents and corn oil at concentrations as low as 1 ppb. Depending on interferences encountered and the solvent being analyzed, the presence or absence of VC can sometimes be detected at levels considerably lower than 1 ppb. However, it must be emphasized that at these low pbb VC levels, confirmation by GLC-MS is highly desirable.

Acknowledgment

The authors thank Virgil Warren, Division of Chemical Technology, Food and Drug Administration, Washington, D.C. for his GLC-MS confirmation of VC in food simulating solvents.

Table 1. Precision in Preparing and Analyzing VC Solutions in 50% Ethanol and Corn Oil

50% Ethanol				Corn Oil			
Set No.	VC Spiked, ppb	VC Found, ppb	% Recovery	Set No.	VC Spiked, ppb	VC Found, ppb	% Recovery
	0.49	0.52	105		1.0	0.9	90%
1	0.52	0.52	100		1.0	0.9	90
	0.50	0.46	92	1	1.0	1.0	100
					1.0	1.1	110
	1.90	2.06	108				
2	1.95	2.00	103		2.5	2.5	100
	1.90	2.02	106	2	2.5	2.6	104
					2.5	2.8	112
	2.82	2.76	98				
3	2.71	2.58	95		5.7	6.0	105
	2.92	3.30	113	3	5.7	5.6	98
	2.86	2.65	93		5.7	5.9	103
		Av.	101%				101%
		Std. dev.	6.9				7.3
		Av. dev. from mean	5.7				5.6

Table 2. VC Migration from PVC Sheets into 50% Ethanol and Corn Oil

Sample	Initial ppm VC in PVC	ppb VC Found in Migration Solutions		% Maximum VC Migration*	
		50% Ethanol (19 days @ 120°F)	Corn Oil (54 Days @ 120°F)	50% ETOH (19 days @ 120°F)	Corn Oil (54 days @ 120°F)
1a	0.28	1.6	2.8 (2.6, 3.0)	28	50 (46,54)
1b		1.5	2.2 (2.1, 2.2)	32	41 (40, 41)
2a	0.44	2.3	4.6 (4.5, 4.6)	31	60 (59,60)
2b		2.5	4.9 (4.7, 5.1)	33	60 (58, 62)

*Uncorrected for VC losses from 1 ppb standards treated identically to the samples. See text for discussion.

References

(1) Federal Register (1973) 38, 12931

(2) Federal Register (1975) 40, 40529-50537

(3) Fuchs, G., Gawell, G. Albanus, L., and Slorach, S. (1975) Var foda 27 (3), 134-145

(4) Williams, D.T., and Miles, W.F. (1975) JAOAC 58, 272-275

(5) Wilks, R.A., Jr., and Gilbert, S.G. (1968) Materials Research and Standards 8, No. 1, 29-32

(6) Breder, C.V., Dennison, J.L., and Brown, M.E. (1975) JAOAC 58, 1214-1220

FIG. 1 - Gas-liquid chromatograms of 3.0 ml headspace aliquots from over 50% ethanol solutions: A, Blank; B, 0.5 ppb VC standard solution, ca 0.5 ng VC injected; $2X10^{-12}$ afs.

FIG. 2 - Gas-liquid chromatogram of 3.0 ml headspace aliquot from over 50% ethanol solution; 5.8 ppb VC standard; ca 6.2 ng VC injected; $8X10^{-12}$ afs.

FIG. 3 - Gas-liquid chromatograms of 4.0 ml headspace aliquots from over corn oil solutions: A, Blank; B, 1.0 ppb VC standard solution; ca 0.35 ng VC injected; $2X10^{-12}$ afs.

FIG. 4 - Gas-liquid chromatogram of 4.0 ml headspace aliquot from over corn oil; 5.7 ppb VC standard solution; ca 1.9 ng VC injected; $2X10^{-12}$ afs.

FIG. 5 - Gas-liquid chromatogram of 3.0 ml headspace aliquot from over 50% ethanol migration solution; PVC lot 1b, representing ca 1.4 ng VC; $2X10^{-12}$ afs.

FIG. 6 - Gas-liquid chromatogram of 4.0 ml headspace aliquot from over corn oil migration solution; PVC lot 1a, representing ca 1.1 ng VC; $2X10^{-12}$ afs.

FIG. 7 - Gas-liquid chromatogram of 3.0 ml headspace aliquot from over 50% ethanol migration solution; PVC sheet contained 0.54 ppm residual VC monomer before migration; concentration in solution ca 10.7 ppb; $16X10^{-12}$ afs.

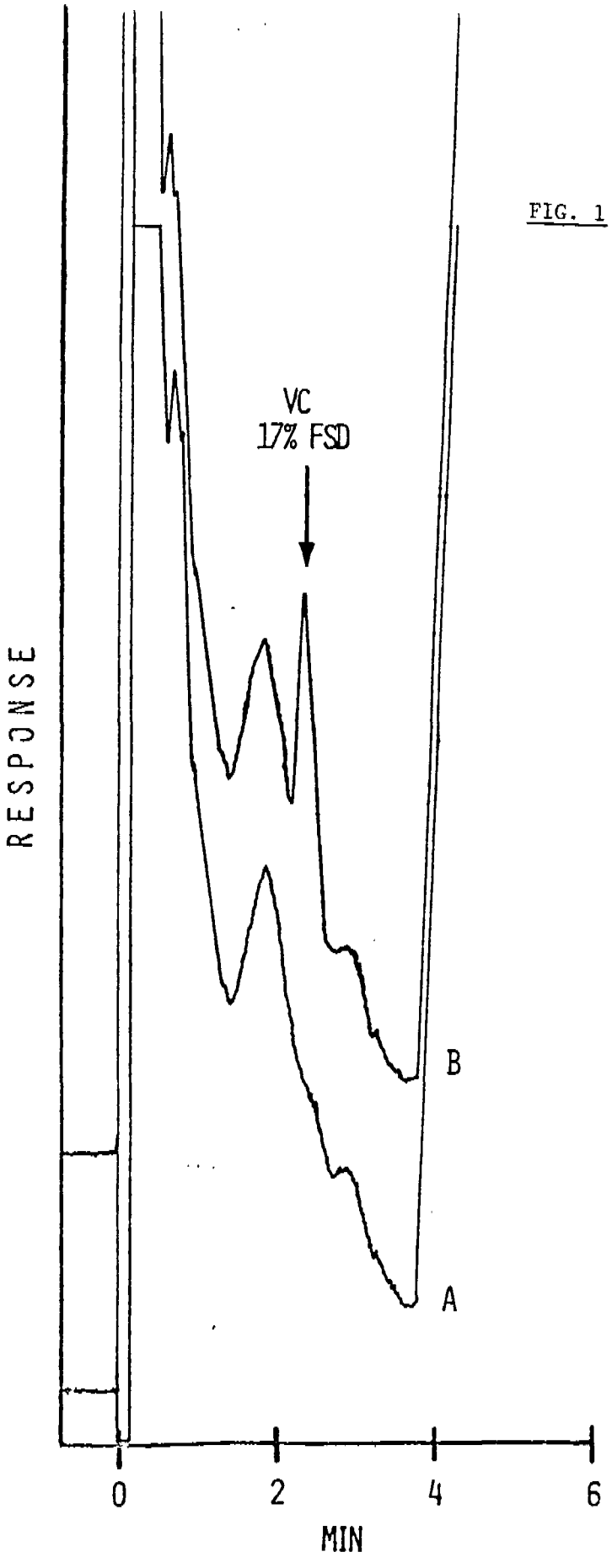


FIG. 1

FIG. 2

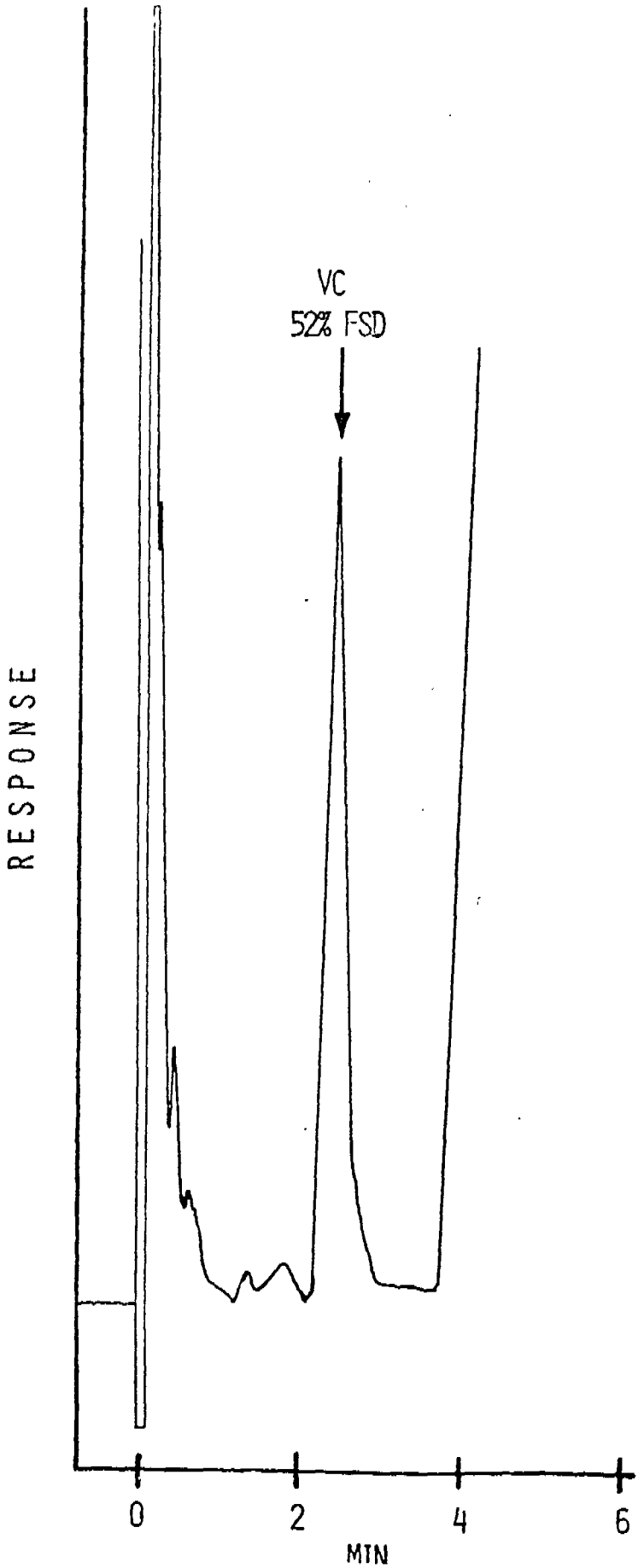


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FIG. 3

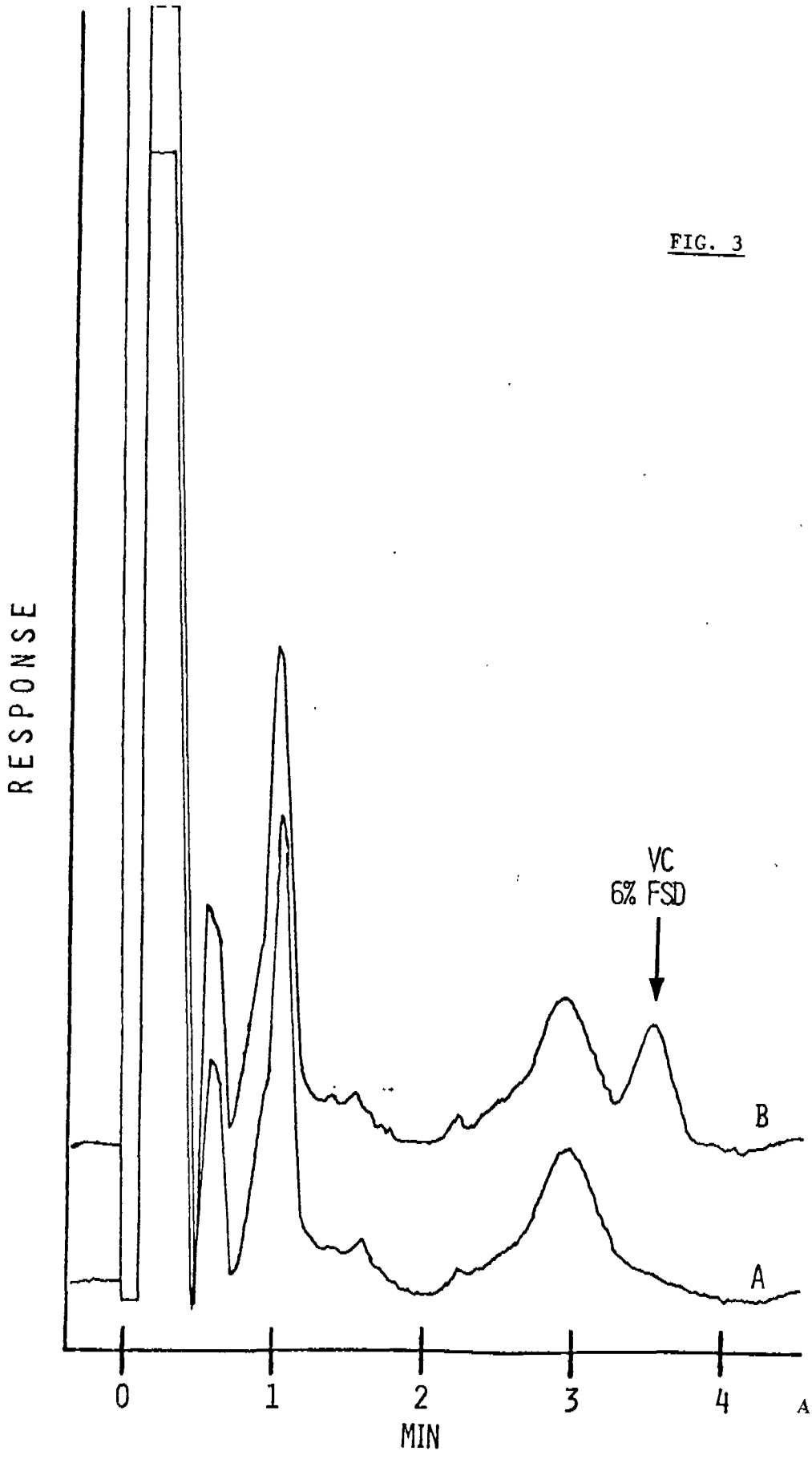

FIG. 4

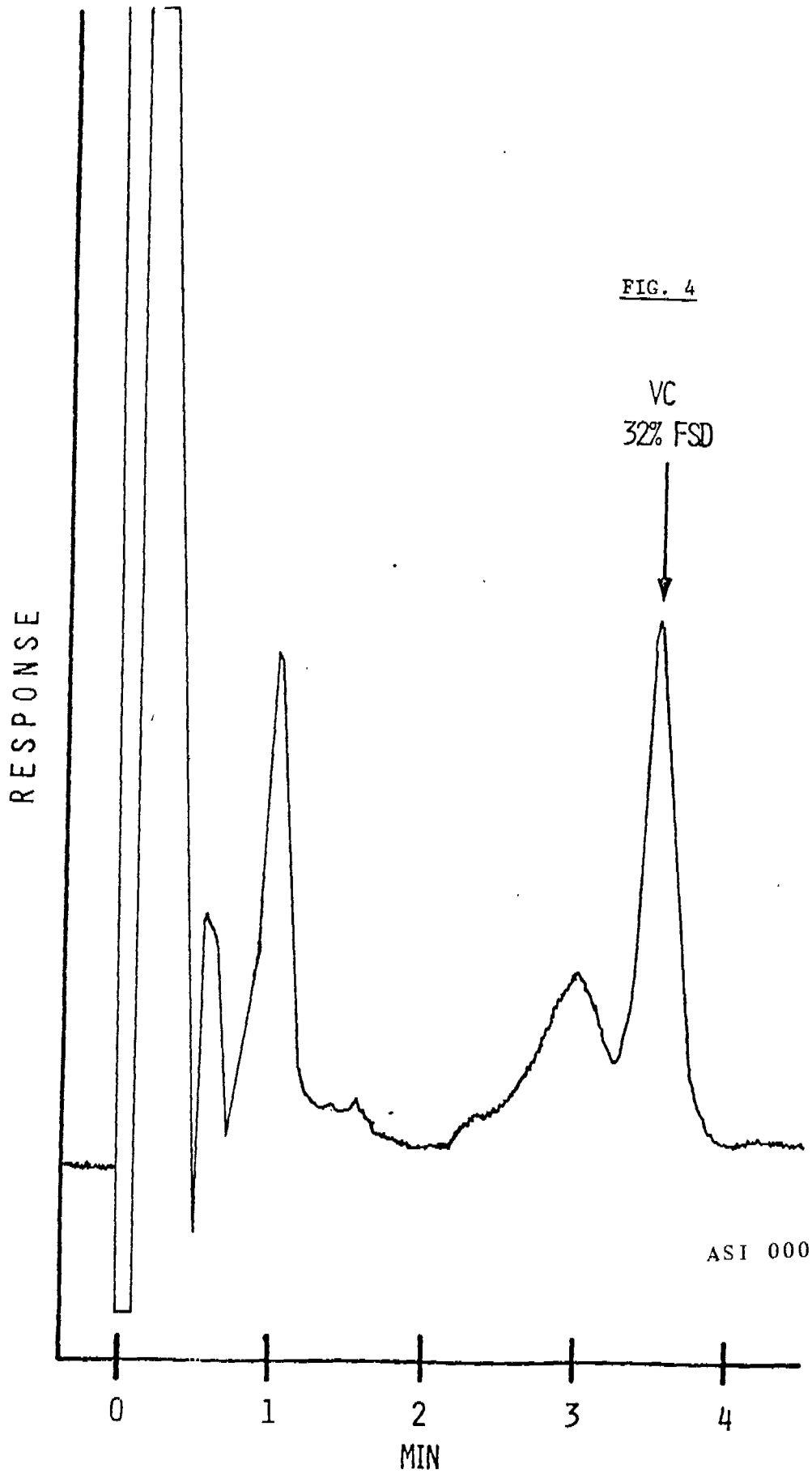

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FIG. 5

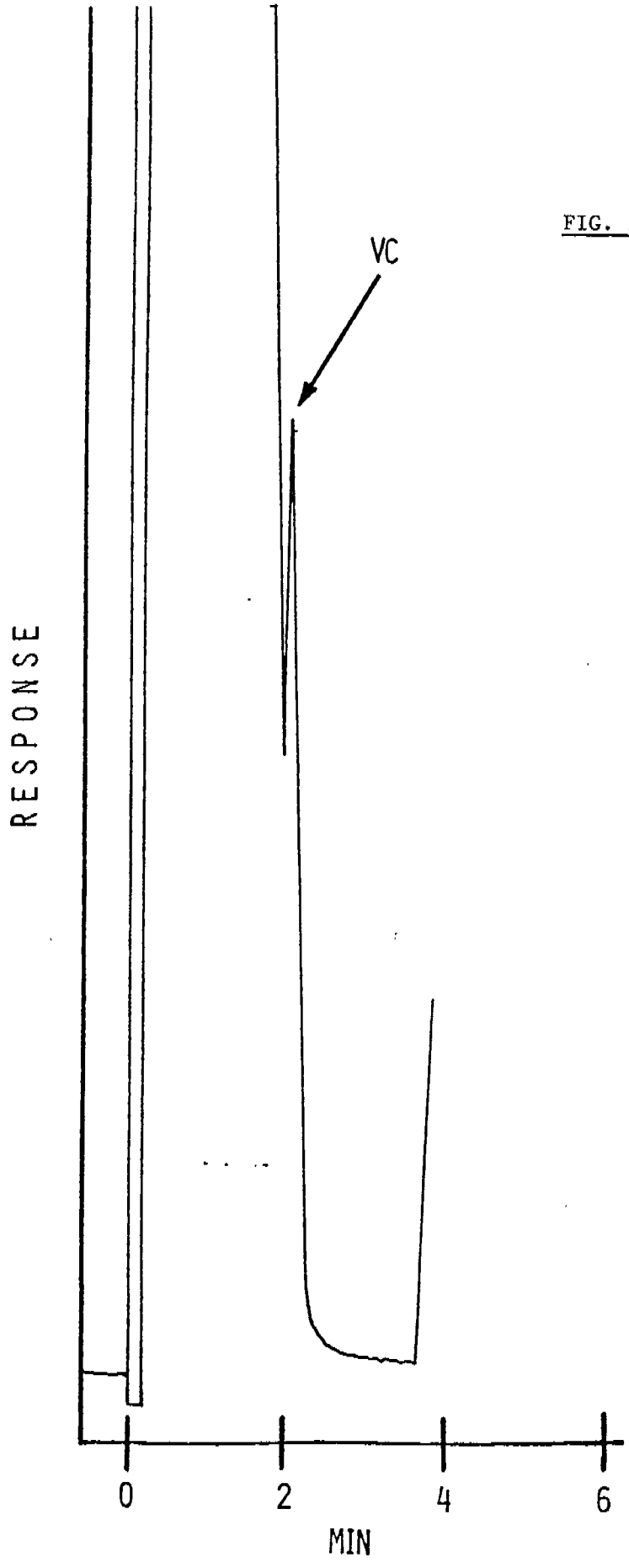

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FIG. 6

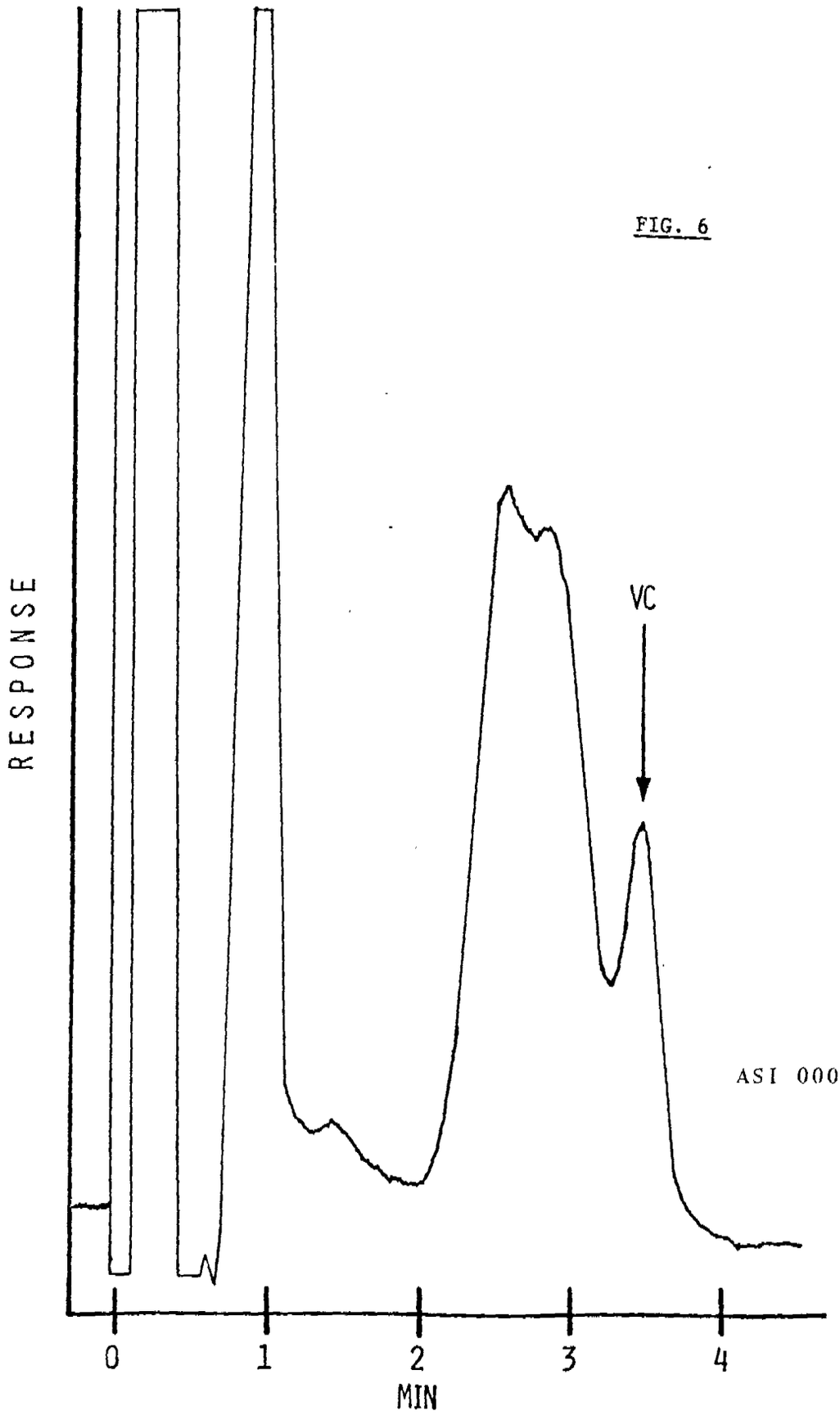

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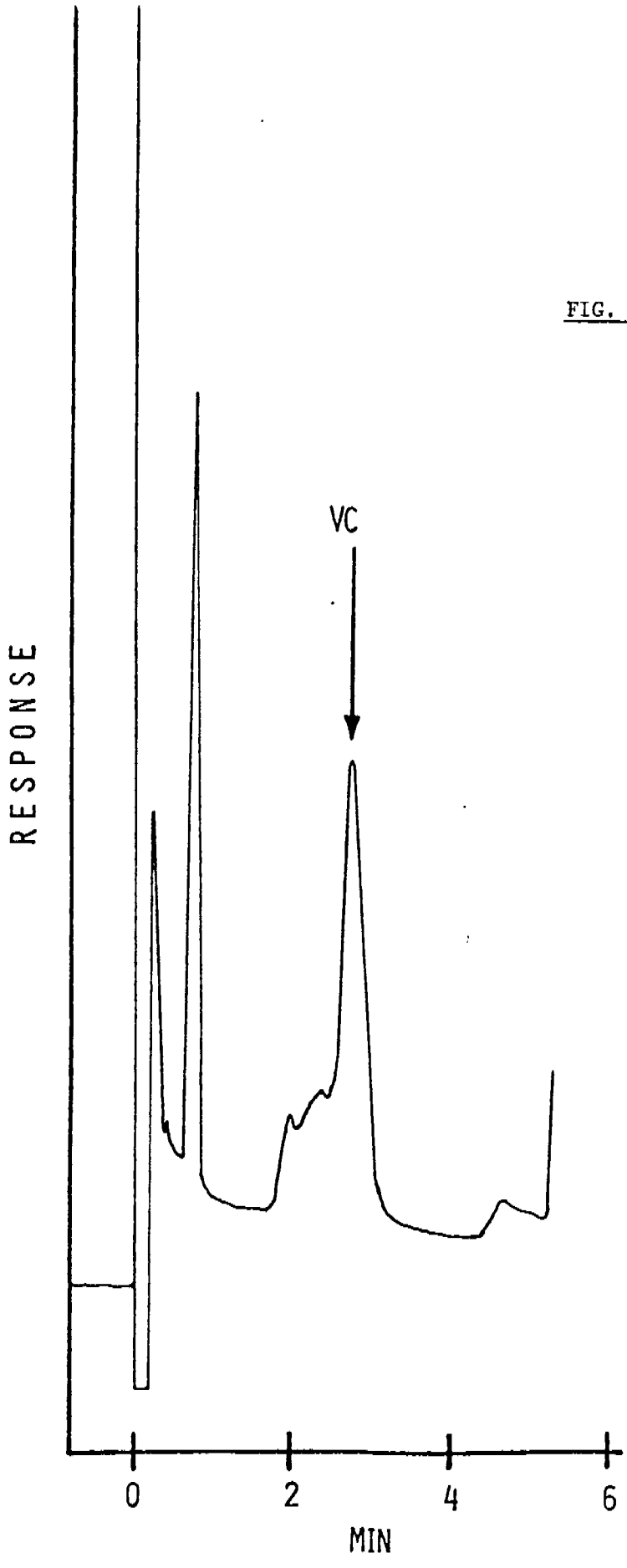
FIG. 7



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December 13, 1976

Mr. Richard J. Ronk
Director
Division of Food and
Color Additives
Food and Drug Administration
200 "C" Street, S.W.
Washington, D.C. 20204

Re: PVC; 90-Week Interim Report of
Two-Year Oral Toxicity Study
Conducted by CIVO-TNO

Dear Mr. Ronk:

Following up on my telephone report to you last week, we are enclosing herewith a copy of the 90-week interim report concerning the chronic oral toxicity study of vinyl chloride now underway at the Central Institute for Nutrition and Food Research (CIVO-TNO) in Holland. Although we received this copy on a confidential basis through informal channels, we felt it necessary and desirable to advise you about it immediately.

Despite the fact that we can see no immediate relevance of a report on a feeding study to the interest of the Environmental Protection Agency or the National Institute of Occupational Safety and Health insofar as their regulatory responsibilities with respect to vinyl chloride monomer are concerned, rather than take any risk that a reporting omission might somehow be misconstrued as constituting some attempt to withhold pertinent data, you will note that copies of this letter and the enclosure have today been sent to the Administrator of the Environmental Protection Agency, Mr. Russell Train,and the Director of the National Institute of Occupational Safety and Health, Dr. John Finklea.

We have heard, but have not confirmed, that various parties have raised questions regarding the actual toxicological data. Consequently, you might wish to follow up on the report and its significance through your own official channels.

Although the enclosed constitutes all the information we now have on this matter, we hope you will not hesitate to contact us if there is anything you feel we can do to be of assistance.

Cordially yours,

Jerome H. Stetkman

Enclosure

cc: Mr. Russell Train
Dr. John Finklea

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Chronic (two-year) oral toxicity study with vinyl chloride in rats

(Interim information III)

1. Conduct of the study

See Interim Information of 15th December 1975, given in Enclosure 1.

Vinyl chloride-treatment by gavage was discontinued in week 84 because the condition of the rats given 300 mg vinylchloride/kg body weight was rapidly declining and mortality in this group was high (55 %). Moreover, most of the rats of this group that died or were killed in extremis showed extensive liver damage (haemorrhages, focal necrosis), liver tumours or tumours at other sites.

2. Results available after a test period of 90 weeks

2.1. Body weights

Not affected.

2.2. Food consumption

Not distinctly affected.

2.3. Mortality

VCM (mg/kg body wt)	Total number of deaths*) at week 90	
	males	females
0	2	5
1	3	4
3	6	16
9	20	40
300 (by gavage)	46	44

*) Initial number of rats: 60 animals/sex/group

2.4. Haematology

Slightly decreased haemoglobin values in males of the 9 mg/kg group after 78 weeks.

2.5. Blood biochemistry

No indications of an adverse effect of vinyl chloride.

See also Interim information II, given in enclosure 2, [illegible]

2.6. Liver function

See Interim information II, given in enclosure 2, § 2.6.

2.7. Urine analyses

No indications of an adverse effect of vinyl chloride.

See also Interim information II, given in enclosure 2, § 2.7.

2.8. Liver and kidney weights

See Interim information II, given in enclosure 2, §2.8.

2.9. Pathology

2.9.1. Rats killed after 26 and 52 weeks

See Interim information II, given in enclosure 2, § 2.9.1

2.9.2. Rats found dead or killed when moribund

See above table for mortality figures.

Gross autopsy findings allow the following preliminary information on both the occurrence of presumable tumours and the number of rats bearing these lesions (in some cases the gross diagnosis was confirmed by histological examination):

Control group:	Thymic tumour	1
	Mammary tumour	1
	Leukaemia	1
	Cervix tumour	1
1 mg/kg group:	Thymic tumour	1
	Uterus tumour	1
	Lymphoreticular tumour	1
	Mammary tumour	1
	Abdominal tumour	1
3 mg/kg group:	Liver nodules (tumours ?)	7
	Subcutaneous tumour	1
	Uterus tumour	1
	Pituitary tumour	1
	Mammary tumour	2
	Ovarian tumour	1

9 mg/kg group:	Liver nodules (tumours ?)
	Pancreas tumour
	Thymic tumour
	Lymphoreticular tumour
	Mammary tumour
	Pituitary tumour
	Subcutaneous tumour
300 mg/kg group:	Liver nodules/haemorrhagic cysts (tumours ??)
	Pancreas tumour
	Pituitary tumour
	Lymphoreticular tumour
	Pulmonary nodules/haemorrhagic lesions (tumou
	Nodules aer-duct area
	Abdominal tumour
	Mammary tumour
	Kidney mass (tumour ?)

3. Preliminary conclusion

From the results so far available it appears that the administration vinyl chloride monomer to rats at levels of 9 (as PVC-powder in diet) and 300 mg/kg body weight (in soyaoil by gavage) resulted in obvious liver ch which in many cases seem to be neoplastic in nature. Moreover, there are i dications that similar lesions also occur at the 3 mg/kg level, but so far are absent at the 1 mg/kg level.