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Description Notes	Includes meeting agenda, list of participants and a phtocopy of Michele Flicker's handwritten notes from the meeting.

DIOXIN DISCUSSION MEETING - VETERANS ADMINISTRATION
Import-Export Building - Room 443
811 Vermont
Washington, D.C.

September 1, 1983

AGENDA

9:30 AM - J. S. Stanley - Opening Remarks, "Status of Adipose Tissue Analysis Programs"

9:45 - A. L. Young, "Status of VA/EPA Efforts in Adipose Tissue Programs"

10:00 - D. Stalling, "Applications of Pattern Recognition for Classification of PCDD/PCDF Data"

10:30 - J. McKinney, "Approaches to Bioincurred TCDD Studies"

11:00 - T. Tiernan, M. Taylor, "Interferences Encountered in the Analysis of Human Adipose Tissues"

11:30 - D. Cox, "Status of Survey Design Using NHMP Adipose Samples"

12:00 PM - Open Discussion

ADIPOSE MEETING

September 1, 1983

Alvin L. Young	VA	Washington, DC	(202) 389-5534
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Larry Keith	Radian	Austin, TX	(512) 454-4797
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Arnold Schecter	Upstate Medical Center - Clinical Campus S.U.N.Y. Binghamton, NY 13901		(607) 798-4809 (607) 772-6067
J. J. Ryan	HPB	Ohawa, ONT	(613) 593-4482
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Lewis Shadoff	Dow Chemical Co.	Midland, MI	(517) 636-5584
Christoffer Rappe	Univ. Umea	S-90187 Umea Sweden	(46) 90-165266
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David Firestone	FDA	Washington, DC	(202) 245-1381
David L. Stalling	USFWS	Columbia Nat. Testing Res. Lab. - Rte. 1 Columbia, MO 65101	(FTS) 276-6399
Ross Norstrom	Com. Wildlife, Sch	Environmental Canada, Ottowa	(613) 997-1410
Michele Flicker	VA	Kansas City, MO	(FTS) 754-1674 (816) 861-4700 ext. 674
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Bob Hill	CDC	Atlanta, GA	(404) 452-4176
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Les Lamparski	Dow Chemical	Midland, MI	(517) 835-6600
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Daniel T. Heggem	EPA	Washington, DC	(202) 382-3582
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REMARKS

Here is a summary of the meeting in note form which I presented to the VA advisory committee on health related effects

(I apologize for the handwriting - I have tried to legibilities - hope this triggers memories of the salient points of the meeting.

I'm working on a typed version but am needing this to expedite available info.

Questions? Before 9/22: FTS 754-1674
After 9/22: (816) 741-5647

FROM

Michele

DATE 9/19/83

TEL. EXT.

VA FORM MAY 1980 3230 — EXISTING STOCKS OF VA FORM 3230, AUG 1976, WILL BE USED. — ☆ U.S. GPO: 1982—508-203

Summary of Dioxin Meeting – presented 9/1/82 to VA Advisory Committee on Health Related Effects of Herbicides

Dioxin — Very recently

Who I am –

VA/EPA coordinated program for the analysis of Dioxin in human adipose Tissue. Purposes – ① Analytical Method ② Detectable in human ③ Higher Levels in male pop'n ④ Correlation with health effects

I. PATTERN RECOGNITION

Highlights

A – Data are now available → Canada
Sweden
Sources
Dioxins, Furans – agents, isomers do exist in the adipose tissue of ordinary citizens
That means we are not merely seeing the Dioxin we know to have been present in Agent Orange, but from other sources – related chemicals
such as fly ash

B – Data also exist which imply a synergism among the chemicals WRT (with respect to) health effects –
Toxicity very much a function of co-
Toxic effects of TCDD (e.g. Teratogenicity)
cleft palate
are magnified many-fold by, for example, the presence of the furans

C – Find higher Dioxin + furans in accidental + occupational exposures

– ∴ Consensus ∴ reached in the panel that our analytic method should be broad enough to be able to detect several of these relatives because such pattern recognition – i.e. analyzing WRT (with respect to) to relative proportions of these related compounds (next sheet)

will enable us to: ① get a handle on the origins - dietary fish vs A.O
② Run a stricter quality control program
~~③ May enable us to~~

II. Bioincurred

Also - because of the global distribution of these chemicals

As part of developing our analytic method, it is also agreed that we ~~should develop~~

Bioincurred Standards

animals fed radioactively labelled representatives of these chemicals so that we can accurately test our methods + calculate yields - not confused by dioxins already "naturally present"

How much is due to exposure vs how much is already there

9 Kg of FAT collected,

In E:
- Dioxin, Furans everywhere
- Analytic Methods will be broader
- Pattern recognition is a valid + necessary tool

Have Started

EPA has begun to ~~analyze~~ identify the adipose tissue in its archives for Vietnam veterans.

Calculations have been completed showing the study is feasible but has many complicating features

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REMARKS

Here are my reworked notes from the Dioxin session.

I hope they are helpful.

Please call me should there be any questions - I have the original copy.

FTS til 9/22 - 754-1674 < at work 10/6

Home 9/22 - 10/5 816-741-5647

FROM

Michele

DATE 9/20/83

TEL. EXT. 674

VA FORM MAY 1960 3230 EXISTING STOCKS OF VA FORM 3230, AUG 1976, WILL BE USED.

☆ U.S. GPO: 1982—508-203

9/1/83 Dioxin Meeting
Washington, D.C.

- Search for methodology
" " baseline

Stanley - Standards
9 Kg Adipose so far — No data on decay of concentration in Adipose tissue

Stalling - Pattern recognition - can be done + very useful for quality assurance as well as recognition + verification of source.
Dunn -> plot conc of arochlors on 3 axes + get pt if 1.0
line (1 factor variable), plane 2 factor variable

Rappe - Human - Serum / Tissue -
Blood - $^{13}C_{12}$ - 2378 TCDD ->

	Yusho		Taiwanese	
Iranian	>12			
	A	B		
2,3 7, 8 Tet CDF	< 3	< 3	< 30	< 30

My note [This is probably fat or blood] ← (I was uncertain which tissue source Rappe was describing)

Decay Rates
occupationally exposed
— 75-85% reduction octa, + hepta in 1 (one) year
in Scandinavia

Yusho - PCB + PCDF
Tissue location
-> 15% reduction } in 1 (one) year
20% reduction }

PCP houses	octa	hept	hexa CDD
	7 PPT	5 ppt	
160:1	14		
165:1	15		

liver / adipose CDF's ~ 2/1

Arnold Frankenberg

Baby

Isomer		Adipose	Liver	Muscle?)	Omentum	Diaphragm?)
2,3,78		17	60			
PCB	ng/g	3.6	27	38	64	48

∴ Different target organs w diff isomers

Swedish, PCDD + (Pg/g) in tissue Mengan Pesticide

(2,4-D 2,4,5-T)

	Liver	Kidney
2,3,78	2(1)	15(1)
Octa-CDD	350 (8)	15(4)
Hepta	?	?

STRIK, Netherlands

	Adipose	Liver	Blood
2,3,78 -	5 PPT	ND	ND
Penta, Hexa, Hepta	?		
Octa	?		
Tetra CDF	?		

} I was unable to copy fast enough

very difficult

c̄ Nordell

2,3,7,8 TCDF	PeCDF PPT	hexa CDF	Σ hexaCDD PPT	hepta CDD	Octa CDD
1	12	9	6	30	150
				56-81	(90-414)

"SAAB" 88

2, 3, 7, 8 - 1.5 PPT

Penta 12 PPT

Hexa-CDD 19

Baltics - Herring, Fish-Eating Bird - Tetra
Penta 1,2,3,7,8
Hexa 1,2,3,4,7,8 -
Furans
2,3,7,8 penta

Yusho liver → 2,3,7,8 - remain of 64 others
(Fish, liver, dioxin ≈ To)

Source of 2,3,7,8 ≠ 2,4,5 T
2,4,5 TP
hexa chlorophen

Comical exposure tetra ≈ penta

Source of Penta 1,2,3,7,8 CDD = Fly Ash ?
∴ Pattern recognition is crucial (crucial)

Bangladesh - 1,500

Nitro → octa CDD 350 (8)] Hijacat liver
Hepta CDF

May be ≠ distribution

∈ Rappe - There is a background but it is complex

McKinney
Biomarkers → during extraction, how much is 2° exposure + how much originally there?
Toxicity ∝ AH receptor + (polarizability) ← electronic
steric - how does the lock go to molecular active site
May want to pattern recognize the toxic compounds vs the source point of Stalling
Toxicity is very much a function of the co-toxins present
(TCDD toxic enhanced by PCB's) PCBs >> Dioxins
e.g. incidence of cleft palate

Chris - Tetrach 1,3,7,8 CDD
Rappe - hexachloro phenoxyphenol acetic esters } Agent Orange
D. Stalling - Very few furans D F ~10 > 1
Phenols + phenoxy phenols are not likely to be stored in adipose because they are readily conjugated + excreted

Don Shadoff → To generate the pattern → feed AO to animals
there exist feeding studies in cattle. 2,3,7,8 →
Saponification will destroy the higher chlorinated dioxins

Firestone - confusing amplifications of Dioxins + Furans in biological tissue

Mike Taylor -
Schecter - Brehm - LLD ~ 10-20 PPT 2° to interference.
Binghamton study:
Found higher Dioxin + furan; exposed people may have had higher levels than control.
Diphenyl ethers are not the major interference.

"Flowers" "weeds"
QA are -> spiked c̄ desired + interferences

Schecter — Dilated ER + microsomal damage in liver bx (biopsy) with ↑ LFT's (elevated liver function tests)
endoplasmic reticulum, microsomal damage

Jake Ryan — variation MS/MS levels -> (8.004 6) range of values on 1 sample
Tandem MS c̄ flash

Advantages
Setup time
Sensitivity
Specificity

Disadvantages
isomer resolution moderate (moderate)
expensive

FAT

Tetra	Penta	Hex	Hepta	Octa
2378 F	D F	D F	D F	D F
10.6 / 2.6	13.1 / 18.4	76 / 15.4	133 / 35	619 ND
				6

	1980	1978
Σ D	801	743
Σ F	71	

(MS)² very good
levels up to PPB.

Joe Carra

Dave Cox - NHMP (National Human Monitoring)

Battelle Columbus (TAC)

- Information retrieval - Toxic + Analysis Samples
- Serum samples come from Vietnam vets
- need to go back to the institutions that the samples were collected to get the ID

- TAC inventory 8,000 persons
- EPA NHATS file 15,000 records TAC information

Birth date / Sex / No SS# (Social security number)

Approach - Mail letters 1937 + 52

MATCH TAC INV. EPA NHATS file

Contact institutions to get SS#

Check VA records

So far 544 potential Vietnam vets - Approx 60 actual veterans

11% samples

92 institutions involved; 22 contacted with 122 records.

50 SS#

Sampling Design: - Age, sex, possible race pair - pull each veteran with a control

- Measure Dioxin levels vet + controls

- Assess statistical significance

Factors affecting detectable ratio (see next page for definition of "detectable ratio")

1. Sample size
2. FP additives due + FN negatives due to falsely conclude vets have higher levels
3. Variable ages of the specimens + no one known effect of storage over time
4. Combined variability - Analytic measurement problem
   - Random variation in dioxin levels.
   - Correlation betw dioxin levels of vets & controls

Detectable ratio = (i.e. ratio of elevated Dioxin levels in vets to controls in order to be detectable + statistically significant)

4.5 → 1.5 Ratio of Dioxin levels detectable

Need sample size of 120 to get a 2 (detectable ratio)

If variability is low, even a sample size of 30 can give useful results

Overall, variability is slightly more important than sample size in determining the detectability ratio.

Question raised over Scalpel objection? differences in manufacture & sterilization procedures

Stan may aware of this as a confounding variable

- Also can ↑ # of controls to improve the ratio

Eventually will or may model on region

Eventually may want to do a ~~metal~~ profile

Concentrations may indeed change in time in the fat samples

Many pit falls — body weight, height

May need a prospective study

Fatty acids marker for example

Total body burden important ← already have this

Q: Does vietnam veteran have > Dioxin?

Does the Dioxin cause a decrement in health?

Someday we may tap into Ranch Hand

Sandra Stroumon Sandy's phone #

352 335 84 11

Shadoff – look for a unique property in AD – such as carbon dating
Type – e.g. phenylene –

Barnes
– National Dioxin Study
–