

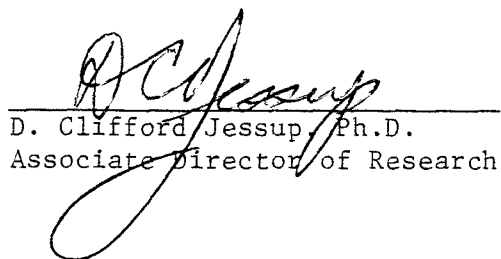
## *International Research and Development Corporation*

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SPONSOR: Velsicol Chemical Corporation  
TEST MATERIAL: Tetrabromobisphenol A  
SUBJECT: Modified Draize Multiple Insult  
Test in Humans.



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I. SYNOPSIS

Fifty-five male and female human volunteer subjects were used to examine the irritation and contact sensitization potential of Tetra-bromobisphenol A.

A modified Draize Multiple Insult Test was conducted. Tetra-bromobisphenol A produced no significant irritation and gave no evidence of contact sensitization in the 54 subjects who completed the study.

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### II. TEST MATERIAL

The test material was received from the Velsicol Chemical Corporation, Chicago, Illinois on October 28, 1977. It was identified as "Tetrabromobisphenol A, Lot 1021 - 85" and was received as a white powder.

III. METHOD

Fifty-five male and female human volunteers were used for this study. The subjects used consisted of a cross-section of the available population and were as follows:

Sex: Male (26%), Female (74%)

Race: White (78%), Black (13%), Oriental (9%)

Age: Average age 39.3 years, range 18 to 74 years

Tetrabromobisphenol A was mixed with water to produce a thick slurry (50-70% concentration) of paste like consistency. Approximately 3 to 5 milligrams of the test material was applied with a spatula to a tape identified as "clinical plastic patch", which was obtained from Johnson and Johnson. The tape, which was occlusive, was applied to the upper arm of each volunteer. Because of the location of the application site, it was not necessary to shave the site. If the tape did not readily stick to the arm, it was sprayed with Hollister Medical Adhesive. The test sites were approximately 15 millimeters square and were not abraded. The test material was applied fresh every other day or every third day (total application period 48 to 72 hours) for a total of 10 applications. Following each application period, any excess test material was wiped off, and the site was scored in accordance with the scale on page 4. The same site was used for each of the 10 applications.

Following the last (10th) application, a rest period of 10-14 days was introduced. Following the rest period, the volunteers were re-exposed to the test material.

For the challenge dose, the test material was applied in a manner identical to that used for the 10 sensitizing doses. A different application site was used for the challenge dose and following the 48 hour application period, the site was examined at 48 and 72 hours. Whenever a questionable reaction occurred, the subject was retested one week later, at another site, in exactly the same manner.

SCORING CODE FOR MODIFIED DRAIZE MULTIPLE INSULT TEST IN HUMANS

- 0 - No reaction
- + - - Questionable reaction<sup>a</sup>
- 1 - Erythema to half the area
- 2 - Erythema and Slight Edema to the full patch test area
- 3 - Beginning denudation<sup>b</sup>
- 4 - Denuded skin surface<sup>c</sup>
- H - Healing
- X - Patch not applied

<sup>a</sup>This score is used to indicate a reaction whose presence is questionable or a reaction which is not considered a true irritant reaction (e.g. tape or pressure reaction).

<sup>b</sup>This score is evidenced by the stratum corneum and upper epidermal cells beginning to slough off.

<sup>c</sup>This score is given when the stratum corneum has completely sloughed off. When a score of 4 occurs patching is stopped at the site until it heals.

IV. RESULTS (Tables 1 and 2)

Fifty-five healthy subjects were screened for the study and fifty-four completed the study period. During the sensitizing phase of the study, one subject (#18) exhibited a 1+ irritant reaction which was considered low-grade and hardly notable. Three other subjects exhibited  $\frac{+}{-}$  reactions at varied times during the study period.

In the challenge (elicitation) phase of the study, one subject (#28) showed a low grade (1+) erythema reaction when the patch was removed and this rapidly healed. It was considered to be an irritant reaction aggravated by tape. None of these reactions appeared allergic in nature; all were considered superficial burns.

V. CONCLUSION

Tetrabromobisphenol A produced almost no irritant reactions during the sensitizing phase and gave virtually no responses that were considered irritant or allergic in the challenge phase in 54 subjects who completed the study. These results suggest that this material should be well tolerated when applied to human skin.



## Modified Draize Multiple Insult Test in Humans with Tetrabromobisphenol A.

TABLE 1.

Test Designation: WLE 12.

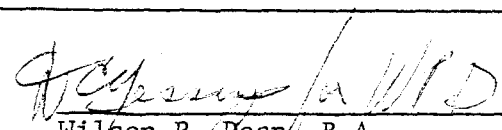
Subject		Personal Subject Data			Challenge Dose Results	
No.	Name	Race	Age	Sex	48 hours	72 hours
1.	Zoe Vivier	W	74	F	0	0
2.	Kendra Schmidt	W	34	F	0	0
3.	Barbara Kearney	W	27	F	0	0
4.	Mary Labagh	W	59	F	0	0
5.	David Jaramillo	W	65	M	0	0
6.	Ramon Quinonez	W	22	M	0	0
7.	Rafael Salinsa	W	66	M	0	0
8.	Joan Smith	W	36	F	0	0
9.	Robert Jovez	Or	18	M	0	0
10.	Nancy Singleton	W	36	F	0	0
11.	Ned Mabanglo	Or	23	M	0	0
12.	Linda Ralls	W	21	F	0	0
13.	CANCEL					
14.	Anne Fisher	W	50	F	0	0
15.	Georgia Vhalos	W	40	F	0	0
16.	Joey Shelton	W	23	M	0	0
17.	Steve Brice	W	26	M	0	0
18.	Happy Kramer	W	41	F	0	0
19.	Susan Lucey	W	28	F	0	0
20.	Evelyn Sanchez	Or	25	F	0	0
21.	Carmen Cortez	W	69	F	0	0
22.	Mary Lawrince	W	19	F	0	0
23.	Esther Magarice	W	63	F	0	0
24.	Joan Knutson	W	41	F	0	0
25.	Mary Brunner	W	46	F	0	0
26.	Patrisa Romeroz	W	50	F	0	0
27.	Angela Dinkas	B	20	F	0	0
28.	Ina Kellman	W	50	F	1/1H	0
29.	Mary Fergus	W	35	F	0	0
30.	Elizabeth Flenning	W	68	F	0	0
31.	Margaret Casey	W	39	F	0	0
32.	Eileen O'Sullivan	W	52	F	0	0
33.	Kathy Cavalli	W	35	F	0	0
34.	Marian Sullivan	W	36	F	0	0
35.	Jeanne Haugh	W	32	F	0	0
36.	Susan Thomas	W	26	F	0	0
37.	Kathleen Maning	W	38	F	0	0
38.	Lawrence Toyooka	Or	50	M	0	0
39.	Lynn Schmidlapp	W	27	M	0	0
40.	Marta Flores	B	20	F	0	0
41.	Shirldy O'Connor	W	60	F	0	0
42.	Barbara Paganini	W	30	F	0	0

W - White

B - Black

Or - Oriental (Includes Phillipino)

H - Healed

  
 Wilson P. Dean, B.A.

 Director of Acute Toxicology  
 and Special Studies  
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## Modified Draize Multiple Insult Test in Humans with Tetrabromobisphenol A.

TABLE 1 (Cont.)

Test Designation: WLE 12.

Subject		Personal Subject Data			Challenge Dose Results	
No.	Name	Race	Age	Sex	48 hours	72 hours
43.	Joan McKeever	W	41	F	0	0
44.	Muriel Strauss	W	36	F	0	0
45.	Versey Tuggle	B	56	F	0	0
46.	Carlos Jones	B	21	M	0	0
47.	Herschel Jones	B	21	M	0	0
48.	Katharine Shea	W	39	F	0	0
49.	Nedra Neeland	W	43	F	0	0
50.	Clotilde Peebles	W	54	F	0	0
51.	Mary Lou Orley	W	25	F	0	0
52.	Jessie Washington	B	21	M	0	0
53.	Brooks Peebles	B	67	M	0	0
54.	Byron Blackwell	W	36	M	0	0
55.	Barbara Hom	Or	41	F	0	0

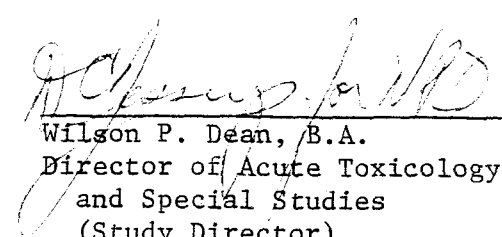
W - White

B - Black

Or - Oriental (Includes Phillipino)

H - Healed

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Modified Draize Multiple Insult Test in Humans with Tetrabromobisphenol A.

TABLE 2.

Individual Scores.

Subject			Sensitizing Dose Results										Challenge Dose Results	
No.	Name	Dose #	1	2	3	4	5	6	7	8	9	10	48 hours	72 hours
1.	Zoe Vivier		0	0	0	0	0	0	0	0	0	0	0	0
2.	Kendra Schmidt		0	0	0	0	0	0	0	0	0	0	0	0
3.	Barbara Kearney		0	0	0	0	0	0	0	0	0	0	0	0
4.	Mary Labagh		0	0	0	0	0	0	0	0	0	0	0	0
5.	David Jamarillo		0	0	0	0	0	0	0	0	0	0	0	0
6.	Ramon Quinonez		0	0	0	0	0	0	0	0	0	0	0	0
7.	Rafael Salinsa		0	0	0	0	0	0	0	0	0	0	0	0
8.	Joan Smith		0	0	0	0	0	0	0	0	0	0	0	0
9.	Robert Jovez		0	0	0	0	0	0	0	0	0	0	0	0
10.	Nancy Singleton		0	0	0	0	0	0	0	0	0	0	0	0
11.	Ned Mabanglo		0	0	0	0	0	0	0	0	0	0	0	0
12.	Linda Ralls		0	0	0	0	0	0	0	0	0	0	0	0
13.	CANCEL													
14.	Anne Fisher		0	0	0	0	0	0	0	0	0	0	0	0
15.	Georgia Vhalos		0	0	0	0	0	0	0	0	0	0	0	0
16.	Joey Shelton		0	0	0	0	0	0	0	0	0	0	0	0
17.	Steve Brice		0	0	0	0	0	0	0	0	0	0	0	0
18.	Happy Kramer		0	0	0	+	-	1	1	+	-	0	0	0
19.	Susan Lucey		0	0	0	0	0	0	0	0	0	0	0	0
20.	Evelyn Sanchez		0	0	0	0	0	0	0	0	0	0	0	0
21.	Carmen Cortez		0	0	0	0	0	0	0	0	0	0	0	0
22.	Mary Lawrince		0	0	0	0	0	0	0	0	0	0	0	0
23.	Esther Margarice		0	+	-	+	-	+	-	0	0	0	0	0
24.	Joan Knutson		0	0	0	0	0	0	0	0	0	0	0	0
25.	Mary Brunner		0	0	0	0	0	0	0	0	0	0	0	0
26.	Patrisa Romeroz		0	0	0	0	0	0	0	0	0	0	0	0
27.	Angela Dinkas		0	0	0	0	0	0	0	0	0	0	0	0
28.	Ina Kellman		0	0	0	0	0	0	0	0	0	0	1/1H*	0
29.	Mary Fergus		0	0	0	0	0	0	0	0	0	0	0	0

\* This score indicates at a 1+ reaction was observed at 48 hours which had healed by 72 hours.

Modified Draize Multiple Insult Test in Humans with Tetrabromobisphenol A.

TABLE 2. Cont.

Individual Scores.

Subject			Sensitizing Dose Results										Challenge Dose Results	
No.	Name	Dose #	1	2	3	4	5	6	7	8	9	10	48 hours	72 hours
30.	Elizabeth Flenning		0	0	0	0	0	0	0	0	0	0	0	0
31.	Margaret Casey		0	0	0	0	0	0	0	0	0	0	0	0
32.	Eileen O'Sullivan		0	0	0	0	0	0	0	0	0	0	0	0
33.	Kathy Cavalli		0	0	0	0	0	0	0	0	0	0	0	0
34.	Marian Sullivan		0	0	0	0	0	0	0	0	0	0	0	0
35.	Jeanne Haugh		0	0	0	0	0	0	0	0	0	0	0	0
36.	Susan Thomas		0	0	0	0	0	0	0	0	0	0	0	0
37.	Kathleen Maning		0	0	0	0	0	0	0	0	0	0	0	0
38.	Lawrence Toyooka		0	0	0	0	0	0	0	0	0	0	0	0
39.	Lynn Schmidlapp		0	0	0	0	0	0	0	0	0	0	0	0
40.	Marta Flores		0	0	+	-	0	0	0	0	0	0	0	0
41.	Shirldy O'Conner		0	0	+	-	0	0	0	0	0	0	0	0
42.	Barbara Paganini		0	0	0	0	0	0	0	0	0	0	0	0
43.	Joan McKeever		0	0	0	0	0	0	0	0	0	0	0	0
44.	Muriel Strauss		0	0	0	0	0	0	0	0	0	0	0	0
45.	Versey Tuggle		0	0	0	0	0	0	0	0	0	0	0	0
46.	Carlos Jones		0	0	0	0	0	0	0	0	0	0	0	0
47.	Herschel Jones		0	0	0	0	0	0	0	0	0	0	0	0
48.	Katharine Shea		0	0	0	0	0	0	0	0	0	0	0	0
49.	Nedra Neeland		0	0	0	0	0	0	0	0	0	0	0	0
50.	Clotilde Peebles		0	0	0	0	0	0	0	0	0	0	0	0
51.	Mary Lou Orley		0	0	0	0	0	0	0	0	0	0	0	0
52.	Jessie Washington		0	0	0	0	0	0	0	0	0	0	0	0
53.	Brooks Peebles		0	0	0	0	0	0	0	0	0	0	0	0
54.	Brian Blackwell		0	0	0	0	0	0	0	0	0	0	0	0
55.	Barbara Hom		0	0	0	0	0	0	0	0	0	0	0	0