LEVELS OF CHLORINATED PESTICIDES IN THE SERA OF OCCUPATIONALLY EXPOSED SPRAYMEN IN VENEZUELA, 1984[1]

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INTRODUCTION

Since 1945, Venezuela's antimalaria programs have used three chlorinated insecticides—first DDT, then HCH and dieldrin. Because of their high degree of chemical and physical stability, these products tend to remain in the environment—to such an extent that virtually no place or organism can escape exposure to them.

Such chlorinated insecticides continue to constitute key tools for many vector control programs—especially those directed against malaria mosquitoes. However, application of any residual insecticide spray inside dwellings (as in antimalaria programs) inevitably involves considerable exposure of the applicators and measurable exposure of the inhabitants of sprayed dwellings. With regard to applicators, their contact with the insecticide is commonly much more prolonged in public health activities than in agricultural activities, and it is common for a single chemical to be applied by the same individuals for extended periods, sometimes exceeding 15 years.

In many parts of the world, studies of residual levels of these toxic substances in the environment, foods, directly exposed people, and indirectly exposed people have indicated levels of contamination that have encouraged restrictions on the manufacture and use of these products. However, countries such as ours that are currently battling malaria with limited resources have no good alternative to using pesticides such as DDT that are the most economical and effective to be had. Hence, procurement of appropriate information and proper training of spraymen and their supervisors in the safe use of these pesticides are our first real lines of defense against the health risks involved.

In this vein, the necessarily prolonged use of chlorinated pesticides in our programs and the risks to which they expose our sprayers justifies studying the actual contamination levels found in groups of people subjected to varying degrees of exposure. This article

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reports the results of serologic assessments made to determine the levels of DDT and its metabolites, dieldrin, and the gamma isomer of HCH in workers occupationally exposed to these pesticides during domiciliary spraying activities. The principal aim of the assessments was to determine the levels of DDT and its metabolites that were present in professionals exposed in the course of domiciliary spraying activities.

MATERIALS AND METHODS

Serum samples were obtained from 289 full-time professional spraymen occupationally exposed to DDT who were selected from the 13 federal departments where malaria had been eradicated (Area 1) or where attack phase antimalaria activities were underway (Area 2). The sera were obtained monthly by personnel of the Toxicology Service and were analyzed within 30 days. The numbers of workers (all men) tested in the various departments involved are shown in Table 1.

The DDT and DDT metabolites in these sera were extracted and measured according to the method described by Dale et al. *(1)*.

Each blood sample was centrifuged for 10 minutes at 3,000 rpm, and the sera obtained were stored in test tubes at −15°C.

A portion (0.5 ml) of each serum was subsequently transferred to a 15 ml centrifuge tube, an equal volume of formic acid was added, and the tube was agitated for one minute. Hexane (2.5 ml) was then added, and the tube was again agitated for one minute. The phases were allowed to separate, after which the tube was agitated for another minute before being centrifuged for three to five minutes to re-separate the phases.

TABLE 1. Serum samples obtained from occupationally exposed workers in places where malaria had been eradicated (Area 1) or where attack phase antimalaria activities were underway (Area 2), by department.

Area	Federal department	No. of serum samples
1	Anzoátegui	25
1	Aragua	9
1	Cojedes	9
1	Federal District	10
1	Miranda	7
1	Trujillo	23
2	Amazonas	25
2	Apure	29
2	Barinas	44
2	Bolívar	22
2	Mérida	23
2	Táchira	19
2	Zulia	47

After this the hexane layer was carefully transferred to another centrifuge tube, another 2.5 ml of hexane were added to the tube with the serum, and the extraction was repeated. The two hexane extracts were then mixed, 0.5 ml of a 5% potassium carbonate solution was added to the extract, this mixture was agitated for one minute, 4 ml of the hexane layer were transferred to another 15 ml centrifuge tube, and the solvent was carefully evaporated in a water bath at 60–70°C until dry. More hexane (1 ml) was then added to the tube, which was agitated again for one minute, and one microliter (or more, depending on the response obtained) was injected into the chromatograph *(1, 2)*.

RESULTS AND DISCUSSION

Table 2 shows the range, arithmetic mean, and standard error for serum levels of DDT, DDE (DDT's principal metabolite),[4] dieldrin, and the gamma isomer of HCH expressed in parts per billion (corresponding to micrograms per liter of serum) in the study subjects' sera, by department. The location of each of these departments and the status of malaria eradication efforts in Venezuela as of 1983, the year before the serum samples were obtained, are shown in Figure 1. Regarding HCH and dieldrin, chromatogram curves characteristic of these products were found in some samples during the course of the analysis. All of these samples were obtained from spraymen in departments where the national Chagas' disease control program was being conducted.

Figure 2 shows the serum levels of total DDT,[5] expressed in parts per billion (ppb), that were found in the sera studied by department, listing the departments by ascending serum levels. The average serum levels found ranged from 23 ppb in Miranda to 1,850 ppb in Bolívar. To understand these variations, one must consider the amounts of DDT previously used in the antimalaria campaign in different departments, as well as the intensity and duration of the study subjects' exposure to it.

Overall, during the 1973–1983 period the amount of DDT used by the antimalaria campaign declined significantly (Table 3). In general, however, far greater amounts were used by departments in Area 2 than by those in Area 1, as indicated in Table 4. Also, in most cases the average serum levels of DDT and DDE that were found in the spraymen studied appeared to correspond to the amount of DDT being used in the departments where they were occupationally exposed (see Table 4). The main exception occurs in the case of Apure, where the average serum level appears high relative to the amount of DDT applied. This suggests unusually great exposure of the Apure workers for unknown reasons that could include neglect of safety measures, improper use of protective devices, faulty equipment maintenance, or poor personal hygiene.

Table 5 compares the average levels of DDT and DDE found in study sera from Area 1 and Area 2. Overall, the average level found in the Area 2 sera (1,067 ppb) was five times the average Area 1 level (213 ppb).

If we group the Area 1 and Area 2 workers by years of contact with DDT, as in Table 6, it appears that the serum levels were substantially higher in the workers exposed for longer times.

Regarding past and recent exposure, the data in Table 5 indicate that DDE accounted for 78% of the DDT and DDE encountered in Area 1 sera. This suggests past exposure levels were relatively high. In addition, the average levels of p,p'DDT found in these sera (44 ppb) were relatively low, indicating

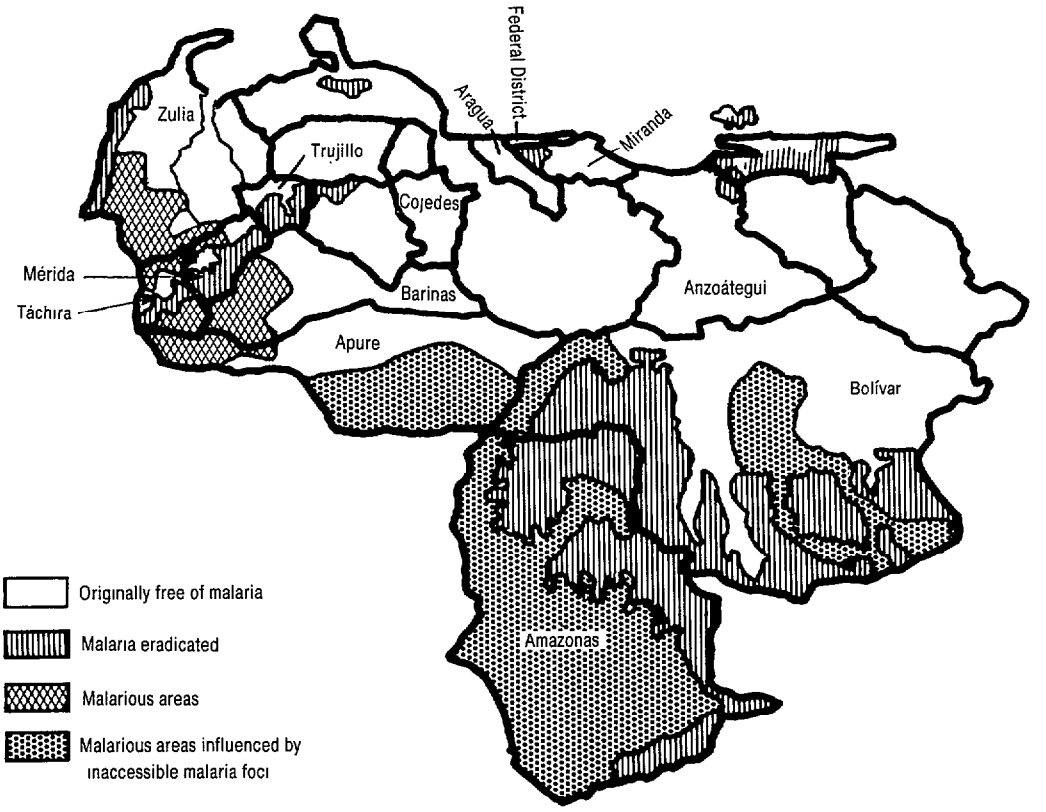
[4] The principal metabolite of DDT (p,p'DDT) detected was DDE. Trace amounts of o,p DDT were found, but these were so small that they have not been included in the data presented.

[5] Pure DDT is 1,1,1-trichloro-2,2-bis(p-chlorophenyl) ethane, also known as p,p'dichlorodiphenyltrichloroethane, or more simply as p,p'DDT. In the human organism, and also in DDT-resistant insects, it is transformed into p,p'DDE (p,p'dichlorodiphenylethylene) with liberation of HCl from the molecule. The sum of p,p'DDE (converted to DDT) and of p,p'DDT gives the "total DDT" figure shown in Table 2.

TABLE 2. Concentrations of dieldrin, HCH (gamma isomer), DDT, and DDT metabolites found in sera from the 289 study subjects, by department and area.

Area	Department	Parts per billion (ppb) of: HCH (gamma isomer) Range	HCH (gamma isomer) $\bar{X}$±S.E.	Dieldrin Range	Dieldrin $\bar{X}$±S.E.	DDT and its metabolites: p,p′DDT Range	p,p′DDT $\bar{X}$±S.E.	p,p′DDE Range	p,p′DDE $\bar{X}$±S.E.	DDE as DDT Range	DDE as DDT $\bar{X}$±S.E.	Total DDT Range	Total DDT $\bar{X}$±S.E.	DDE in total DDT (%)
1	Anzoátegui (N=25)	3–77	5±4	5–34	14±3	12–244	68±12	25–456	106±21	12–508	120±23	27–546	186±29	65%
1	Aragua (N=9)	11–103	28±11	22–182	81±18	19–107	49±10	39–218	113±20	43–243	126±20	62–312	176±30	72%
1	Cojedes (N=9)	8–90	17±10	3–140	53±14	0–34	8±4	11–156	46±15	12–174	52±16	12–193	59±18	88%
1	Federal District (N=10)	—	—	3–18	4±2	8–28	12±3	6–64	18±17	6–71	21±20	6–99	32±27	66%
1	Miranda (N=7)	—	—	22–98	46±26	8–12	10±2	4–22	12±93	5–23	13±8	12–32	23±10	57%
1	Trujillo (N=23)	0–14	2±1	9–290	49±12	18–138	38±8	19–750	186±36	21–840	228±39	21–879	266±43	86%
2	Amazonas (N=25)	—	—	—	—	41–384	113±18	46–568	186±26	52–633	207±28	119–812	320±40	64%
2	Apure (N=29)	—	—	—	—	83–2,267	436±46	93–2,369	664±107	104–2,641	800±120	231–4,907	1,230±197	65%
2	Barinas (N=44)	2–79	6±3	—	—	27–1,840	318±46	23–2,490	588±90	199–2,776	618±95	614–4,540	941±131	66%
2	Bolívar (N=22)	—	—	—	—	194–3,450	895±173	95–2,640	859±134	106–2,940	957±149	300–6,390	1,850±294	52%
2	Mérida (N=23)	—	—	8–84	49±10	52–1,854	305±78	48–1,161	415±68	54–1,290	468±70	106–3,114	772±143	61%
2	Táchira (N=19)	—	—	—	—	26–1,523	284±77	38–1,780	186±93	42–1,989	459±104	69–3,510	744±180	62%
2	Zulia (N=47)	—	—	—	—	44–1,020	213±30	30–925	255±30	31–1,030	272±30	81–1,768	485±56	56%

FIGURE 1. A map of Venezuela showing the departments where study subjects were occupationally exposed and the status of antimalaria efforts as of 1983, the year before the serum samples were obtained.



that recent exposure levels were minimal—as was to be expected in places where malaria had been eliminated.

The Area 2 sera showed a somewhat different pattern. DDE still accounted for a fairly high share (60%) of the total DDE and DDT found; but the average levels of DDT encountered were relatively high (423 ppb). Hence, the data indicate that recent as well as past exposure levels of the Area 2 spraymen had been relatively high—a reasonable finding for places with attack phase activities underway.

Departmental data on recent and past DDT exposure, as indicated by DDT and DDE serum levels, are shown in Figure 3.

Regarding dieldrin, serum samples from 103 occupationally exposed workers participating in Chagas' disease control programs in seven departments (see Table 2) were examined for this pesticide. Levels of dieldrin found in these sera ranged from 3 to 290 parts per billion, the average serum level being 30 ppb with a standard error of ± 4 ppb. The amount of dieldrin applied in the 1973–1983 period in these departments was 168,946 kg, the average annual amount being 15,359 kg.

FIGURE 2. Parts per billion of DDT and DDT metabolites as total DDT (see Table 2) in the sera of occupationally exposed study subjects, by department.

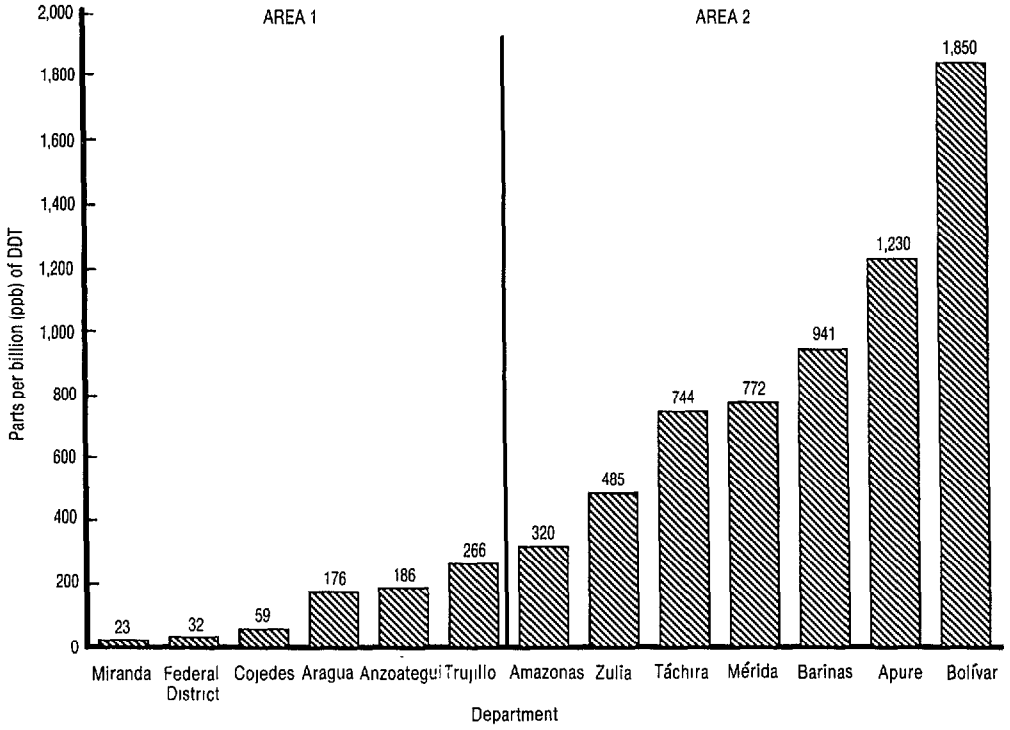


TABLE 3. Technical grade DDT (kg) and 5% DDT suspension (liters) used in the years indicated by Venezuela's antimalaria campaign.

Year	Technical grade (kg)	5% suspension (liters)
1973	234,125	5,697,105
1974	244,134	5,517,378
1975	287,807	5,784,163
1976	294,311	5,941,542
1977	270,316	5,415,317
1978	244,423	4,958,742
1979	223,206	4,464,247
1980	214,014	4,366,847
1981	182,547	3,778,746
1982	165,496	3,431,918
1983	137,902	2,756,654
Total	2,498,281	52,112,659
Annual average	227,116	4,737,514

Regarding HCH (the gamma isomer), the serum samples tested came from 107 occupationally exposed workers in the states of Anzoátegui, Aragua, Barinas, Cojedes, and Trujillo. The serum levels found ranged from 2 to 103 ppb, the average being 10 ppb with a standard error of ± 2 ppb. The amount of HCH used in these departments in 1973–1983 was 153,189 kg, the annual average being 13,926 kg.

TABLE 4. DDT applied and serum concentrations found in Area 1 and Area 2 spraymen, by department. The amounts applied are the average number of liters of 5% DDT applied per year in 1973–1983. The serum levels are the average amounts of DDT plus metabolites in parts per billion that were found in the study sera.

Area 1			Area 2		
Department	Liters of 5% DDT applied (annual average, 1973–1983)	Serum level in ppb of DDT and metabolites (departmental averages of spraymen studied)	Department	Liters of 5% DDT applied (annual average, 1973–1983)	Serum level in ppb of DDT and metabolites (departmental averages of spraymen studied)
Miranda	21	23	Amazonas	153,000	320
Federal District	25	32	Apure	421,000	1,230
Cojedes	115	59	Zulia	511,000	485
Aragua	2,500	176	Táchira	513,000	744
Anzoátegui	83,000	186	Mérida	516,000	772
Trujillo	151,000	266	Barinas	930,000	941
			Bolívar	972,000	1,850
Multistate averages	236,611			4,242,661	

CONCLUSIONS

To help assess the average daily amount of DDT absorbed by our Area 1 and Area 2 spraymen, who had been subjected to prolonged contact with the insecticide, we estimated the approximate concentrations of DDT in their adipose tissue. This was done by multiplying the average serum concentration of total DDT by 344—a factor found by various authors *(3, 4)* to express the ratio between the DDT level in adipose tissue and that in blood serum among individuals who had worked for five years or more in factories where DDT was synthesized or where DDT formulations were prepared. Based upon the concentrations estimated for adipose tissue, we estimated the daily absorption of total DDT in mg per man using Durham's graph *(5)*. The results, shown in Table 7, indicate that the Area 1 study subjects were absorbing DDT at an average rate of approximately 5 mg per day, while for those in Area 2 the daily absorption rate was approximately 55 mg per day.

The implications of this are hard to gauge from the literature, because of the broad range of values spanned by different standards. According to a joint FAO/WHO Expert Committee on Pesticide Residues convened in 1970 *(6)*, the maximum acceptable daily intake of DDT for humans is 0.35 mg per individual (based on an average weight of 70 kg). This is approximately one fourteenth of the estimated daily intake (5 mg) of the Area 1 spraymen and one one-hundred-and-fifty-seventh of the estimated daily intake (55 mg) of the Area 2 spraymen.

TABLE 5. Average levels of DDT and DDE (parts per billion) that were found in the sera of spraymen occupationally exposed in the two study areas.

Area	DDT (ppb)	DDE (ppb)	DDE as DDT (ppb)	Total DDT (ppb)	DDE in total DDT
Area 1	44	149	166	213	78%
Area 2	423	572	638	1,067	60%

TABLE 6. Comparison of DDT and DDE levels in sera of Area 1 and Area 2 spraymen exposed for different lengths of time.

Years of contact	Compound	Area 1 sera (average ppb±S.E.; N=80)	Area 2 sera (average ppb±S.E.; N=209)
1–5	DDT	36±5	259±23
	DDE	77±12	362±37
	Total DDT (ppb)	122±17	662±60
6–10	DDT	52±12	396±72
	DDE	222±52	496±61
	Total DDT (ppb)	299±62	949±135
11–15	DDT	—	614±113
	DDE	—	859±137
	Total DDT (ppb)	—	1,572±204

On the other hand, Ferreira de Almeida *(2)* indicate that the smallest one-time dose producing clinical signs and symptoms of intoxication in humans is 10 mg/kg (equivalent to 700 mg for a 70 kg sprayman). Information provided by this and other sources *(4, 7)*, together with the fact that toxicologic medical examinations of the occupationally exposed spraymen revealed no signs or symptoms of intoxication, seem to suggest that the estimated average dose of 55 mg per man per day posed no substantial health hazards.

With respect to the other pesticides tested, the observed serum levels of dieldrin (averaging 30 ppb) were high relative to levels found in the sera of occupationally exposed workers in the United States—levels averaging 2.3 ppb *(8)*. However, they were considerably lower than levels averaging 490 ppb that were found in sera from occupationally exposed farm workers in São Paulo, Brazil *(9)*. In this same vein, the average serum level of the gamma isomer of HCH (10 ppb) was somewhat higher than the average level found in the sera of occupationally exposed U.S. workers (2.9 ppb) and also higher than the average level found in members of the general U.S. population (1.2 ppb).

FIGURE 3. Average levels (parts per billion) of DDT and DDE found in the study sera, by department. Levels of DDT indicate recent levels of exposure, while levels of the metabolite DDE indicate past exposure levels.

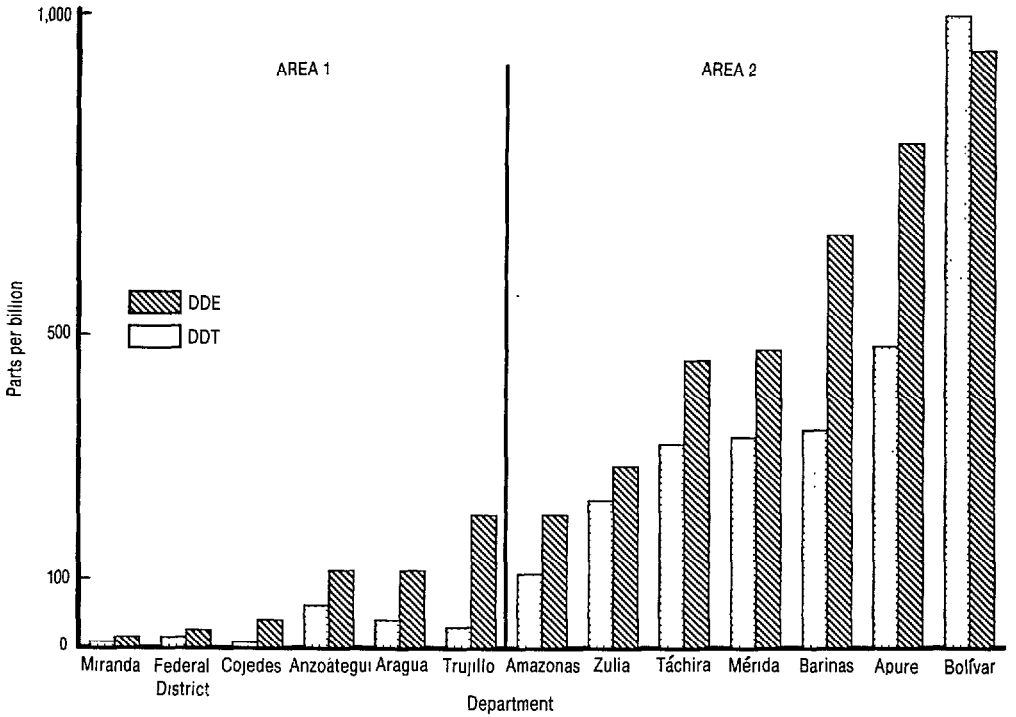


TABLE 7. Assessment of average daily DDT absorption by the Area 1 and Area 2 spraymen tested, based on their average levels of serum DDT and DDE.

Area	Average DDE and DDT as total serum DDT (ppb)	Estimated DDT in adipose tissue (ppm)	Estimated average daily DDT absorption (mg per man)
Area 1	213	73	5
Area 2	1,067	367	55

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Summary

A serologic analysis was made of Venezuelan spraymen in 13 geographic departments who had been occupationally exposed to the chlorinated hydrocarbon pesticides DDT, dieldrin, and HCH through house spraying activities.

Regarding DDT, 80 samples were obtained from spraymen in departments where malaria had been eradicated and 209 were obtained from spraymen in departments where attack phase activities were underway. The average level of DDT (as DDT and the metabolite DDE) found in the 80 sera was 213 parts per billion, while the average level found in the 209 sera was 1,067 parts per billion. Absorption figures based on these findings appear to exceed levels considered acceptable by a WHO Expert Committee in 1970 *(6)*, but below levels known to induce clinical symptoms of poisoning in humans *(2, 4, 7)*.

Regarding serologic levels of dieldrin and the gamma isomer of HCH, 103 dieldrin applicators in Bolívar Department were found to have average serum levels of that pesticide that were above the average serum levels found among occupationally exposed U.S. workers but considerably below levels found in Brazilian agricultural workers. Similarly, 107 HCH applicators were found to have serum HCH levels exceeding the average serum HCH levels found among occupationally exposed U.S. workers.

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