since the Giant Fell

Federal investigators uncovered evidence in 1975 that the then commercial chemical-testing goliath Industrial Bio-Test Laboratories (IBT) was doctoring data. IBT's questionable test results continue to haunt the government.

BY LINDA GARMON

Joseph Calandra, Moreno Keplinger, Paul Wright and James Plank are the most recent reminders of a fallen giant. The four — indicted June 22 by a federal grand jury in Chicago on counts of giving false documents to the government and mail and wire fraud — are former employees of Industrial Bio-Test Laboratories Inc., of Northbrook, Ill.

In its heyday, IBT was one of the largest of some 200 independent labs that test the safety of new drugs, cosmetics, pesticides, plastics and food additives. In 1975, however, a U.S. Food and Drug Administration official fortuitously (the official apparently pulled an IBT file by mistake when checking a potential problem with another laboratory) discovered "serious deficiencies" in one of that lab's studies. More spot checks of IBT's data revealed, for example, a feeding study that IBT reported lasted 24 months but that actually was terminated after 18 months and reports of the use of live test animals after they had been reported killed in earlier experiments. So in a letter to pesticide manufacturers for which IBT had tested products, U.S. Environmental Protection Agency officials warned that IBT's records showed evidence of haphazard research and data that had been doctored to obscure potential harmful effects of chemicals. The giant had been slain.

But its ghosts — the more than 4,000 IBT health effect studies that supported the registration of 123 pesticides and the establishment of 160 pesticide tolerances (maximum permissible residue levels) — continue to haunt the government. According to the latest EPA estimates, nearly 1,800 of those tests must be reviewed — a task that has been divided between EPA and the Canadian government. Thus far, the inspectors have found that 100 percent of the chronic rodent tests and the majority of most other types of IBT tests reviewed are invalid (see chart A).

If most of the IBT tests for a particular pesticide are deemed invalid, then reviewers must search the literature for other health effect studies of that chemical. (To date, only 40 chemicals have been reassessed in this manner; see chart B.) If important tests still are lacking, then the information base for the pesticide is said to suffer from "major data gaps," and EPA — under the authority of the Federal Insecticide, Fungicide and Rodenticide Act — can request the pesticide manufacturers to fill in those gaps. During this case-by-case review, or EPA's "Data Call-In" program, all chemicals involved in the IBT case remain on the market.

EPA's method of handling the IBT case has met with criticism. Since evidence has amassed that IBT produced bogus data on a large scale, says Paul Merrell of the Northwest Coalition for Alternatives to Pesticides in Eugene, Ore., EPA should not bear the cost of case-by-case examinations. Instead, "Wholesale rejection of IBT data and withdrawal of pesticide registrations for products involved would seem to be more in line with EPA's mandate from Congress," he says. EPA officials, on the other hand, explain that under current law, once a pesticide is registered, EPA must bear the burden of proof that a substance can cause adverse health effects. Still, says Merrell, if his recommendation is impractical, it is only "because of industry's influence in the nation's capital."

Merrell also recommends changing the U.S. patent laws. "Strangely enough," he says, "our nation's patent laws are probably the largest single cause of chemical health and safety data falsification." Developers of new chemicals have 17 years to fully test and reap profits from their inventions before competitors can share their market. "A more rational approach might be legislation which would allow the chemical industry a liberal grace period in which to study effects of their chemical inventions before the patent clock begins ticking," Merrell says.

Financial connections between laboratories and chemical companies and financial corner-cutting also probably encourage commercial data falsification, Merrell says. "The problem doesn't end with studies performed by the IBT."

Indeed, results of an EPA audit from 1977 to 1979 of 70 pesticide-testing laboratories — obtained in response to a Freedom of Information Act request — seem to indicate that IBT was not alone in conducting haphazard research. For example, as long as a 99-day lag between times of test animal sacrifice and necropsy (without proper tissue preservation) was noted in bioassays Gulf South Research Institute of New Iberia, La., had conducted for the National Cancer Institute. At Harris Laboratory, Inc., in Lincoln, Neb., "rats listed as 'dead' were also listed as having been mated during the same time frame"; at Howard University College of Medicine in Washington, D.C., there were "autopsy records . . . for several animals which were still alive." And studies performed by Biosafety Research Laboratory in Branchville, N.J., were invalidated by EPA auditors "on the basis of unclear dose determination and lack of proper animal examinations." Such examples are strewn throughout the EPA report.

But EPA employee Diana Horne — former head of the EPA auditing lab program — says the audit report reflected not an epidemic of IBT-like research, but rather the state-of-the-art of toxicological testing years ago. Since then, she says, techniques have improved and most of those laboratories audited now comply with EPA's Good Laboratory Practice regulations. "We think that IBT was a particularly bad situation and that it was not really the norm," says another EPA employee. "We assume that IBT was the worst case." □

In chronic studies animals are fed a test chemical for 2 years; subacute, 7 to 30 days, acute, once. Cholinesterase studies involve measuring a nerve-transmission chemical concentration in test animals.

CHART A
INVALID IBT STUDIES—UPDATE

	JUNE '80	DEC. '80	JUNE '81	# INVALID/TOTALREVIEWED
Chronic Rodent	100%	100%	100%	34/34
Carcinogenicity	94%	94%	94%	17/18
Teratology	76%	75%	78%	42/54
Reproduction	73%	79%	76%	22/29
Chronic Dog	64%	53%	62%	13/21
Subacute	59%	68%	74%	99/134
Neurotoxicity	50%	64%	61%	11/18
Mutagenicity	48%	44%	48%	13/27
Cholinesterase	46%	58%	67%	20/30
Fish & Wildlife	42%	75%	76%	123/162
Acutes	29%	32%	32%	156/481
Residue	—	42%	29%	15/51

CHART B
Status of Regulatory Reassessment Phase of IBT Review

Forty-nine chemicals have completed this phase. They fall into the following categories.

1. IBT review is complete and all studies are valid for: Alanap*, Carbaryl*, Chlorpyrifos*, Dyanap*, Pencap E*, Pencap M*, Fire Prep 1000, Harvade*, FloMo, System E, Sumitol and Pyrethrin*.
2. Metolachlor, 4-Aminopyridine and Terrazole already had been reassessed.
3. Completed because no registration is now in effect: Hinosan, Cycle, Butam, Cypromid, Ethiolate*, Chlorobromuron, Chloroprophylate, Fluorodifen, Metabromuron*, Methylene bis propionate, Malonoben, Dantoin, Heptachlor Epoxide, Potassium Azide, CGA 12223, Potassium Hexafluoro Arsenate, Binapacryl*.
4. Major data gaps have been identified for: Bux, Cobex, Disyston*, Sencor* and Cyanurates.
5. No major data gaps exist as a result of invalid IBT studies for: Brodifacoum, DSMA, Iodine, Merphos, MCPA, Nalco 247, Oxadiazon, Nemagon, Sectrol, Methomyl, Avenge and 2,4-D.

*Chemicals reviewed by Canada.