

pected or have characteristics not ordinarily expected with respect to range, frequency distribution, etc.

Some examples of invalid, spurious, or inaccurate lab reports¹⁰ which the sponsor's summary failed to disclose adequately:

1. Dr. Melvyn Wade, NDA 16-880, Vol. 1.49, 1967-68. Every one of the 44-patients in this study had hematocrits (Hct) below normal¹¹—the range was 31-36; i.e., every patient was anemic if the Hcts listed are accurate. Most of the hemoglobins (Hb) listed for the same dates, however, were within normal¹¹ limits—the range was 10.4-17.5. If we calculate the mean corpuscular hemoglobin concentration (MCHC) for the first three patients we get:

	Hct	Hb	MCHC (percent)
Patient No.:			
1.....	34	17.5	52
2.....	46	15.3	42
3.....	32	15.3	48

Since the normal MCHC is $34 \pm 2\%$, and cannot exceed this value by more than a very few percentage points in any known condition, it is obvious that either the above Hbs or Hcts (or both) are spurious. The accuracy of the MCHC determination = $\pm 0.8\%$.

In spite of the fact that the average Hct in these 44 patients was almost 10 mm, or 25 percent, below normal, the sponsor's summary, Vol. 1.1, p. 362, states that, except for a low WBC in patient 3, "no significant alterations were observed in any of the following parameters: CBC . . ." Judging from the diagnoses listed on the case report forms, it is unlikely that all of the patients were anemic.

2. Dr. Sobotka, NDA 16-880, Vol. 1.29, 1967. Analysis of the frequency distribution of Hb values reveals a rectangular pattern inconsistent with normal biological variation. (41) *Dr. Sobotka was "disqualified" Sept. 21, 1970 by the Commissioner.*

3. Dr. Evangelista, NDA 16-880, Vol. 1.98, 1968 (Samber Research Co., Inc.). A. The cholesterol values fluctuated wildly without explanation, e.g.:

Patient No.:	Volume 1.98, page —	Serum cholesterol, repeated at 1-4 week intervals			
		Number	Number	Number	Number
1.....	13	220	240	118	120
2.....	20	180	200	100	190
3.....	31	230	190	180	148
4.....	40	150	170	280	204

No comment or explanation concerning these values was made by either the investigator or sponsor.

B. *The pulse rates were recorded every 2 wks. for 26 wks.—about 500 pulse rates—and every one was listed as "80."* Although Dr. Evangelista claimed in his letter of 5-5-69 that "80" was a method he used to designate a normal reading, it is noted that in another study¹² the actual pulse rates were listed, and that study was done about the same time as the above study. See also Samber Research Co. letter of 5-19-69. (42)

4. Dr. Dietz, NDA 16-880, Vol. 1.79, 1967. The frequency distribution of Hcts and Hbs and WBC are bizarre; there is an unbelievably narrow range of values for Sp. Gr. of urine, differential white blood counts, etc.

¹⁰ The fact that abnormal lab data could pass through the three levels of surveillance listed above, before being submitted to the FDA, without eliciting any concern or comment raises several questions:

(a) Were the lab tests actually performed by a technician?
(b) Did the investigator look at the lab data? Was the investigator aware of what the normal values were?

(c) Did the sponsor fail to monitor the lab data received from the investigator?

¹¹ Normals: Hct=Male, 42-52; Female, 37-47. Hb=Male, 14-18; Female, 12-16. (Win-trobe M: Clinical Hematology, ed 6, 1967, p. 86)

¹² See NDA 16-421.