show reduced serum levels under this test condition. The fact that erythromycin stearate is dosed at times clearly not recommended by our product literature makes the reason for the difference in serum levels patently obvious.

The last page of this study provides adequate opportunity to point out that the study was conducted with this dosage administration bias. The second paragraph indicates that this is a commonly occurring clinical setting. Numerous references are made to the fact that the medication was given immediately after a meal, but none mention that this is not the recommended dosage schedule for Erythrocin Stearate Filmtab.

STUDY CS NO. 077

This study is essentially a repeat of CS#071 with the exception that both Erythrocin Stearate Filmtab and Erythromycin Base Filmtab are included in the comparison to E-Mycin Tablets. Again, the same deficiencies exist in this study. As we have previously stated, both the Abbott products are to be taken under fasting conditions, not immediately following meals.

Comparisons between any studies must be made cautiously in trying to assess the comparability of drug products. However, we are impressed with the great differences in the shape of the serum curves presented for E-Mycin in Study CS#071 and CS#077. They suggest to us that there must be great variability in individual serum levels. However, since only average values are given, this can only be speculated. Some differences at specific sampling times are shown below:

Hours	CS No. 071	CS No. 077
5	0.5	0.8
24	1.0	1.4
51	.7	1.6
67	1.0	.4

The serum levels reported for Erythrocin Stearate Filmtab in studies CS#071 and CS#077 are low for the reasons discussed above. Our product enclosure, in addition to specifying the proper administration time also indicates that peak serum levels of at least 0.6 mcg./ml. are obtained. (See enclosed insert.) Since this insert is FDA approved, it must be obvious that our data must support this figure. The actual levels are consistently above the 0.6 mcg./ml. figure. In Upjohn Study CS#071 the highest level reported for Erythrocin Stearate is 0.44 mcg/ml. (61 hours) and in Study CS#077 only two sampling periods (60 and 61 hours) show levels of 0.6 mcg./ml. or greater. Such inconsistencies should alert the careful reviewer that some deviation from the recommended use of the drug has occurred. Finally good serum levels are seen with the Abbott Erythromycin Base Filmtab. (See Studies #72-9 and #72-82.)

SUMMARY

I hope the above comments will be helpful. They appear to follow a repeating pattern at this time. It should be obvious that bioavailability studies can be designed to show any product at advantage over some other product if sampling times or protocol conditions (meals, dosing times, blood sampling times, etc.) are adjusted to show the competitive product at its greatest disadvantage and the product to be promoted at its optimum. If he promotional use of bioavailability studies continues along these lines, we would expect that the credibility of bioavailability information will eventually be eroded and be considered meaningless.

ABBOTT INTEROFFICE CORRESPONDENCE

To: Mr. M. J. Henrichs, D-309 (NC)
Re Upjohn Studies CS #037 and CS #056

The following may be used in commenting on the above two Upjohn studies.

Bioavailability information on a pharmaceutical product can be illustrated in a concise and graphic manner by presenting the average serum drug level data obtained after single or multiple dose drug administration. However, there are some serious practical limitations to these data and its applicability to clini-