Attachment 3
Notes abstracted from: "Reproducibility of Dissolution Test Results," J.F. Hamilton, T.W. Moore, and C.M. Kerner, Pharm. Forum, 21, 1995, pp 1383-1386.

"Dissolution testing has been in progress at the FDA, Division of Drug Analysis (DDA)[1] since the 1970s. During this time, at least 15 different units or models of dissolution apparatus have been in use, and individual tests have been performed by many different analysts. ... **Records of long-term testing confirm that when critical parameters are identified and controlled, consistent and reproducible results can be obtained**. ... Since 1979, in a total of 17 different dissolution apparatuses, the NCDA #2 tablets were tested repeatedly in water with the paddle at 50 rpm. There has been remarkably little variation in results; the average of the means for the 17 apparatuses is 37.4%, with a standard deviation of the means of 1.3. ... In 1980 the NCDA #2 tablets were included in a collaborative study conducted by DDA-then the National Center for Drug Analysis-among 11 FDA laboratories ... The mean for 132 tablets from 22 runs was 38.9%, with a standard deviation of the tablets of 4.2 ... Many variations of a non-critical nature have occurred during the 15-year time span of these tests. The most obvious change is the evolution of the dissolution apparatus itself: As improvements in the ease of alignment of the equipment and in producing a more vibration-free apparatus were made, the precision of the individual tablet results improved. Because of fluctuations in price and availability during this time span, different brands of membrane filters were used at different times for both the manual and the automated apparatus. Also, both plastic and glass dissolution vessels were used. Over this extended time period, different lots of USP Prednisone Reference Standard Calibrator Tablets and two different methods of deaerating the dissolution medium were used; at least 20 analysts performed dissolution calibration and testing. ... Recently, using both paddle and basket methods, 3-hour profiles with sampling every 10 minutes were run on the NCDA #2 calibrators, using 36 tablets for each method. At 30 minutes, the average dissolution result for 36 tablets by the paddle method was 34.2%, with a standard deviation of the means of 1.6."

[1] The laboratory was originally founded as the National Center for Drug Analysis (NCDA) which became the Center for Drug Analysis (CDA) and then the Division of Drug Analysis (DDA). The staffing and mission were essentially unchanged through these organizational name changes.

Comparative Dissolution Results for Different Apparatuses in Use at DDA (NCDA)[2] Since 1979 10 mg NCDA #2 Prednisone Calibrator Tablets (6 Tablets per Run).[3]

			% of Declared			
Apparatus	Dates in Use	# of Runs	High	Low	Mean	Stnd. Dev.
Hanson 381	5/79-2/91	30	47.6	30.7	38.2	3.5
Hanson 539	5/79-7/83	26	59.0	31.1	37.8	3.9
WEAC 3M	10/79-3/81	11	44.4	30.2	37.4	2.9
WEAC 1	11/79-2/82	49	51.9	32.4	39.8	3,7
Hanson 723	4/80-12/84	9	51.0	31.3	39.9	4.7
WEAC 11	9/80-4/88	19	45.2	28.7	37.4	4.1
FDA #1	2/82-8/84	46	45.7	29.5	38.0	3.0
Hanson 538	9/82	2	42.1	33.2	36.7	2.7
WEAC 3	12/82-11/84	6	44.4	32.4	36.8	2.9
FDA #2	3/83-2/84	11	44.5	30.7	35.8	3.3
Hanson 1392-19	6/83-5/89	51	50.1	30.4	38.6	3.7
Hanson 2013-11	6/88-10/89	24	46.1	30.3	38.2	3.5
Hanson SR2-36	10/89-1/90	2	39.3	32.5	36.1	2.6
Distek 2100,#4	1/89-present[a]	57	43.9	27.6	35.0	2.5
Distek 2100,#3	11/92-present[a]	14	45.9	31.1	36.8	3.1
Distek 2100,#2	11/92-present[a]	30	45.3	28.8	37.5	3.2
Distek 2100,#1	1993-present[a]	3	42.7	31.6	36.5	3.0
Total/Average/Weighted Average		390	59.0	27.6	37.4	3.4

[a] "Present" for this paper was 1994

[2] Continuing FDA reorganizations resulted in name changes but the staff and mission over this period remained the same. NCDA-National Center for Drug Analysis; CDA-Center for Drug Analysis; and DDA-Division of Drug Analysis were the names used over this period.

[3] "FDA" and "WEAC" refer to units custom-built by FDA machine shops. "Hanson" and "Distek" refer to the commercially available equipment.