FY 76

NATIONAL CENTER FOR DRUG ANALYSIS
Bureau of Drugs, U.S. Food and Drug Administration
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Executive Summary of Accomplishments: Fiscal Year 1976, including Transitional Quarter ending September 30, 1976.

1. Staff Level: 43 persons
   Allocation: 6 persons: Biopharmaceutics Projects
   37 persons: Drug Quality Assurance Projects

2. Dissemination of Methodology.

   Methods developed at the Center were reported via papers in scientific journals (1, 2), in-house publications (3-23), and interim reports (24-32). About 80% of these publications and reports relate to Drug Quality Assurance and 20% to Biopharmaceutics. Advances reported in these papers include development of a new method for dissolution profiling of digitoxin tablets and new methods for quality assurance testing of papaverine hydrochloride, quinine sulfate, phenazopyridine hydrochloride, diethylstilbestrol, reserpine, ferrous sulfate, pentaerythritol tetranitrate, isosorbide dinitrate, dienestrol, ephedrine sulfate, pseudoephedrine hydrochloride, and several antimalarial drugs. The development of a unique, continuous-cycling apparatus, generally applicable to dissolution profiling of many drugs, was also reported.

3. Dissolution Testing.

   In addition to the projects reported above, the Center obtained dissolution profiles on samples of papaverine hydrochloride capsules and thiazide diuretic tablets, which have been or are to be studied in vivo by extramural contractors. The Center organized and conducted an FDA-wide dissolution seminar, attended by one USP official and about 30 FDA personnel from six districts and headquarters, and trained 16 chemists from district and headquarters laboratories in the techniques of dissolution testing. A videotape of the seminar has been used subsequently to train other scientists. The Center developed a new, highly sensitive method for obtaining dissolution profiles of phenytoin tablets and capsules (32).

4. Surveillance/Regulatory Analyses.

   In addition to the projects reported under Item 2, the Center developed an automated method of analysis for steroid estrogens. A gas-chromatographic method was adapted from the literature to perform qualitative and quantitative analyses of estrone and equilin in conjugated estrogens. A thin-layer chromatographic method for the qualitative detection of nitrofurazone, furazolidone, and 5-nitro-2-furfuraldazine in nitrofurantoin was developed. A semiautomated method of analysis for reserpine in the presence of most thiazide diuretics was validated in

preparation for an AOAC collaborative study. The compendial methods for the drugs listed in Sections 2 and 4 were evaluated for precision and accuracy.

Thirteen Drug Quality Assurance studies were completed in the last five quarters (see Table 1).

5. Development of New Technology.

Several automated systems were developed to collect and analyze aliquots of dissolution media. The continuous-cycling system (28), which has been used for testing aminophylline tablets and quinidine sulfate tablets and capsules, is best suited for high-dosage drug forms. Other systems, which collect discrete aliquots for later analysis on separate, stand-alone analytical trains, are best suited for testing low-dosage drug forms, e.g., prednisone tablets and digitoxin tablets (29).

The Center developed extensive software involving NCDA's computer-based Laboratory Data Acquisition System and Management Information System. Major projects include programming to allow on-line testing and calibration of instrument-computer interfaces, programming to utilize recently acquired moving-head disk storage systems, programming to store and process specialized data acquired on-line from dissolution and multipoint-analysis experimentation, programming to make computer sorts of completed and uncompleted samples by manufacturer, collecting district, or date of receipt and to generate summary reports of these samples, and programming to do extensive statistical analyses of analytical data acquired at NCDA.

NCDA has also completed the following hardware-related projects: design and construction of electronic interfaces to allow new instrumentation to be placed on-line to the computer, isolation and correction of power-line disturbances that have frequently interrupted computer services over the last several years, isolation and elimination of noise sources in NCDA's data-transmission system, identification of a commercial radio transmitter as the source of electrical interference in several of NCDA's laboratory areas, and expansion and enhancement of the Center's instrument-calibration and repair capabilities.

6. Other Activities.

The Center participated in eight AOAC collaborative studies that were initiated by other government laboratories and conducted one AOAC collaborative study of its own.

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Table 1. Drug Quality Assurance Studies Completed at NCDA in FY 76 and Interim Quarter

This Table presents results of laboratory findings and includes the percentage of all types of defects observed. These percentages do not necessarily reflect the quality of all the drugs on the market since the Studies are conducted on drug categories where high defect rates are suspected.

Study No. and Name	Batches Analyzed	Defective Batches, %[a]	
538 Progestins	42	2.4	1
539 Androgenic Hormones	72		1
540 Sedatives	282	5.0	14
547 Antithyroids	15	6.7	1
548 Antimalarials	37	5.4	2
556 Papaverine	48	6.2	3
557 Phenazopyridine	13	0	0
562 Nitrofurantoin	37	8.1	3
564 Ferrous Sulfate	83	2.4	2
565 Oral Contraceptives	69	0	0
566 Digitoxin) Continuous) Certification	69	10.1	7
567 Digoxin) Studies	52	9.6	5
568 Local Anesthetics	218	0.9	2
573 Nitrate Coronary Vasodilators	165	3.7	6
579 Reserpine	133	6.0	8
	1335		55

4.1%

[a]Percent of batches not meeting compendial or FDA-imposed requirements.