PART IV

ANALYTICAL

A. ANALYZING LABORATORIES

The district will make all the necessary arrangements for proper handling of samples with the following designated testing facilities:

TYPES OF DEVICES	ANALYZING LABORATORIES
All General Medical Devices	Winchester Engineering and Analytical Center (WEAC) 109 Holton Street Winchester, Massachusetts 01890-1197
Radioimmunoassay	WEAC
All Other In Vitro Diagnostic Devices	Micro—WEAC Chem—WEAC
Testing for sterility of finished devices, package integrity, bioburden, and endotoxins:	WEAC
Testing of biological indicators:	WEAC

See PART VI regarding those persons designated as contacts for WEAC and specific products.

SPECIAL NOTE: For all other devices and questions concerning sampling of devices and laboratory capabilities, contact Division of Field Science (DFS), HFC-140.

B. ANALYSES TO BE CONDUCTED

Sample collection and analysis will be determined on a case-by-case basis through consideration of inspectional findings, compliance and scientific capabilities and expertise. Full collaboration between investigations and analytical personnel is essential. See Part III for additional information.

C. METHODOLOGY

1. Testing Finished Device Samples for Sterility

   a. Visually examine each unit to ascertain that its packaging is intact. Report all defects observed by describing the size, type and location of the defects. Units with defective packaging need not be examined for sterility.

   b. Finished device samples are to be tested in accordance with the requirements of current USP methodology for Sterility Tests. **Reference the FDA Sterility Analytical Manual for guidance on applying the USP methods.**

   c. Device samples are to consist of 60 units, as follows:

      20 units tested in Soybean-Casein Digest Broth
      20 units tested in Fluid Thioglycollate Broth
      10 units for bacteriostasis/fungistasis testing
      2 units for system control
      8 units for method development
      60 units for re-test, if required under USP methodology

      When 120 units are not available because of lot size or cost, follow the current USP recommendations for the minimum number of articles to be tested in each media, as follows:

Number of Articles in the Batch	Number of Articles to be tested
Not more than 100 articles	10% or 4 articles, whichever is greater
More than 100, but not more 500 articles	10 articles
More than 500 articles	2% or 20 articles whichever is less

      Note that the USP permits the division of articles into equal portions for addition to each of the specified media when the contents of the article are of sufficient quantity (see the current USP to determine what is a sufficient quantity).

      NOTE: For the purposes of this compliance program, the “articles” referred to in the USP may be interpreted as devices.

d. Positive subsamples

Check cultures for growth daily and begin qualitative analysis of growth immediately upon detection of growth. Follow subculturing procedures in the Sterility Analytical Manual. Continue to incubate growth vessels after subculture for full term analysis to detect slow growing bacteria and molds. For each subsample found to be non-sterile, prepare a pure culture of each contaminant. All isolates from sterility tests must be maintained until otherwise notified by CDRH or for one year.

2. Presterilization Microbial Contamination (Bioburden)

Bioburden testing is to be performed in accordance with the guidance provided in ISO 11737-1, Sterilization of medical devices - Microbiological methods - Part I: Estimation of population of microorganisms on products. The methodology used for estimating the bioburden is to be validated. Twenty units are to be tested.

3. Analysis of Biological Indicators

Test 40 biological indicators according to current USP methodology using sterilization conditions specified on the indicator label. "Survival time and kill time" and "Resistance performance tests" are to be used. 80 additional biological indicators may be required if either performance test fails. Under some conditions, the D-Value may also be determined. That determination requires a minimum of 45 biological indicators. These determinations will be performed according to the claims of the manufacturer of the indicator or inoculated product. Pertinent test specifics will be required.

4. Analysis of Packaging Defects

Perform a visual, non-destructive, inspection of the package noting the existence and location of seal or material defects. Normally 20 packaged devices will be collected for analysis. Further testing is to be performed using consensus standards such as those identified in the Part VI.A.1 references for the American Society for Testing and Materials (ASTM). Selection of the test will depend on the materials and construction of the package, and on the nature of the noted or suspected problem.

5. Analysis of Endotoxins

Samples will be analyzed using the Bacterial Endotoxins Test found in the current USP and the Sterility Analytical Manual. Ten units are required for endotoxin testing.

6. Antimicrobial Effectiveness Testing

Samples will be analyzed using the Antimicrobial Effectiveness Test found in the current USP and the Sterility Analytical Manual. Ten units are required for testing.