a) Investigations into pyrogen failures for Prolastin Lots 601U036, 601U052, and 601U054 were limited to the column 02U02 eluate through bulking operation and did not include any processes prior to the eluate collection.

The investigations into pyrogen failures for Prolastin Lots 601U036, 601U052, and 601U054 did not involve processes prior to the eluate collection because in-process data was not gathered on production material prior to eluate collection. For the investigations of the lots noted above, Bayer collected all available data, from pre-sterile filtration to bulking. Because the three Prolastin lots failed the pyrogen test, those lots were rejected in accordance with Clayton Standard Operating Procedure CQAB 09-130, "Rabbit Pyrogen Test Dose Schedule Biological Products (except Gamma Globulins)." Other Prolastin lots were released based on in-specification microbial anaytical assays and LAL tests for production steps after eluate collection, and normal pyrogen testing of final containers, which ensured product safety and efficacy.

As a result of the FDA inspection, however, Bayer recognizes the need for collecting data throughout the production process to strengthen its investigation systems. Bayer has now identified points in the production process prior to eluate collection for sampling. In addition, Bayer is validating its microbial analytical assay and LAL testing methods, both for the newly established sampling points and for all other key product steps after the eluate collection. Indeed, Bayer has already validated microbial testing for samples from the plasma pool IV-1 paste. Bayer is scheduled to complete validation for the microbial analytical assays by the fourth quarter of 2001 and LAL testing by the first quarter of 2002. Data from sampling points prior to eluate collection is being collected and evaluated in order to establish alert and action levels. Once sufficient data is available, Bayer will implement in-process bioburden monitoring of production steps prior to eluate collection based on these alert and action levels. It is expected that this monitoring will be in place by the second quarter of 2002. Once validated in-process monitoring is in place, Bayer will be collecting data from throughout the production process and will develop procedures requiring the evaluation of this bioburden and LAL data in all future investigations of pyrogen failures and sterility related discrepancies.