sequencing using an ABI Prism Model 377 DNA Sequencer, confirming the high quality of the purified DNA. This is reflected by the high $A_{260}/A_{280}$ ratio (Table I) and was confirmed by agarose gel electrophoresis.

The silica matrix offers a degree of flexibility in optimizing the mass of matrix required to bind sufficient DNA for the application, whereas the silica discs provide a laminar format perhaps more suitable for molecular diagnostic device development because of their ease of handling. Furthermore, the silica matrix used in this study is nonporous, which not only reduces the likelihood of contaminant carryover from step to step, a consideration when using conventional porous silica materials, but also permits small elution volumes with high recovery.

DNA isolation is gaining importance in the fields of molecular diagnostics. In the present study, we report two approaches to isolation of high-quality DNA from a prokaryotic source in a relatively short time. By way of comparison, we report a similar purification by ion exchange using DEAE-Magarose (6). Although this yields DNA of greater purity, it is a slower process, and the DNA eluted requires desalting by precipitation before use. Depending on the intended use of the DNA, these issues may be of importance in selecting the most appropriate technique. Although the applications presented here are not clinical examples, they serve the purpose of demonstrating proof of concept for this type of diagnostic application. We feel that the adsorptive methods described here could be considered when developing a molecular diagnostic test protocol, and depending on the process requirements, an interaction with silica under chaotropic conditions using either particulate or laminar matrices may be suitable.

References

Transference of Reference Intervals in the Validation of Automated Chemiluminescent Immunoassays on a New Platform, Michael Lynch,1 Anne Thompson, Bruce Gaumond, John Kilroy, Holly Leonard, Ann Jacob, and Thomas Jackson (Chiron Diagnostics Corporation, East Walpole, MA 02032, * author for correspondence: fax 508-660-8100, e-mail michael.lynnch@chirondiag.com)

Integrating highly evolved automated immunoassay platforms into the laboratory provides long-term advantages such as improvements in workflow, performance, and data handling. However, to make the transition from a current platform to a new platform the end user is often required to revise reference intervals, a time-consuming and often tedious process. According to the guidelines of the NCCLS (C28-A) (1), transference may be used to confirm that an established reference interval can be applied between two methods that show substantially the same precision and interferences, use comparable calibrators, and yield comparable values. Establishing transference was a fundamental component of the strategy for validating ACS:180® thyroid, fertility, and oncology assays on the ACS:Centaur™ system. Laboratories currently using the ACS:180 system will find introducing an ACS:Centaur system simpler because the reference intervals they established on the ACS:180 system apply to the ACS:Centaur system.

A minimum of three ACS:180 systems and three ACS:Centaur systems were included in the evaluation. Both platforms used the same reagents, calibrators, and controls. The results for six fertility assays (follicle-stimulating hormone, luteinizing hormone, prolactin, human chorionic gonadotropin, estradiol, and progesterone), seven thyroid assays [thyroid-stimulating hormone (TSH), TSH-3, thyroxine, triiodothyronine, thyroxine uptake, free thyroxine, and free triiodothyronine], and four oncology markers ($\alpha$-fetoprotein, breast cancer antigen, gastrointestinal cancer antigen, and ovarian cancer antigen) were reviewed. Reagents, controls, and calibrators for each of the assays were obtained from in-stock inventory.

The protocol for verifying the validity of transference involved three steps: demonstrating accuracy, demonstrating precision, and demonstrating diagnostic concordance.

Accuracy was demonstrated by running method comparisons relative to the ACS:180 assays using >100 clinical specimens. Data were analyzed using unweighted least-squares regression to obtain estimates of the slope, intercept, and correlation coefficient ($r$). Bias between the methods was tested by analyzing bias plots and mountain plots of the cumulative distribution of partitioned biases (2, 3). Estimates of within-run precision were obtained from replicate observations in the method comparison (4).

Diagnostic concordance between the two devices was demonstrated by selecting a population of specimens the analyte concentrations of which fell within the reference intervals for the ACS:180 system. These specimens were also tested by the ACS:Centaur system and determined to be concordant if the results fell within the reference interval established for the ACS:180 system.

The slopes of linear regression equations ranged from 0.95 to 1.05 for all assays. Correlation coefficients were $\geq 0.98$ for all assays. The scatter plot and bias plot for TSH are shown in Fig. 1, A and B, respectively. To demonstrate the lack of bias at different analyte ranges, the data were partitioned into three segments and displayed in mountain plots (Fig. 1, C–E). The median bias for each segment is represented by the peak of the mountain plot. The data for TSH clearly show that the median bias is $\sim 0\%$ over the ranges tested. Similarly low bias was demonstrated when the mountain
Fig. 1. Analysis of bias between the ACS:Centaur and ACS:180 systems.

Scatter (A) and bias (B) plots of ACS Centaur vs ACS:180 for the TSH assay. (C–E) Summaries of partitioned bias analysis showing mountain plots of percentage of bias over three segments of the assay range. (F) Tabular summary of the mean concentrations and pooled within-run imprecision by assay segment for the TSH assay.
plots and bias plots were analyzed for the rest of the thyroid assays as well as the fertility and oncology assays.

Pooled estimates of within-run imprecision for the replicate results were calculated in each of the segments. The results are summarized in Fig. 1F. The precision for the ACS:Centaur system was demonstrated to be equivalent to that of the ACS:180 system.

Diagnostic concordance between the systems was also verified using patients with results within the reference interval. Diagnostic concordance of the ACS:180 thyroid, fertility, and oncology assays on the ACS:Centaur system was 96% for all assays. Data from regression analysis and diagnostic concordance studies are summarized in Table 1.

We conclude that according to testing guidelines recommended by the NCCLS, the reference intervals of the ACS:Centaur assays analyzed in this study are equivalent to those of the ACS:180 system. Given these results, laboratorians can be confident that the reference intervals they established on the ACS:180 system will apply to the ACS:Centaur system. For laboratories already using the ACS:180 system, this feature will speed implementation of the ACS:Centaur system.

### References


### Fully Automated Enzyme Immunoassay System for the Determination of Activator-specific Histamine Release from Basophils in Whole Blood, Priscilla K Zia, Nazrin Namei, Ashok Patel, Kris J. Kontis, Narayan Nayak, Roy Chen, and Thomas M. Li (1 Hycoir Biomedical Inc., Garden Grove, CA 92841; 2 Becton Dickinson, San Jose, CA 95131; *author for correspondence: fax 714-895-6920, e-mail kjkontis@ix.netcom.com)

Histamine release from washed leukocytes and/or whole blood has been extensively utilized for in vitro studies of allergy (1–5). It has been shown that when the history and skin test of an individual are positive for a given activator, the probability is very high that the in vitro tests will also be positive for histamine release (6). Throughout the past 10 years, numerous methods have been developed for the determination of histamine release. The commercially available RIA and enzyme immunoassay (EIA) kits for histamine release are not automated and require the investigator to provide the activators or compounds to be used in stimulating histamine release. This study de-