Evaluation of AMPLILINK Software for the COBAS AMPLICOR System

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The use of AMPLILINK version 1.0 software was evaluated for the operation and control of one COBAS AMPLICOR instrument and for two COBAS AMPLICOR instruments run simultaneously to perform and detect nucleic acid amplification reactions. A total of 3,384 results were analyzed. The initial accuracy of the results was 99.91%. Three errors of omission of transfer of data from the COBAS AMPLICOR to the AMPLILINK system were observed. Two of these errors were from a single specimen, where both the analyte and internal control results were not transmitted. These errors did not interfere with the correctness of any other data. There were no interruptions of runs, and no data were mixed. AMPLILINK increased convenience, saved labor, and was found to be a very useful addition for clinical laboratories performing molecular-diagnostic procedures with the COBAS AMPLICOR system.

PCR-based molecular assays are gaining importance in the diagnosis and monitoring of infectious diseases. In-house assays do not always meet the high-volume needs of the routine-diagnostic laboratory. They have been reported to be susceptible to false-positive results because of carryover contamination due to frequent transfer of reagents (3, 9). False-negative results may occur because of amplification failure due to interference from PCR inhibitors (11). The hands-on time required by an in-house assay further limits its utility in the routine-diagnostic laboratory. To overcome these problems, the COBAS AMPLICOR instrument, which allows the automation of the amplification and detection steps of a PCR test, has been introduced (4, 6). The amplification reagents of qualitative assays include an internal control to uncover false-negative results due to PCR inhibitors (8). The COBAS AMPLICOR allows significant reduction of manual steps and automated calculation of quantitative test results. When manual quantitative test methods are used instead of this instrument, serial dilutions have to be prepared, in-range background-corrected optical densities of the amplified genome and the quantitation standard must be chosen, and genome copies per milliliter have to be calculated with a formula that includes total genome and total quantitation standard optical densities, input quantitation standard copies, and a conversion factor. The COBAS AMPLICOR can be used as an unattended system and has been found to be an easy, quick, and reliable way to perform high-volume PCR (1, 2, 5, 7, 10). However, for additional labor saving and convenience, a final area needing improvement in this amplification and detection system was the user interface. Users interact with the system via a small keypad to manually enter PCR run profiles, to create each test order for each specimen, and to perform other instrument maintenance functions. The improvements needed were the ability to link multiple instruments, to coordinate testing, to simplify startup by creating run profiles, to create orders, to manage reagent inventory, to read barcodes to improve the accuracy of identification of samples, and to manage patient data. Additional help was also needed with the recording of service and quality control data.

Software (AMPLILINK) was recently developed which proposed to meet these needs. It was designed to permit the control of up to three COBAS AMPLICOR instruments as well as to improve the other areas mentioned above. In the present study, AMPLILINK version 1.0 software, run on a Windows-based Pentium computer, was evaluated for operation and control of first one COBAS AMPLICOR instrument and then two instruments run simultaneously. Printers attached directly to each COBAS AMPLICOR instrument recorded all data prior to its manipulation by the AMPLILINK system. A printer was also attached to the AMPLILINK system, and the results were compared. Besides data manipulation accuracy, other features of the software were evaluated during the course of the study at two sites, one in Europe and one in the United States. Technologists experienced in the use of the COBAS AMPLICOR system performed the testing.

A total of 2,640 qualitative amplification and detection tests were run, including 1,200 amplifications and detections of internal controls (Table 1). All samples had earlier been processed with the corresponding COBAS AMPLICOR specimen preparation protocols following the manufacturer's instructions. Additionally, 744 quantitative amplification and detection tests were run (Table 1). In the first week, one COBAS AMPLICOR was run; in weeks 2 to 4, two COBAS AMPLICOR instruments were run simultaneously. In weeks 1 to 4, basic and parallel modes were run, patient identification was entered with AMPLILINK, and profiles were created and then used to create orders with AMPLILINK. Status and reagent reports, results, and system and error messages were collected daily. On a weekly basis, results were archived and reviewed for consistency of information transfer. All results were then purged once the data had been collected. The AMPLILINK service icon was used to follow all maintenance of the COBAS AMPLICOR instruments. The results reported by AMPLILINK were compared to printouts created by a printer which was directly connected to COBAS AMPLICOR.
There was no direct link with the LIS in AMPLILINK version 1.0 software. The automated calculation for quantitative tests was the best feature of AMPLILINK. Maintenance records, and other records that could be useful in tracking performance, were missed on page reports, and it was not possible to create a user-defined patient identification field. Furthermore, the help access, while greatly improved, could be improved further. Finally, we found that the cassette inventory of reagents required that partially used reagents always be reused on the same instrument.

In summary, we found that AMPLILINK could conveniently operate and control one or two COBAS AMPLICOR instruments. The new software showed good overall functionality and user friendliness. The AMPLILINK operator’s manual and tutorial proved very useful. Although the existing minor problems are expected to be eliminated in future versions of the software, AMPLILINK version 1.0 already represents a great improvement in the user interface with the instruments.

A total of 3,384 results were obtained by data transfer. AMPLILINK correctly reported 3,381 results. In data transfers for two specimens, an interface failure occurred. Errors (for both the target and the internal control) were observed in one sample dedicated for Mycobacterium tuberculosis detection and in another sample dedicated for quantitative human immunodeficiency virus type 1 detection (Table 1). However, these were errors of omission of transfer of data; i.e., they were not printed. In all three events, the COBAS AMPLICOR had the data and printed them. The overall accuracy rate was 99.91%.

During the whole study, there were no interruptions of runs. Only several minor errors were displayed. No data were mixed, and no data errors were printed.

The new software was easy to load and easy to use. The package was found to be complete, and the format, graphics, and order of presentation were acceptable. The software successfully implemented a complete self-help tutorial and an on-line help menu for reference. The complete status of the COBAS AMPLICOR systems could be seen by looking at the graphical-style screens. Orders could be created by using various options, such as typing the test information or scrolling through a list and then copying and pasting or dragging and dropping the information that was required. Results could be outputted directly from the printer allocated to the computer or archived and copied to a floppy disk. Once saved to a disk, the data could be loaded into a laboratory information system (LIS) or manipulated in a personal computer program. There was a notepad, which was convenient for sharing messages between operators. This was found to be especially useful for communication between shifts when the instruments were run throughout the extended day. There was a message log, which was the instrument’s way of letting the operator know when reagents might be running low or if there was a problem with the COBAS AMPLICOR system. A system maintenance log recorded each time that the system was serviced, each daily maintenance session, and other records that could be useful in tracking performance. One of the best features of AMPLILINK was the automated calculation for quantitative tests.

Several minor problems were observed with AMPLILINK. There was no direct link with the LIS in AMPLILINK version 1.0. The only way to transfer data to a main LIS computer is indirect, by downloading data to a disk, and it will only work if the LIS will accept data in one of the AMPLILINK output formats, such as a text-only file. The printouts of quantitative results would be clearer if the raw data was printed on a page separate from the calculated data. Important messages, such as, for example, comments and instrument number, were missed on page reports, and it was not possible to create a user-defined patient identification field. Furthermore, the help access, while greatly improved, could be improved further. Finally, we found that the cassette inventory of reagents required that partially used reagents always be reused on the same instrument.

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**REFERENCES**


