

Final Progress Report - Contract N01-LM-6-3550
Decision Support Deployment in Diverse Clinical Settings
Health Applications for the National Information Infrastructure

Reporting Period Nov 30, 1999 through June 30, 2000

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1 EXECUTIVE SUMMARY

This report covers the period from Nov 30, 1999 through June 30, 2000 and constitutes the final progress report for this contract. The report shows completion of the work articulated in our original proposal. During this reporting period, we successfully ported our real-time drug order screening and clinical alert notification systems to Christian Northeast/Northwest Hospital, another major facility in the BJC Health System, building on our previous success at putting these systems into production at Barnes Jewish Hospital. From these experiences, we learned valuable lessons regarding expert system behavior and the complexity of processing real-time drug orders, and the differences in these processes from our prior process of batch mode screening. We also learned a great deal about clinical alert notification methodologies, user preferences, and notification escalation strategies.

2 DETAILED REPORT

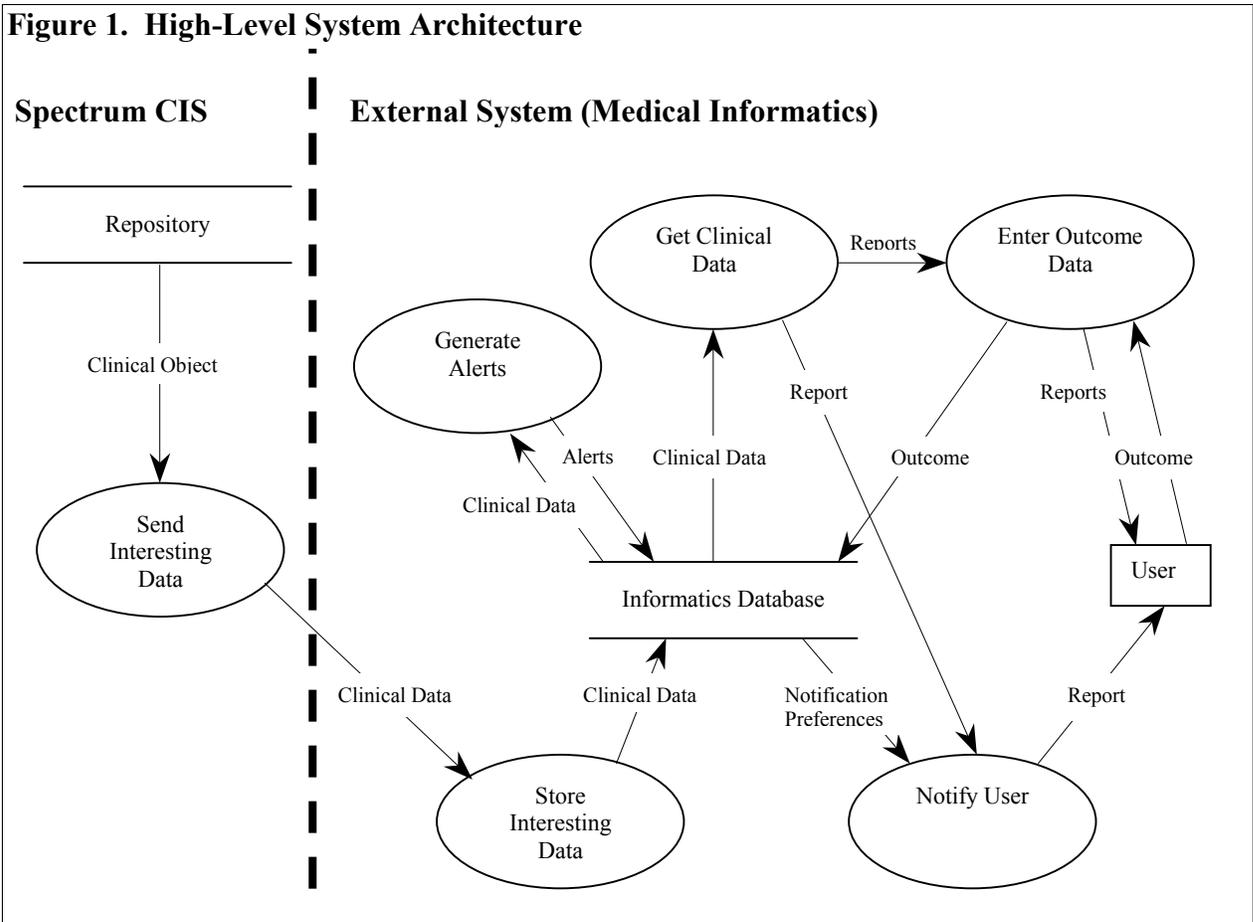
2.1 Introduction

This report covers the period from November 30, 1999 to June 30, 2000 and summarizes the work completed for the entire project. Our work is focused on three major goals: 1) conversion of two production quality expert systems—DoseChecker and PharmADE — from batch mode to real time, 2) development and evaluation of notification strategies for clinical alerts generated by these expert systems, and 3) porting the expert systems to other facilities within the BJC_{SM} Health System. By integrating data from disparate sources, our distributed computing environment allows for more specific and, therefore, more effective rule sets than would be possible by adding alerts onto individual pharmacy or laboratory systems; real *synergy* takes place through data integration. Because the systems are developed using simple database triggers and common standards, they can be adapted rapidly to meet the needs of local health care professionals. Because the systems are secure and WWW-enabled, they can be distributed *where* professionals need them *when* they need them. Because the system is heavily integrated *through established data standards* with both legacy systems and newly developed systems, it can serve as a “safe harbor” during the inevitable information systems consolidations and migrations that are at times crippling health care delivery organizations. In all of these ways, the application is an exemplar of the power of distributed computing and standards in the promotion of regional health care.

During this project, we completed real-time implementation and testing of both pharmacy expert systems, successfully collaborated with Motorola to better understand issues surrounding clinical alert notification, implemented and tested our expert systems, the user interface, and the notification engine on a single pharmacy satellite at Barnes Jewish Hospital (BJH), successfully completed a full roll out of these systems at BJH in September 1999, and accomplished the final task of porting these systems to another BJC system hospital, Christian Northeast Hospital (CHNE) where they have been in production since April 2000. The next section briefly describes how all the components of the system work together.

2.2 Technical Overview

Figure 1 depicts an overview of the system architecture, which is briefly reviewed in this



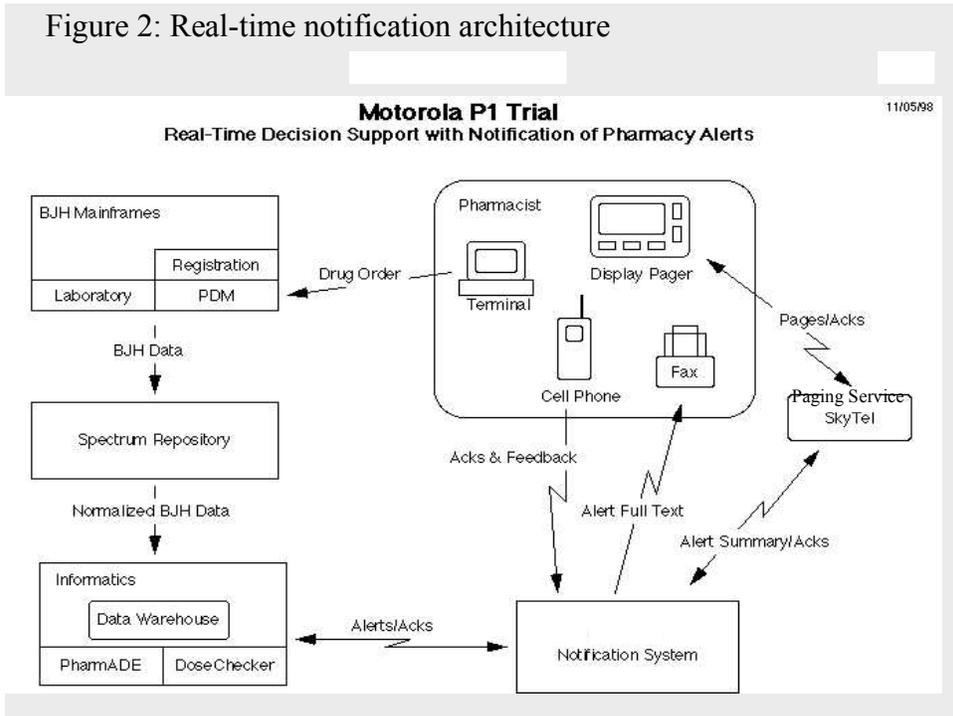
section. In the figure, processes are depicted as ovals, data stores (or databases) as open-ended rectangles, and data flows as arrows, with arrowheads pointing in the direction of “flow.” The heavy dashed line represents an interface between the Project Spectrum Clinical Information System (CIS) and a Medical Informatics managed system used for this project. This figure was presented in previous quarterly reports and was discussed the site visit on August 12, 1997. A brief review of how the system works is presented here, to set the context for the information that follows.

Most of the clinical data needed for this project are obtained from the Project Spectrum Repository, which receives its data in “real time” from several BJC hospital facility mainframes. The incoming data are normalized and encoded using Spectrum’s SNOMED-based Medical Entities Dictionary (MED) before being stored in Spectrum’s repository. The process *Send Interesting Data* represents a Medical Logic Module (MLM) that is invoked by the Spectrum Decision Support Engine at the moment that clinical data is stored in Spectrum. This relatively simple MLM determines whether the data is “interesting” for the purposes of

this contract, formats the data into an HL7-like message, and sends it to the Medical Informatics computer.

Store Interesting Data is a process that receives the clinical data from Spectrum as they arrive and uses them to update the Informatics Database. *Generate Alerts*, which represents our two expert systems, examines the new clinical data after they are stored in the database and applies the appropriate rules to determine whether to issue an alert or not. Some rules fire as soon as new data arrives (high priority alerts) and some rules fire at scheduled times during the day (medium and low priority alerts). Whenever an alert is generated, *Notify User* creates an alert-specific report and delivers it to the “appropriate user,” as defined in a set of user-specified Notification Preferences. Later, the user enters outcome data for the alert via a web-based application.

Figure 2 depicts an overview of the notification architecture for the alpha trial conducted in conjunction with Motorola.



There are certain features of the Motorola notification system that we did not replicate. For example, acknowledgement of page transmission and user receipt of the page was not possible at the time of development and implementation of these systems using existing technology and paging services used by BJC. However, alerts designated as high-priority that are not "closed" by the user are reissued until the user does close the alert, the instigating drug order is changed, or a patient factor changes that negates the need for an alert. Otherwise, our notification process is conceptually similar.

2.3 Work Completed for the Contract

We focused our efforts in six major areas: the design of the Informatics Database, the interface between the Informatics computer and the Spectrum CIS, the Expert Systems, the Notification Engine, Porting the Expert Systems to Another BJC Facility, and the Evaluation Studies. A detailed description of our work in each of these areas is provided in the following subsections.

2.3.1 Informatics Database Design

The tasks from our schedule (refer to Section 2.4) that comprise the database design are:

DB-1	Identify required clinical data
DB-2	Identify required MED terms
DB-3	Design database: clinical and MED
DB-4	Acquire tool to process data feeds

These tasks were all completed. Physical schemas of the Clinical and Notification portions of the Informatics Database are provided in Appendix A, Figure 5 (page 16) and Figure 6 (page 17).

2.3.2 Interface to Project Spectrum Repository

Two processes comprise this interface: *Send Interesting Data* and *Store Interesting Data*. The implementation portion and final testing and Y2K re-testing of this interface are complete.

2.3.2.1 Send Interesting Data

The tasks from our schedule (refer to Section 2.4) that comprise the *Send Interesting Data* process fall into two groups.

Each task in the first group involves setting up a real time data feed for one type of clinical data using the Spectrum repository as the data source. For each task, an MLM must be written which the Spectrum decision support engine executes. The MLM is triggered immediately when data are stored in the Spectrum repository, and its logic is fairly straightforward: if the data meet the simple criteria of being “interesting” to us for the contract (for example, if the lab test result is a gentamicin drug level), then they are immediately written to an MQ Series queue. MQ Series, an IBM guaranteed message delivery software package that we purchased for this contract, is used to transfer the data across the network from Spectrum to Informatics.

Tasks in the first task group are:

DB-5	Lab
DB-6	Demographic
DB-7	Visit
DB-8	Vitals

Tasks DB-5 through DB-8 are all complete.

The second group of tasks that comprise *Send Interesting Data* involves implementing data feeds that are not available from Spectrum because it has not yet implemented a pharmacy data model. Tasks in this group are:

DB-9	Pharmacy
DB-10	NDC codes

These tasks are also complete.

2.3.2.2 Store Interesting Data

Store Interesting Data is the “mirror image” of the *Send Interesting Data* process: this half of the Spectrum/Informatics messaging interface must receive messages arriving asynchronously and use the clinical data contained in them to immediately update the Informatics Database. Hence, there is a program on Informatics to handle each incoming data feed, regardless of its source. The tasks from our schedule (refer to Section 2.4) that comprise the *Store Interesting Data* process are:

DB-11	Lab
DB-12	Demographic
DB-13	Visit
DB-14	Vitals
DB-15	Pharmacy
DB-16	NDC Codes

Following the 1997 August site visit, we purchased Orion Systems’ Symphonia HL-7 parser product to facilitate the development of these programs.

Tasks DB-11 through DB-16 are all complete.

2.3.3 Expert System Architecture Redesign

The original versions of the DoseChecker and PharmADE expert systems were written in CLIPS, an expert system “shell” developed by NASA. Runtime access to our Sybase clinical database was provided by a set of CLIPS functions that we developed and placed in the public domain. While this architecture was adequate for our “batch” mode of operation, it did not lend itself to real time processing, so a new architecture was needed.

We continued to support the existing “batch” versions of these systems while reimplementing them for real time processing, in order to understand the differences in behavior of the real time and batch systems. In order to convert from batch mode to real time, we designed and implemented a new architecture to support real-time operation. We have also added new rules to both expert systems. See Appendix B for a paper detailing the process of DoseChecker redesign presented at AMIA in 1999.

The tasks from our schedule (refer to Section 2.4) that comprise the *Generate Alerts* process are:

DoseChecker:		ADE Monitor:	
DC-1	Analysis/Design	ADE-1	Analysis/Design
DC-2	Programming	ADE-2	Programming
DC-3	Develop test plans	ADE-3	Develop test plans
DC-4	Unit test expert system	ADE-4	Unit test expert system
DC-5	Integrated system testing	ADE-5	Integrated system testing

Tasks DC-1 through DC-5 are complete, as are tasks ADE-1 through ADE-5.

Re-testing of this interface was also performed to assure that it was Y2K compliant.

2.3.4 Notification Engine

Shortly after the 1997 August site visit, BJC Health System entered into an agreement with Motorola whereby Motorola would develop—with our assistance—a general-purpose Notification Engine that would become one of its commercial products. Prior to this contract being signed, we had completed a significant amount of the analysis and design work for this portion of our system. The user requirements on which our design was based were provided to Motorola in exchange for its help with implementation and the use of some notification devices, such as two-way pagers.

In mid-1998, BJC Health System suspended its contract with Motorola on the Notification Engine. Because a portion of the NLM Contract depended upon our evaluating notification technology, we (Washington University School of Medicine) successfully negotiated a separate agreement with Motorola so that work could continue on the Notification Engine as previously planned. An “alpha” version of the phase I system was deployed and tested in the fourth quarter of 1998 and first quarter of 1999. See appendix B for a paper related to this notification work that was presented at the AMIA conference in the fall of 1999. After completing this alpha trial, it was clear that we could develop an alternative notification strategy that would satisfy the needs of our users as well as meet our timelines.

The tasks from our schedule (refer to Section 2.4) that comprise the *Notify User* process are:

N-1:8	Analysis/Design
N-9	Acquire telephony package
N-10:16	Programming

The Analysis/Design tasks are complete. Programming and testing is also complete for this phase of the project. We conducted a trial of the expert systems and real time notification of high priority alerts using alpha pagers on a single pharmacy satellite at BJH from June 16, 1999 through September 1, 1999. On September 1, we went live with the entire hospital. After working through implementation issues related to this go-live, the conversion was successful and the systems remain in full production, with the hospital continuing support for maintenance and further development.

2.3.5 Porting the Expert Systems to Another BJC Facility

Real time DoseChecker and PharmADE went into house-wide production at BJH in September 1999. Following construction of a pharmacy orders interface from Christian Hospital NE/NW (CHNE), these systems were successfully ported to this facility and have been in production since April 2000.

2.3.6 Evaluation Studies

We planned and conducted three types of evaluations. First, we compared the alerting behavior and performance of the real-time and batch mode systems. Second, we are evaluated user preferences for alerting methodologies (FAX, EMAIL, and alpha paging). Third, as a means to evaluate the performance of our rules in diverse clinical settings, we compared user agreement with alerting rules at BJH and at CHNE.

Alerting Behaviors

DoseChecker: Real-time operation of DoseChecker went into production at BJH in September 1999. Batch mode DoseChecker continued to run until April 2000 but its output was not directed to the users. Over this period of time, batch mode DoseChecker screened an average of 4800 orders per month while real-time screened 7300 orders per month. The monthly alert rate for batch mode DoseChecker was 6.9% (95% CI 6.3-7.5), while the alert rate for real-time DoseChecker was 9.4% (95% CI 8.5-10.4); $p=0.0001$ paired t-test for equal variances. The higher alert rate for real-time DoseChecker is attributable to a greater

Pharmacy orders with potentially inappropriate dosages detected by DoseChecker

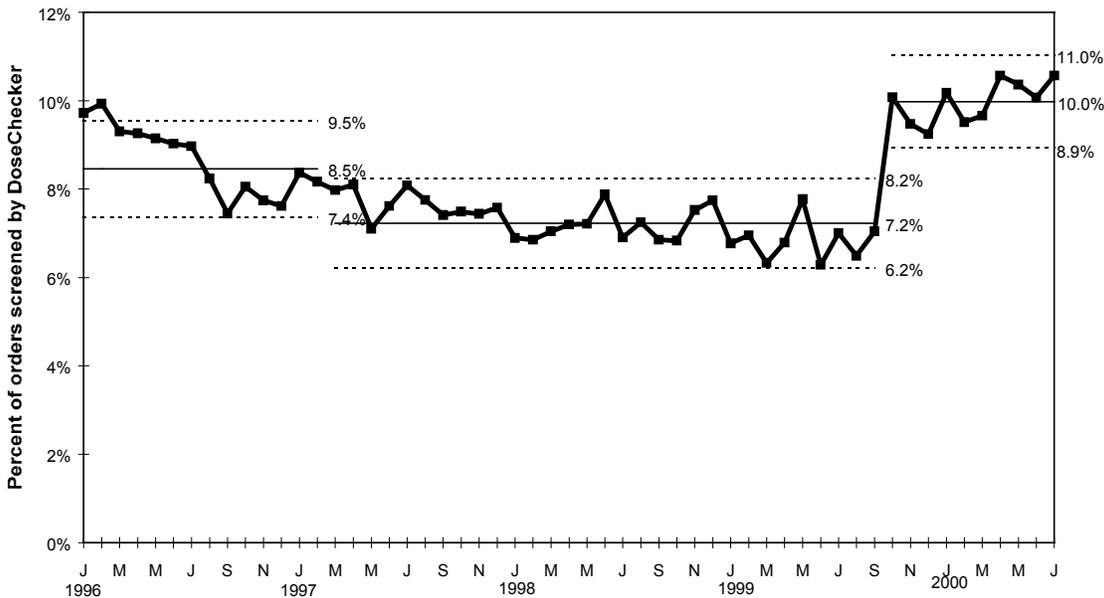


Figure 3

proportion of orders of shorter duration being screened and a greater proportion of violations with these orders, and the addition of new rules to the knowledge base. Another view of the impact of conversion from batch mode to real time DoseChecker in September 1999 can be readily seen in the statistical process control chart depicted in Figure 3.

PharmADE: Real-time operation of PharmADE went into production at BJH in September 1999. Batch mode PharmADE continued to run until April 2000 but its output was not directed to the users. Over this period of time, both batch mode and real-time PharmADE issued 46 unique alerts.

Performance:

User Preference for alerting methodologies: An iterative process was used to determine user preferences for clinical alert notification. During the Motorola alpha trial, all clinical alerts were directed to alpha pagers. The recipients of the alerts were eleven highly motivated clinical pharmacists. One hundred forty seven alerts were generated over the period of the trial, comprising 30 operational days. As a means to assess notification preferences each alert was assessed individually for pharmacist agreement with the alert itself, and whether the notification timing was appropriate, too early or too late. One hundred fourteen responses to this question were received. The majority (84, 74%) felt that timing was appropriate. In addition, the pharmacists were directly surveyed regarding their preferences for alert notification modality. When given the option of choosing a single alerting modality, 50% of the trial pharmacists preferred alpha pagers, with smaller percentages preferring fax or e-mail notification. However, it was clear from this alpha trial and from user feedback prior to real-time go-live that not all alerts were regarded with equal weight, and a need for prioritization was needed, with higher priority alerts being delivered by alpha pager and lower priority alerts being delivered by fax or e-mail. Furthermore, the users expressed the desire to batch lower priority alerts in order to decrease workflow disruption. Finally, although the pharmacists desired to be paged with high priority alerts, and agreed that the format for the alpha page contained all the pertinent clinical information they needed to act upon it, they desired a paper copy of the alert as a worksheet in addition to the alpha page. All of these features have been incorporated in the production versions of DoseChecker and PharmADE. High priority alerts are defined as all drug-drug interactions detected by PharmADE, and a single rule in DoseChecker (meperidine dosing in patients with severe renal insufficiency). These alerts are sent by alpha page and fax to the pharmacist responsible for the patient. Reminders alerts and an escalation feature help assure that these alerts are attended to promptly. Lower priority alerts are batched and sent by fax to the responsible pharmacists three times a day, with times chosen to correspond to pharmacy order volume and integrate with pharmacist workflow. Alert information can also be viewed by means of a web interface and the same interface can be used for alert outcome feedback. Faxed alert forms can also be used for alert outcome feedback. At BJH, the pharmacists almost exclusively use these faxed forms to provide this feedback, while at CHNE the web interface is exclusively used for this purpose. This is a matter of user preference and the fact that responsibility for addressing clinical alert outcomes is distributed over many users at BJH, while at CHNE there is a single designated pharmacist to provide this feedback.

User agreement with alerting rules:

We measured agreement rate with clinical alerts in two user groups (pharmacists and physicians) at two BJC facilities (BJH and CHNE). Pharmacists are the direct recipients of clinical alerts and physicians receive them indirectly after the pharmacist has assessed alert validity. BJH pharmacists use a paper-based system to record agreement with alerts, while

CHNE uses a web interface. The response rate is much better with the web interface than with the paper-based system: approximately 60% with the former and 100% with the latter. Since implementation, we have data addressing agreement with 5273 DoseChecker alerts at BJH and 1588 DoseChecker alerts at CHNE. BJH pharmacists agreed with and contacted physicians regarding 1960 of 5273 alerts (37%), while CHNE pharmacists agreed with and contacted physicians regarding 420 of 1588 alerts (26%). When pharmacists contacted physicians with these alerts, physicians agreed to change the order 72% (1417 of 1960) of time at BJH, and 50% (210 of 420) of the time at CHNE. The effective rate of agreement (pharmacist+physician) was 27% (1417 of 5273) at BJH and 13% (210 of 1588 at CHNE). Alert agreement by drug at each facility is seen in the following table:

Drug	Facility	N	Effective Agree	95% CI	Rph Agree	95% CI
Acyclovir	BJH	291	9.3%	5.9-12.6%	13.7%	9.7-17.7%
	CHNE	19	5.3%	0-16.3%	15.8%	0-33.8%
Allopurinol	BJH	2	100%	-	100%	-
	CHNE	9	33%	0-72%	55%	15-96%
Ampicillin-sulbactam*	BJH	90	46%	35-56%	53%	43-65%
	CHNE	31	19%	4.6-34%	45%	27-64%
Ampicillin*	BJH	138	38%	29-46%	46%	38-55%
	CHNE	19	0	-	10%	0-26%
Atenolol*	BJH	93	14%	6.8-21.1%	26%	16.7-34.9%
	CHNE	25	0	-	12%	0-26%
Aztreonam	BJH	29	21%	5.0-36%	31%	13-49%
	CHNE	18	5.6%	0-17%	39%	14-64%
Cefazolin	BJH	300	25%	20-30%	31%	26-37%
	CHNE	125	15%	8.8-22%	26%	19-34%
Cefepime	BJH	670	35%	32-39%	44%	40-47%
	CHNE	82	32%	21-42%	51%	40-62%
Cefotetan	BJH	122	21%	14-29%	25%	18-33%
	CHNE	87	8%	2.2-14%	26%	17-36%
Ceftazidime	BJH	14	14%	0-35%	36%	7.0-64%
	CHNE	33	12%	0-24%	27%	11-43%
Ceftriaxone	BJH	85	25%	15-34%	47%	36-58%
	CHNE	40	12%	1.8-23%	35%	20-50%
Ciprofloxacin IV	BJH	205	27%	21-33%	34%	28-40%
	CHNE	47	17%	5.9-28%	43%	28-57%
Ciprofloxacin PO*	BJH	276	32%	26-37%	40%	34-46%
	CHNE	107	8.4%	3.0-14%	41%	32-50%
Clindamycin	BJH	32	47%	29-65%	59%	41-77%
	CHNE	37	30%	14-45%	32%	17-48%
Famotidine*	BJH	152	38%	30-46%	46%	38-54%
	CHNE	69	56%	44-68%	74%	63-84%
Fluconazole	BJH	79	20%	11-29%	34%	23-45%

	CHNE	11	27%	0-59%	64%	29-98%
Gabapentin	BJH	20	20%	1-39%	45%	21-69%
	CHNE	5	60%	0-100%	60%	0-100%
Gentamicin*	BJH	314	22%	28-27%	38%	32-43%
	CHNE	146	2%	0-4%	2	0-4%
Imipenem*	BJH	214	48%	41-55%	62%	56-69%
	CHNE	15	6.7%	0-21%	6.7%	0-21%
Ketorolac	BJH	96	31%	22-41%	35%	26-45%
	CHNE	47	32%	18-46%	36%	33-50%
Lamivudine	BJH	18	17%	0-36%	44%	19-70%
	CHNE	9	11%	0-37%	56%	15-96%
Meperidine*	BJH	40	50%	34-66%	72%	58-87%
	CHNE	143	0%	-	3.5%	0-6.5%
Metformin	BJH	309	9.7%	6.4-13%	26%	22-31%
	CHNE	56	7.1%	0.2-14%	32%	20-45%
Metronidazole	BJH	26	31%	23-50%	42%	22-63%
	CHNE	44	59%	44-74%	64%	49-78%
Piperacillin-Tazobactam*	BJH	88	38%	27-48%	44%	34-55%
	CHNE	85	8.2%	2.3%-14%	26%	16%-35%
Stavudine	BJH	21	4.8%	0-15%	33%	11-55%
	CHNE	5	40%	0-100%	60%	0-100%
Vancomycin*	BJH	1161	24%	22-26%	33%	30-36%
	CHNE	222	1.4%	0-2.9%	2.2%	0.3-4.2%

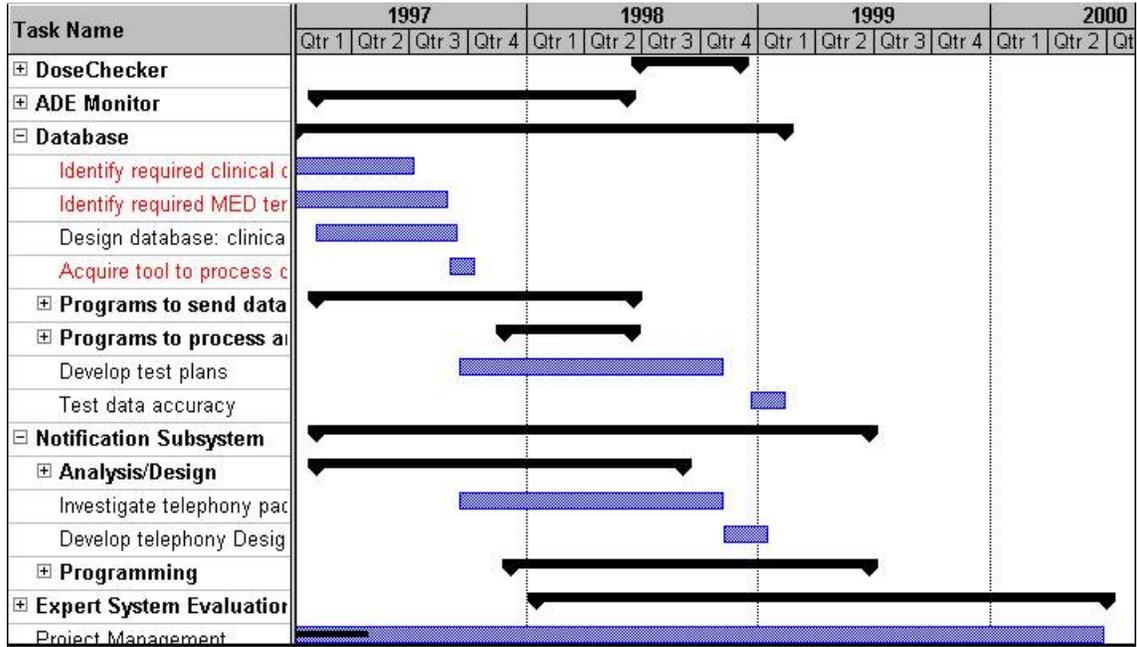
* Indicates statistically significant differences (shown in bold).

Statistically significant differences in effective agreement rate existed between facilities for nine drugs: ampicillin-sulbactam, ampicillin, atenolol, oral ciprofloxacin, gentamicin, imipenem, meperidine, piperacillin-tazobactam, and vancomycin. In six of these nine cases pharmacists between the facilities differed in the proportion of alerts with which they agreed, contributing to the observed difference in effective agreement. In the remaining three cases, physicians disagreed with pharmacist recommendations. The level of agreement is lower at CHNE than at BJH. Only one drug (famotidine) had a significantly higher rate of agreement among pharmacists at CHNE when compared to BJH, but the effective rate of agreement was not significantly different between the facilities. In no case was MD rate of agreement higher at CHNE. We saw similarly low rates of agreement among pharmacists with initial implementation of the expert systems in batch mode at BJH, and pharmacist education and experience with the expert systems and physician interaction have resulted in increased rates of agreement over time. We anticipate a similar phenomenon at CHNE.

2.4 Schedule

Figure shows the completed project schedule.

Figure 4. Completed Project Schedule



2.5 Summary

We deployed a fully functional, integrated, near real-time expert system and notification package to screen pharmacy orders for appropriate dosing and for contraindicated drug combinations at BJH on September 1, 1999 and at CHNE on April 1, 2000. Acceptance of these systems is good, both by the pharmacists who receive clinical alerts and by physicians who are contacted by pharmacists as a result of these alerts. However, significant differences exist between facilities in agree rates for some drugs. Preferences for notification modality vary by the severity of the type of error detected, and the user.

The most common source of prescribing error is failure to adjust doses based upon patients' renal function. Hospitalized patients often have unstable renal function requiring constant monitoring of prescriptions for appropriateness. Approximately 30% of our dosing errors occur as the result of information that changes after the opportunity to first screen the order. Our systems catch dosing errors and contraindicated drug combinations that have evaded existing systems designed to catch them. Order entry systems equipped with alerting mechanisms to intercept prescribing errors only at the time of order entry may be substantially less effective than alerting strategies that periodically evaluate all active orders as our systems do. Our asynchronous alerting strategy is a practical response to existing technologic and workflow constraints, disrupting physician workflow only when necessary to correct possible errors.

These systems represent a valuable safety net for medication errors that slip past existing safeguards. Wireless and web technologies deliver significant advantages in terms of efficiency and convenience for pharmacists, and serves as an important adjunct to paper-based technologies. The systems funded by this contract continue in operation at the writing of this report, with plans being made to further expand deployment within BJC. A significant and interesting open question raised by this work is whether direct notification of physicians rather than using pharmacists as intermediaries would be similarly acceptable, more efficient, and possibly more effective.

APPENDIX A. DATABASE SCHEMAS

This appendix contains the physical schemas of both the clinical and notification portions of the Informatics Database.

APPENDIX B. PAPERS AND PRESENTATIONS

This appendix contains the papers and meeting presentations related to our work.