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Research Article

Autoverification in a core clinical chemistry laboratory at an academic medical center

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Abstract

Background: Autoverification is a process of using computer-based rules to verify clinical laboratory test results without manual intervention. To date, there is little published data on the use of autoverification over the course of years in a clinical laboratory. We describe the evolution and application of autoverification in an academic medical center clinical chemistry core laboratory. **Subjects and Methods:** At the institution of the study, autoverification developed from rudimentary rules in the laboratory information system (LIS) to extensive and sophisticated rules mostly in middleware software. Rules incorporated decisions based on instrument error flags, interference indices, analytical measurement ranges (AMRs), delta checks, dilution protocols, results suggestive of compromised or contaminated specimens, and 'absurd' (physiologically improbable) values. **Results:** The autoverification rate for tests performed in the core clinical chemistry laboratory has increased over the course of 13 years from 40% to the current overall rate of 99.5%. A high percentage of critical values now autoverify. The highest rates of autoverification occurred with the most frequently ordered tests such as the basic metabolic panel (sodium, potassium, chloride, carbon dioxide, creatinine, blood urea nitrogen, calcium, glucose; 99.6%), albumin (99.8%), and alanine aminotransferase (99.7%). The lowest rates of autoverification occurred with some therapeutic drug levels (gentamicin, lithium, and methotrexate) and with serum free light chains (kappa/lambda), mostly due to need for offline dilution and manual filing of results. Rules also caught very rare occurrences such as plasma albumin exceeding total protein (usually indicative of an error such as short sample or bubble that evaded detection) and marked discrepancy between total bilirubin and the spectrophotometric icteric index (usually due to interference of the bilirubin assay by immunoglobulin (Ig) M monoclonal gammopathy). **Conclusions:** Our results suggest that a high rate of autoverification is possible with modern clinical chemistry analyzers. The ability to autoverify a high percentage of results increases productivity and allows clinical laboratory staff to focus attention on the small number of specimens and results that require manual review and investigation.

Key words: Algorithms, clinical chemistry, clinical laboratory information system, Epstein-Barr virus, informatics

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INTRODUCTION

Autoverification is a process whereby clinical laboratory results are released without manual human intervention.[1-6] Autoverification uses predefined computer rules to govern release of results.[1] Autoverification rules may include decisions based on instrument error flags (e.g. short sample, possible bubbles, or clot), interference indices (e.g. hemolysis, icterus, and lipemia),[7] reference ranges, analytical measurement range (AMR), critical values, and delta checks (comparison of current value to previous values, if available, from the same patient).[8-13] Rules may also define potentially absurd (physiologically improbable) values for some analytes and additionally may control automated dilutions and conditions for repeat analysis of specimens. More sophisticated application of autoverification rules can generate customized interpretive text based on patterns of laboratory values.[3,14] Autoverification is commonly performed using the laboratory information system (LIS) and/or middleware software that resides between the laboratory instruments and the LIS.[1-6]

Autoverification can greatly reduce manual review time and effort by laboratory staff, limiting staff screen fatigue caused by reviewing and verifying hundreds to thousands of results per shift. Ideally, autoverification allows laboratory staff to focus manual review on a small portion of potentially problematic specimens and test results.[6] However, improperly designed autoverification can lead to release of results that should have been held, potentially negatively impacting patient management.

There is relatively little published literature on practical use of autoverification. There is a guideline document produced by the Clinical and Laboratory Standards Institute (CLSI) on autoverification of clinical laboratory test results which focuses on the process for validating and implementing autoverification protocols.[15] In this study, we present data on autoverification used in a clinical chemistry core laboratory in an academic medical center. The rules in this laboratory evolved over more than a decade and now result in a high autoverification rate of clinical chemistry tests.

SUBJECTS AND METHODS

The institution of this study is a 734-bed tertiary care academic medical center that includes an emergency room with level one trauma capability, adult and pediatric inpatient floors, and multiple intensive care units (neonatal, pediatric, cardiovascular, medical, and surgical/neurologic). Primary care and specialty outpatient services are provided at the main medical center campus as well as a multispecialty outpatient facility located 3 miles away. Pneumatic tube transportation of specimens is available throughout the medical center. Smaller primary care clinics affiliated with the academic health system are dispersed throughout the local region. A core laboratory within the Department of Pathology provides clinical chemistry and hematopathology testing for both outpatient and inpatient services. This study focuses on the clinical chemistry division from 1/1/2000 to 9/21/2013. This study was approved by the University of Iowa Institutional Review Board as a retrospective study.

Throughout the time period of retrospective analysis, the main chemistry instrumentation in the core laboratory was from Roche Diagnostics (Indianapolis, IN, USA). By 2010, the chemistry automation line included five Modular *P* and four Modular E170 analyzers, with front-end automation provided by a Modular Pre-Analytic (MPA)-7 unit. In 2013, the chemistry instrumentation was replaced with a Cobas 8000 system with two c702, three C502, and five e602 analyzers, still using MPA-7 as the front-end automation. This chemistry automation system currently supports 131 Roche assays and 14 non-Roche assays run as either open or partner channels. Other instrumentation in the core chemistry laboratory includes: Abbott Diagnostics (Abbott Park, IL, USA) Architect i1000 (running cyclosporine, sirolimus, and tacrolimus drug levels, along with human immunodeficiency virus (HIV) testing); Bio-Rad (Hercules, CA, USA) Bioplex 2200 (variety of serologic assays), and Advanced Instruments (Norwood, MA, USA) A2O automated osmometer for serum/plasma and urine osmolality measurements.

The LIS throughout the period of retrospective analysis has been Cerner (Kansas City, MO, USA) "Classic", currently version 015. The LIS is managed by University of Iowa Hospital Computing and Information Services. Roche instruments are interfaced to the LIS via Data Innovations (South Burlington, VT, USA) Instrument Manager ("Middleware") version 8.10. Instruments other than Roche are interfaced to the LIS via Data Innovations Instrument Manager version 8.12. The majority of autoverification rules are in Middleware. A small number of rules are in the LIS. The Roche and non-Roche Middleware production servers each have "shadow" backups in a separate location that can be used if the corresponding main production server fails. There are also separate "test" servers for each system that allow for initial testing and validation of rules without affecting the production servers. Service agreements for instrumentation and middleware are at a level that provides rapid response to problems.

The core laboratory has a supervisor that primarily focuses on middleware, and three clinical laboratory scientists that are tasked with implementing, validating, and maintaining autoverification rules. The core laboratory employs a full-time medical technologist for quality control and improvement. A process improvement team within the chemistry division meets

regularly with the medical director to review and discuss laboratory issues. Many of the core laboratory staff is cross-trained on both chemistry and hematology automated instrumentation. This provides important cross-coverage, particularly in periods of instrument, LIS, or middleware downtime.

All autoverification rules require approval by medical director. Core laboratory staff can suspend autoverification, if necessary. The goal of the core laboratory is to have continuous flow of specimens onto the automated line as much as possible, regardless of the inpatient or outpatient unit origin of the specimens. Specimens that are not suitable for the automated line (e.g. small pediatric tubes or tubes requiring manual aliquoting) are handled by a manual exception bench. There is no designation of routine versus stat for ordering of laboratory tests. By 2010, the option to order any chemistry assay on a stat basis was removed from the electronic medical record provider ordering system and on paper requisitions. This change was based on consistent turnaround times and had approval from the hospital subcommittee overseeing laboratory testing.

The autoverification rules currently used were developed mainly over the course of 8 years, although rudimentary autoverification rules within the LIS were first used starting in 2000. Manual review and absurd limits were developed based on analysis of patient data and consultation with clinical services. More involved use of autoverification followed with use of introduction of middleware.

Validation of autoverification rules followed CLSI guideline AUTO10-A.[15] Key elements of the validation protocol are pretesting, simulated patient testing, testing using clinical specimens, approval of documentation, and finally, implementation and maintenance of rules. Where possible, clinical specimens with unusual properties (e.g. extremely low or high concentrations of a specific analyte, very icteric or lipemic specimens) were saved to allow for testing of rules using real specimens. Validation included thorough testing of upper and lower limits of ranges (e.g. reference ranges, absurd ranges), including the boundaries of these ranges. Rules were tested individually and in combination. Finally, integrity of the results to the LIS and finally to the hospital electronic medical record were tested. Common pitfalls encountered in the evolution of autoverification rules were unexpected instrument errors or finding samples with values sought after for testing. In the cases that specimens cannot be found with certain properties, simulated testing had to suffice. Table 1 contains parameters for all the chemistry assays including manual review limits, critical values, delta checks, interference indices (hemolysis, icterus, lipemia), AMR, and auto-extended range (for automated dilution protocols).

The protocols permit autoverification of critical values provided all other rules are met. Whether a critical value autoverifies or not, a printout is generated that directs laboratory staff to notify the ordering provider by telephone and to document this notification (including read-back and verification of the result by the recipient of the call). A call center within the core laboratory handles the majority of critical value reporting during business hours. When the call center is not open, technologists within the laboratory handle critical value reporting. Critical value reporting and appropriate documentation of the provider call is monitored as a quality metric. Late reports detect failure to document notification of provider of critical values.

RESULTS

Figure 1 shows a schematic diagram of autoverification rules used for the chemistry assays. Table 2 specifies in greater detail the consequences of each step of this process. Some steps such as instrument error flags or violation of manual review limits or delta checks outright prevent autoverification. Note that a test result generating a critical value does not preclude autoverification.

Figure 2 shows the increasing rate of autoverification over the course of years in the core chemistry laboratory. Starting from an autoverification rate of 40% in 2000 using rudimentary rules within the LIS, the rate increased to 95% by 2007 by initial implementation of middleware rules and then to 99.0% by 2010. The time period from 2005 to 2010 also saw an increase in staff productivity, with an increase of billable tests per hour from 14.9 to 19.7 [Figure 2]. During this time period, the annual testing volume increased from 2.7 million tests/year (2005) to 3.2 million tests/year (2010). Annual test volumes have remained relatively steady since 2010.

The further increase in autoverification rate from 99.0% in 2010 to the current rate of 99.5% in 2013 was achieved by allowing autoverification of critical values (provided manual review limits or absurd ranges are not violated) and by auto-release of results with interference by hemolysis, lipemia, or icterus. Exceeding interference limits results in text result of "hemolyzed", "lipemic", or "icteric" (i.e. no numeric result is provided), coupled with crediting of charges for that assay. Tests cancelled due to interference can only be overridden at clinician request, with a disclaimer then appended. For critical values that autoverify, the notification of clinical service occurs after autoverification (i.e. as long as autoverification conditions are met, filing of critical value results does not wait for clinician notification).

Table 3 shows current rates of autoverification for a variety of panels and individual assays. The overall rate of autoverification for all chemistry tests was 99.5% measured

Table 1: Parameters for all the chemistry assays including manual review limits, critical values, delta checks, interference indices (hemolysis, icterus, lipemia), AMR, and auto-extended range (for automated dilution protocols)

Test name	Units	Instrumentation (previous/ current)	Assay vendor	Current assay version	Manual review, low value	Manual review, high value	Critical low value below	Critical high value above	Delta	Hemolysis index	Lipemic index	Icteric index	AMR	Auto extended range	Final result, if above AMR
Acetaminophen	µg/mL	Modular P/Cobas 8000 c502	Sekisui	Acetaminophen-SL, 8/16/2011				40		200	1,200	40	1.2-378	NA	Full value
Adrenocorticotropic hormone	pg/mL	Modular E/Cobas 8000 e602	Roche	ACTH, 2011-12, V7						400	1,500	25	1-2,000	NA	>2,000
Alanine aminotransferase	U/L	Modular P/Cobas 8000 c702	Roche	ALT, 2011-03,V3						200	150	60	5-700	5-7,000	Full value
Albumin	g/dL	Modular P/Cobas 8000 c702	Roche	Albumin, 2010-12,V3						1,000	550	60	0.2-6.0	0.2-30.0	Full value
Alkaline phosphatase	U/L	Modular P/Cobas 8000 c702	Roche	ALP, 2012-08,V3						200	2,000	60	5-1,200	5-6,000	Full value
Alpha-1 antitrypsin	mg/dL	Modular P/Cobas 8000 c502	Roche	A1AT, 2012-03, V8						1,000	350	60	20-600	20-1,200	Full value
Alpha-fetoprotein	ng/mL	Modular E/Cobas 8000 e602	Roche	AFP, 2010-04,V4						2,200	1,500	65	0.6-1,210	0.6-60,500	Full value
Amikacin	µg/mL	Modular P/Cobas 8000 c502	Roche	AMIK2, 2012-02,V8				35		1,000	2,000	50	0.8-40.0	NA	Full value
Ammonia	µmol/L	Modular P/Cobas 8000 c502	Roche	NH3L, 2012-03, V7						200	50	30	10 -700	10-1,400	Full result
Amylase	U/L	Modular P/Cobas 8000 c702	Roche	AMYL, 2010-12, V3						500	1,500	60	3-1,500	3-7,500	Full value
Amylase, urine	U/L	Modular P/Cobas 8000 c502	Roche	AMYL, 2010-12, V3						NA	NA	NA	3-1,500	3-7,500	Full value
Angiotensin converting enzyme	U/L	Modular P/Cobas 8000 c502	Trinity Biotech	ACE, 3/2011						NA	NA	NA	1-120	1-240	Full value
Anticyclic citrullinated peptide	U/mL	Modular E/Cobas 8000 e602	Roche	Anti-CCP, 2010-08,V2						500	1,500	25	8-1,500	NA	>500
Antinuclear antigen-anticentromere B antibodies	Antibody index	BioPlex 2200	Bio-Rad	ANA Screen, 3/2012						NA	NA	NA	0.2-8.0	NA	>8.0
ANA-antichromatin antibodies	AI	BioPlex 2200	Bio-Rad	ANA Screen, 3/2012						NA	NA	NA	0.2-8.0	NA	>8.0
ANA-double-stranded deosyribonucleic acid antibodies	IU/mL	BioPlex 2200	Bio-Rad	ANA Screen, 3/2012						NA	NA	NA	1-300	NA	Full value
ANA-Jo1 antibodies	AI	BioPlex 2200	Bio-Rad	ANA Screen, 3/2012						NA	NA	NA	0.2-8.0	NA	>8.0
ANA-ribosomal P antibodies	AI	BioPlex 2200	Bio-Rad	ANA Screen, 3/2012						NA	NA	NA	0.2-8.0	NA	>8.0

Contd

Table 1: Contd...

Test name	Units	Instrumentation (previous/ current)	Assay vendor	Current assay version	Manual review, low value	Manual review, high value	Critical low value below	Critical high value above	Delta	Hemolysis index	Lipemic index	Icteric index	AMR	Auto extended range	Final result, if above AMR
ANA-RNP antibodies	AI	BioPlex 2200	Bio-Rad	ANA Screen, 3/2012						NA	NA	NA	0.2-8.0	NA	>8.0
ANA-RNP/ Smith (common motif) antibodies	AI	BioPlex 2200	Bio-Rad	ANA Screen, 3/2012						NA	NA	NA	0.2-8.0	NA	>8.0
ANA-Smith antibodies	AI	BioPlex 2200	Bio-Rad	ANA Screen, 3/2012						NA	NA	NA	0.2-8.0	NA	>8.0
ANA-SS-A antibodies	AI	BioPlex 2200	Bio-Rad	ANA Screen, 3/2012						NA	NA	NA	0.2-8.0	NA	>8.0
ANA-SS-B antibodies	AI	BioPlex 2200	Bio-Rad	ANA Screen, 3/2012						NA	NA	NA	0.2-8.0	NA	>8.0
Aspartate aminotransferase	U/L	Modular P/Cobas 8000 c702	Roche	AST, 2011-03, V3						40	150	60	5-700	5-7,000	Full result
Beta-2 microglobulin	mg/L	Modular P/Cobas 8000 c502	Roche	2012-01, V4						1,000	1,000	60	0.1-8.0	0.1-88.0	>88.0
Beta-hydroxybutyrate	mEq/L	Modular P/Cobas 8000 c502	Stanbio	LiquiColor 06/2004						2,000	417	36	0.1-5.0	0.1-10.0	Full result
Bilirubin, direct	mg/dL	Modular P/Cobas 8000 c502	Roche	D-BILI, 2011-12, V9						30	60	None	0.2-40.0	NA	Full result
Bilirubin, total	mg/dL	Modular P/Cobas 8000 c702	Roche	TBILI, 2012-12, V4				>10 (younger than 1-day-old) >13 (1–31-days-old)		500	90	None	0.1-35.1	0.1-175.5	Full result
C3 complement	mg/dL	Modular P/Cobas 8000 c502	Roche	C3c, 2012-01, V6						1,000	2,000	60	4-500	4-1,000	Full result
C4 complement	mg/dL	Modular P/Cobas 8000 c502	Roche	C4, 2012-01, V7						500	1,000	60	2-100	2-200	Full result
Calcium, total	mg/dL	Modular P/Cobas 8000 c702	Roche	2012-08, V2			6.0	13.0	±20% to previous if <7.5 mg/dL; ±10% to previous if >15.0 mg/dL	1,000	1,000	60	0.8-20.1	NA	Full result
Calcium, urine	mg/dL	Modular P/Cobas 8000 c502	Roche	2012-08, V2						NA	NA	NA	0.8-30.1	0.8-150.5	Full result
Cancer antigen -125	U/mL	Modular E/ Cobas 8000 e602	Roche	CA 125 II, 2011-05, V2						3,200	2,000	66	1-5,000	1-25,000	>25,000

Contd

Table 1: Contd...

Test name	Units	Instrumentation (previous/ current)	Assay vendor	Current assay version	Manual review, low value	Manual review, high value	Critical low value below	Critical high value above	Delta	Hemolysis index	Lipemic index	Icteric index	AMR	Auto extended range	Final result, if above AMR
Carbamazepine	µg/mL	Modular P/Cobas 8000 c502	Roche	CEDIA Carbamazepine II, 2012-10,V11				12		1,000	1,000	60	0.5-20.0	NA	Full result
Carbohydrate antigen-19-9	U/mL	Modular E/Cobas 8000 e602	Roche	CA 19-9, 2010-09,V4						2,200	1,500	66	0.6-1,000	0.6-10,000	>10,000
Carbon dioxide	mEq/L	Modular P/Cobas 8000 c502	Roche	CO2-L, 2012-02,V6			10	50	±66% to previous if <10 mEq/L	600	1,800	60	2-50	NA	Full result
Carcinoembryonic antigen	ng/mL	Modular E/Cobas 8000 e602	Roche	CEA, 2012-05, V4						2,200	1,500	66	0.2-1,000	0.2-50,000	>50,000
Ceruloplasmin	mg/dL	Modular P/Cobas 8000 c502	Roche	2012-04,V7						1,000	200	60	3-140	3-420	Full result
Chloride	mmol/L	Modular P/Cobas 8000 c702	Roche	ISE N, K, Cl; 2010-09,V1					±20% to previous if <80 mmol/L; ±10% to previous if >120 mmol/L	None	2,000	60	60-140	NA	Full result
Chloride, urine	mmol/L	Modular P/Cobas 8000 c502	Roche	ISE N, K, Cl; 2010-09,V1						NA	NA	NA	10-250	NA	Full result
Cholesterol, total	mg/dL	Modular P/Cobas 8000 c702	Roche	CHOL, 2010-12,V3			2.0 (clinically significant)			700	2,000	16	4-800	4-8,000	Full result
Cortisol	µg/dL	Modular E/Cobas 8000 e602	Roche	2010-08,V4						1,900	2,700	60	0.3-63.4	0.3-634	Full result
C-peptide	ng/mL	Modular E/Cobas 8000 e602	Roche	2011-12,V7						300	2,000	50	0.01-40.0	NA	>40.0
C-reactive protein	mg/dL	Modular P/Cobas 8000 c702	Roche	CRPL3, 2011-12,V6						1,000	1,000	60	0.5-35.0	0.5-70.0	Full result
CRP, high sensitivity	mg/L	Modular P/Cobas 8000 c502	Roche	CRPHS, 2012-03,V8						1,000	600	60	0.2-20.0	NA	>20.0
Creatine kinase	U/L	Modular P/Cobas 8000 c702	Roche	CKm 2012-03, V3						100	1,000	60	7-2,000	7-22,000	Full result
Creatinine	mg/dL	Modular P/ Cobas 8000 c702	Roche	CREP2, 2011-03,V4					±50% to previous if <0.15 mg/dL	800	2,000	15	0.1-30.5	0.1-120	Full result

Contd

Table 1: Contd...

Test name	Units	Instrumentation (previous/ current)	Assay vendor	Current assay version	Manual review, low value	Manual review, high value	Critical low value below	Critical high value above	Delta	Hemolysis index	Lipemic index	Icteric index	AMR	Auto extended range	Final result, if above AMR
Creatinine, urine	mg/dL	Modular P/Cobas 8000 c502	Roche	CREP2, 2011- 03,V4						NA	NA	NA	0.1-610	0.1-1,525	Full result
Cyclosporine	ng/mL	Abbott Architect	Abbott	Cyclosporine, October 2010	24	1,501				NA	NA	NA	25-1,500	NA	>1,500
Cystatin C	mg/L	Modular P/Cobas 8000 c502	Roche	CYSC, 2012-04, V6						700	1,000	60	0.3-8.0	0.3-12.0	Full result
Cytomegalovirus antibodies, IgG	IU/mL	BioPlex 2200	Bio-Rad	ToRC IgG, 3/2012						Avoid hemolysis	NA	NA	0.2-8.0	NA	>8.0
CMV antibodies, IgM	IU/mL	BioPlex 2200	Bio-Rad	RC-M, 8/2011						Avoid hemolysis	NA	NA	0.2-4.0	NA	>4.0
D-Dimer	µg/mL	Modular P/Cobas 8000 c502	Roche	2012-04,V7						500	750	20	0.10-9.0	0.1-21.6	Full result
Dehydroepiandrosterone sulfate	µg/dL	Modular E/Cobas 8000 e602	Roche	2011-01,V15						560	2,000	13	0.1-1,000	NA	>1,000
Digoxin	ng/mL	Modular E/Cobas 8000 e602	Roche	2012-10,V4					2.1	1,000	1,500	65	0.15-5.0	0.15-10.0	Full result
Drug of abuse-amphetamines	Qualitative	Modular P/Cobas 8000 c502	Roche	Amphetamines II, 2012-02,V6						NA	NA	NA	NA	NA	NA
Drug of abuse-benzodiazepines	Qualitative	Modular P/Cobas 8000 c502	Roche	Benzodiazepines Plus, 2012-03, V6						NA	NA	NA	NA	NA	NA
Drug of abuse-cocaine metabolite	Qualitative	Modular P/Cobas 8000 c502	Roche	Cocaine II, 2012-04,V6						NA	NA	NA	NA	NA	NA
Drug of abuse-opiates	Qualitative	Modular P/Cobas 8000 c502	Roche	Opiates II, 2012-05,V9						NA	NA	NA	NA	NA	NA
Drug of abuse-oxycodone/ oxymorphone	Qualitative	Modular P/Cobas 8000 c502	Roche	Oxycodone, 2012-04,V5						NA	NA	NA	NA	NA	NA
Drug of abuse-tetrahydrocannabinol	Qualitative	Modular P/Cobas 8000 c502	Roche	Cannabinoids II, 2012-03,V8						NA	NA	NA	NA	NA	NA
Epstein-barr virus early nuclear antibody	AI	BioPlex 2200	Bio-Rad	EBV IgG, 3/2012						NA	NA	NA	0.2-8.0	NA	>8.0
EBV heterophile antibodies	Qualitative	BioPlex 2200	Bio-Rad	EBV IgM, 3/2012						NA	NA	NA	NA	NA	NA
EBV viral capsid antibodies, immunoglobulin (Ig) G	AI	BioPlex 2200	Bio-Rad	EBV IgG, 3/2012						NA	NA	NA	0.2-8.0	NA	>8.0
EBV viral capsid antibodies, IgM	AI	BioPlex 2200	Bio-Rad	EBV IgM, 3/2012						NA	NA	NA	0.2-8.0	NA	>8.0
Estradiol	pg/mL	Modular E/Cobas 8000 e602	Roche	Estradiol II, 2012-03,V2						1,000	1,000	66	5-4,300	5-21,500	Full result

Contd

Table 1: Contd...

Test name	Units	Instrumentation (previous/ current)	Assay vendor	Current assay version	Manual review, low value	Manual review, high value	Critical low value below	Critical high value above	Delta	Hemolysis index	Lipemic index	Icteric index	AMR	Auto extended range	Final result, if above AMR
Ethanol	mg/dL	Modular P/Cobas 8000 c502	Roche	2012-04,V9				300		200	500	60	10-498	NA	Full result
Ethanol, urine	mg/dL	Modular P/Cobas 8000 c502	Roche	2012-04,V9						NA	NA	NA	10-498	NA	Full result
Ethylene glycol	mg/dL	Modular P/Cobas 8000 c502	Catachem	Catachem AB162007				9		200	1,000	15	0.1-300	NA	Full result
Everolimus	ng/mL	Modular P/Cobas 8000 c502	Thermo-scientific	QMS Everolimus, 2/2011						NA	NA	NA	2.0-20.0	NA	>20.0
Ferritin	ng/mL	Modular E/Cobas 8000 e602	Roche	2012-06,V2						500	3,300	65	0.5-2,000	0.5-100,000	Full result
Folate	ng/mL	Modular E/Cobas 8000 e602	Roche	Folate III, 2012-02,V6						40	1,500	33	1.5-20.0	NA	>20.0
Follicle stimulating hormone	mIU/mL	Modular E/Cobas 8000 e602	Roche	FSH, 2010-08, V17						1,000	1,900	64	0.1-200	NA	>200
Gamma-glutamyl transpeptidase	U/L	Modular P/Cobas 8000 c702	Roche	GGT-2, 2012-07, V4						200	1,000	35	3-1,200	3-3,000	Full result
Gentamicin	µg/mL	Modular P/Cobas 8000 c502	Thermo-fisher	Gentamicin, 9/2010				15		1,000	2,000	60	0.3-10.0	NA	Full result
Glucose	mg/dL	Modular P/Cobas 8000 c702	Roche	GLUC3, 2010-12,V3			40 (less than 1-month-old); 50 (1 month or older)	300 (less than 1-month-old); 450 (1 month or older)	±25% to previous if <20 mg/dL	1,000	1,000	60	2-750	2-1,500	Full result
Glucose, body fluid or cerebrospinal fluid	mg/dL	Modular P/Cobas 8000 c502	Roche	2010-12,V3	5					NA	NA	NA	2-750	2-1,500	Full result
Glucose, urine	mg/dL	Modular P/Cobas 8000 c502	Roche	2010-12,V3						NA	NA	NA	2-750	2-1,500	Full result
Haptoglobin	mg/dL	Modular P/Cobas 8000 c502	Roche	2012-03,V8						10	200	60	10-750	10-1,140	Full result
Hemoglobin A1C-absolute value %A1C	g/dL %	Modular P/Cobas 8000 c502	Roche	HBA1C II, 2012-08,V11	0.29, 4	3, 17				NA	NA	NA	0.9-3.1	NA	Full result
Hemoglobin, plasma	mg/dL	Modular P/Cobas 8000 c502	Roche	SI2, 2011-02,V2						NA	NA	NA	1-1,200	NA	>1,200
Hepatitis A IgM antibodies	Cutoff index	Modular E/Cobas 8000 e602	Roche	Anti-HAV IgM, 2010-09,V2						1,000	2,000	50	NA	NA	NA
Hepatitis A total (IgG+IgM) antibodies	IU/mL	Modular E/Cobas 8000 e602	Roche	Anti-HAV, 2011-08,V3						100	1,500	50	NA	NA	NA
Hepatitis B core IgM antibodies	COI	Modular E/Cobas 8000 e602	Roche	Anti-Hbc IgM, 2011-11,V1						2,000	1,000	25	NA	NA	NA

Contd

Table 1: Contd...

Test name	Units	Instrumentation (previous/ current)	Assay vendor	Current assay version	Manual review, low value	Manual review, high value	Critical low value below	Critical high value above	Delta	Hemolysis index	Lipemic index	Icteric index	AMR	Auto extended range	Final result, if above AMR
Hepatitis B core total (IgG+IgM) antibodies	COI	Modular E/Cobas 8000 e602	Roche	Anti-HBc, 2011-05,V1						800	1,000	25	NA	NA	NA
Hepatitis B surface antibody	mIU/mL	Modular E/Cobas 8000 e602	Roche	Anti-HBs, 2012-05,V14						1,600	1,500	60	3.5-1,000	NA	>1,000
Hepatitis B surface antigen	IU/mL	Modular E/Cobas 8000 e602	Roche	HBsAg, 2012-04,V9						1,400	1,500	60	0.041 (lower limit)	NA	NA
Hepatitis C antibody	COI	Modular E/Cobas 8000 e602	Roche	HEPC, 2011-03, V3						100	2,100	50	NA	NA	NA
Herpes simplex virus (HSV) type 1 antibodies	COI	Modular E/Cobas 8000 e602	Roche	HSV-1 IgG, 2012-09,V1						1,000	2,000	66	NA	NA	NA
Herpes simplex virus (HSV) type 2 antibodies	COI	Modular E/Cobas 8000 e602	Roche	HSV-2 IgG, 2012-09,V1						1,000	2,000	66	NA	NA	NA
High density lipoprotein	mg/dL	Modular P/Cobas 8000 c702	Roche	HDL-3 PLUS 3rd generation, 2010-12,V3						1,200	1,800	60	3-120	3-240	Full result
Human immunodeficiency virus antigeNAntibody combo	Sample/ cutoff, relative light units	Abbott Architect	Abbott	2010-07						Avoid hemolysis	NA	NA	NA	NA	NA
Homocysteine	µmol/L	Modular P/Cobas 8000 c502	Axis-Shield	Homocysteine, 6/2011						500	500	20	3-50	NA	Full result
Human chorionic gonadotropin-pregnancy, serum	mIU/mL	Modular E/Cobas 8000 e602	Roche	HCG STAT, 2012-04,V15						1,500	2,400	29	2-1,0000	2-1,000,000	Full result
hCG-tumor marker, serum	mIU/mL	Modular E/Cobas 8000 e602	Roche	HCG+-, 2010-08,V14						1,000	1,400	24	2-1,0000	2-1,000,000	Full result
hCG-urine pregnancy	Qualitative	Modular E/Cobas 8000 e602	Roche	HCG STAT, 2012-04,V15						NA	NA	NA	2-1,0000	2-1,000,000	NA
Human growth hormone	ng/mL	Modular E/Cobas 8000 e602	Roche	hGH, 2011-02, V2						500	1,500	25	0.03-50	NA	>50
IgA	mg/dL	Modular P/Cobas 8000 c502	Roche	IgA, 2012-03,V8						1,000	2,000	60	50-800	5-6,400	Full result
IgE	mg/dL	Modular E/Cobas 8000 e602	Roche	IgE, 2010-08,V5						100	2,200	37	1-2,500	1-50,000	Full result

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Table 1: Contd...

Test name	Units	Instrumentation (previous/ current)	Assay vendor	Current assay version	Manual review, low value	Manual review, high value	Critical low value below	Critical high value above	Delta	Hemolysis index	Lipemic index	Icteric index	AMR	Auto extended range	Final result, if above AMR
IgG	mg/dL	Modular P/Cobas 8000 c502	Roche	IgG-2, 2012-02, V7						1,000	2,000	60	300-5,000	30-27,500	Full result
IgM	IU/mL	Modular P/Cobas 8000 c502	Roche	IgM-2, 2012-03, V7						1,000	2,000	60	25-650	5-5,850	Full result
N-terminal pro B-type natriuretic peptide	pg/mL	Modular E/Cobas 8000 e602	Roche	proBNP II STAT, 2012-09,V4						1,000	1,500	25	5.0-35,000	5.0-70,000	Full result
Osmolality, plasma/ serum	mOsm/kg	A2 Advanced Automated Osmometer	Advanced Instruments	3LA028, version 3IP027, rev 9						NA	NA	NA	0-2,000	NA	Full result
Osmolality, urine	mOsm/kg	A2 Advanced Automated Osmometer	Advanced Instruments	3LA028, version 3IP027, rev 9						NA	NA	NA	0-2,000	NA	Full result
Parathyroid hormone	pg/mL	Modular E/Cobas 8000 e602	Roche	2010-07,V6						200	1,500	65	1.2-5,000	NA	>5,000
Phenobarbital	µg/mL	Modular P/Cobas 8000 c502	Roche	PHNO2, 2012-01,V7				60		1,000	600	60	2.4-60.0	NA	Full result
Phenytoin, free	µg/mL	Modular P/Cobas 8000 c502	Siemens	Emit 2000 Phenytoin, 8/2009						800	750	30	0.5-40	NA	>40
Phenytoin, total	µg/mL	Modular P/Cobas 8000 c502	Roche	2012-02,V9				40		1,000	800	50	0.8-40.0	NA	Full result
Phosphorus, inorganic	mg/dL	Modular P/Cobas 8000 c702	Roche	2011-01,V5			1.0 (clinically significant)		±0.6 to previous if <1.0 mg/dL	300	800	60	0.3-20.0	0.3-40.0	Full result
Phosphorus, inorganic, urine	mg/dL	Modular P/Cobas 8000 c502	Roche	2011-01,V5						NA	NA	NA	3.4-285.0	3.4-570.0	Full result
Potassium	mmol/L	Modular P/Cobas 8000 c702	Roche	ISE N, K, Cl; 2010-09,V1			3.0 (birth to 15 years); 2.8 (16 years and older)	6.5 (birth to 15 years); 6.2 (16 years and older)	±15% to previous if <2.9 mmol/L; ±10% to previous if >6.2 mmol/L	60	2,000	60	1.5-10	NA	Full result
Potassium, urine	mEq/L	Modular P/Cobas 8000 c502	Roche	ISE N, K, Cl; 2010-09,V1						NA	NA	NA	1.5-100	NA	Full result

Contd

Table 1: Contd...

Test name	Units	Instrumentation (previous/ current)	Assay vendor	Current assay version	Manual review, low value	Manual review, high value	Critical low value below	Critical high value above	Delta	Hemolysis index	Lipemic index	Icteric index	AMR	Auto extended range	Final result, if above AMR
Prealbumin	mg/dL	Modular P/Cobas 8000 c502	Roche	PREA, 2012-04, V7						1,000	100	60	3-80	3-240	Full result
Progesterone	ng/mL	Modular E/Cobas 8000 e602	Roche	Progesterone II, 2012-09,V2						1,000	720	54	0.2-60	NA	Full result
Prolactin	ng/mL	Modular E/Cobas 8000 e602	Roche	Prolactin II, 2012-03,V5						1,500	1,500	30	0.1-470	0.1-4,700	Full result
N-terminal pro B-type natriuretic peptide	pg/mL	Modular E/Cobas 8000 e602	Roche	proBNP II STAT, 2012-09,V4						1,000	1,500	25	5.0-35,000	5.0-70,000	Full result
Osmolality, plasma/ serum	mOsm/kg	A2 Advanced Automated Osmometer	Advanced Instruments	3LA028, version 3IP027, rev 9						NA	NA	NA	0-2,000	NA	Full result
Osmolality, urine	mOsm/kg	A2 Advanced Automated Osmometer	Advanced Instruments	3LA028, version 3IP027, rev 9						NA	NA	NA	0-2,000	NA	Full result
Parathyroid hormone	pg/mL	Modular E/Cobas 8000 e602	Roche	2010-07,V6						200	1,500	65	1.2-5,000	NA	>5,000
Phenobarbital	µg/mL	Modular P/Cobas 8000 c502	Roche	PHNO2, 2012-01,V7				60		1,000	600	60	2.4-60.0	NA	Full result
Phenytoin, free	µg/mL	Modular P/Cobas 8000 c502	Siemens	Emit 2000 Phenytoin, 8/2009						800	750	30	0.5-40	NA	>40
Phenytoin, total	µg/mL	Modular P/Cobas 8000 c502	Roche	2012-02,V9				40		1,000	800	50	0.8-40.0	NA	Full result
Phosphorus, inorganic	mg/dL	Modular P/Cobas 8000 c702	Roche	2011-01,V5			1.0 (clinically significant)		±0.6 to previous if <1.0 mg/dL	300	800	60	0.3-20.0	0.3-40.0	Full result
Phosphorus, inorganic, urine	mg/dL	Modular P/Cobas 8000 c502	Roche	2011-01,V5						NA	NA	NA	3.4-285.0	3.4-570.0	Full result
Potassium	mmol/L	Modular P/Cobas 8000 c702	Roche	ISE N, K, Cl; 2010-09,V1			3.0 (birth to 15 years); 2.8 (16 years and older)	6.5 (birth to 15 years); 6.2 (16 years and older)	±15% to previous if <2.9 mmol/L; ±10% to previous if >6.2 mmol/L	60	2,000	60	1.5-10	NA	Full result

Contd

Table 1: Contd...

Test name	Units	Instrumentation (previous/ current)	Assay vendor	Current assay version	Manual review, low value	Manual review, high value	Critical low value below	Critical high value above	Delta	Hemolysis index	Lipemic index	Icteric index	AMR	Auto extended range	Final result, if above AMR
Potassium, urine	mEq/L	Modular P/ Cobas 8000 c502	Roche	ISE N, K, Cl; 2010-09,V1						NA	NA	NA	1.5-100	NA	Full result
Prealbumin	mg/dL	Modular P/ Cobas 8000 c502	Roche	PREA, 2012-04,V7						1,000	100	60	3-80	3-240	Full result
Progesterone	ng/mL	Modular E/ Cobas 8000 e602	Roche	Progesterone II, 2012-09,V2						1,000	720	54	0.2-60	NA	Full result
Prolactin	ng/mL	Modular E/ Cobas 8000 e602	Roche	Prolactin II, 2012-03,V5						1,500	1,500	30	0.1-470	0.1-4,700	Full result
Syphilis IgG	AI	BioPlex 2200	Bio-Rad	Syphilis IgG, 3/2012						Avoid hemolysis	NA	NA	0.1-8.0	NA	>8.0
Tacrolimus	ng/mL	Abbott Architect	Abbott	Tacrolimus, 4/2009	1.9					NA	NA	NA	2-30	NA	>30
Testosterone, total	ng/dL	Modular E/Cobas 8000 e602	Roche	TST II, 2010-07, V2						600	1,000	30	5-1,500	NA	>1,500
Theophylline	µg/dL	Modular P/Cobas 8000 c502	Roche	Theophylline Online, 2012-01, V7				20		1,000	300	50	0.8-40.0	NA	Full result
Thyroglobulin autoantibodies	IU/mL	Modular E/Cobas 8000 e602	Roche	Anti-Tg, 2010-10,V3						1,690	2,000	66	10-4,000	NA	>4,000
Thyroid peroxidase autoantibodies	IU/mL	Modular E/Cobas 8000 e602	Roche	Anti-TPO, 2011-08,V2						1,500	2,100	66	5.0-600	NA	>600
Thyroid stimulating hormone (TSH)	mIU/mL	Modular E/Cobas 8000 e602	Roche	2012-02,V1						1,000	1,500	41	0.01-100	NA	Full result
Thyroxine (T4), free	ng/dL	Modular E/Cobas 8000 e602	Roche	FT4, 2012-11, V2						2,000	2,000	41	0.02-7.77	NA	>7.77
T4, total	µg/dL	Modular E/Cobas 8000 e602	Roche	T4, 2011-10,V4						2,300	2,500	37	0.4-24.9	0.4-124.5	Full result
Tobramycin	µg/mL	Modular P/Cobas 8000 c502	Roche	2012-02,V6				10.1		800	750	30	0.3-10.0	NA	Full result
Toxoplasma antibodies, IgG	IU/mL	BioPlex 2200	Bio-Rad	ToRC IgG, 3/2012						Avoid hemolysis	NA	NA	3-	NA	NA
Transferrin	mg/dL	Modular P/Cobas 8000 c502	Roche	TRFS2, 2011-01, V3						1,000	500	60	10-520	10-780	Full result
Triglycerides	mg/dL	Modular P/Cobas 8000 c702	Roche	2011-01,V3						700	2,000	35	9-885	9-4,425	Full result

Contd

Table 1: Contd...

Test name	Units	Instrumentation (previous/ current)	Assay vendor	Current assay version	Manual review, low value	Manual review, high value	Critical low value below	Critical high value above	Delta	Hemolysis index	Lipemic index	Icteric index	AMR	Auto extended range	Final result, if above AMR
Triiodothyronine (T3), free	pg/mL	Modular E/Cobas 8000 e602	Roche	FT3, 2011-09, V14						4,300	2,000	33	0.26-32.55	NA	>32.55
T3, total	ng/mL	Modular E/Cobas 8000 e602	Roche	T3, 2011-08, V20						2,000	1,800	35	0.19-6.51	NA	>6.51
Troponin T	ng/mL	Modular E/Cobas 8000 e602	Roche	Troponin T Stat, 2012-07,V7						300	1,500	27	0.03-25	0.03-250	Full result
Unsaturated iron binding capacity	µmol/L	Modular P/Cobas 8000 c502	Roche	UIBC, 2011-04, V3						40	300	60	3-125	NA	Full result
Urea nitrogen, blood (BUN)	mg/dL	Modular P/Cobas 8000 c702	Roche	BUN, 2011-03, V3					±50% to previous if <2 mg/dL	1,000	1,000	60	2-112	2-336	Full result
Urea nitrogen, urine	mg/dL	Modular P/Cobas 8000 c502	Roche	BUN, 2011-03, V3						NA	NA	NA	3-5,600	3-10,080	Full result
Uric acid	mg/dL	Modular P/Cobas 8000 c502	Roche	Uric Acid Plus, 2010-09,V7						1,000	1,500	40	0.2-25	0.2-62.5	Full result
Valproic acid	µg/mL	Modular P/Cobas 8000 c502	Roche	2012-03,V9				150		500	500	30	2.8-150	NA	Full result
Vancomycin	µg/mL	Modular P/Cobas 8000 c502	Roche	2012-04,V10				50		650	500	30	1.7-80	NA	Full result
Varicella zoster virus antibodies, IgG	AI	BioPlex 2200	Bio-Rad	MMRV IgG, 3/2012						Avoid hemolysis	NA	NA	0.2-8.0	NA	>8.0
Vasculitis-glomerular basement membrane antibodies, IgG	AI	BioPlex 2200	Bio-Rad	Vasculitis IgG, 4/2012						Avoid hemolysis	NA	NA	0.2-8.0	NA	>8.0
Vasculitis-myeloperoxidase antibodies, IgG	AI	BioPlex 2200	Bio-Rad	Vasculitis IgG, 4/2012						Avoid hemolysis	NA	NA	0.2-8.0	NA	>8.0
Vasculitis-proteinase 3 antibodies, IgG	AI	BioPlex 2200	Bio-Rad	Vasculitis IgG, 4/2012						Avoid hemolysis	NA	NA	0.2-8.0	NA	>8.0
Vitamin B12	pg/dL	Modular E/Cobas 8000 e602	Roche	2012-01,V2						1,000	1,500	65	30-2,000	NA	>2,000
Vitamin D, 25-hydroxy	ng/mL	Modular E/Cobas 8000 e602	Roche	Vitamin D, 2012-07,V1						2,000	400	66	5-60	NA	Full result

ACTH: Adrenocorticotropic hormone, ALT: Alanine aminotransferase, AFP: Alpha-fetoprotein, ACE: Angiotensin converting enzyme, CCP: Anticyclic citrullinated peptide, ANA: Antinuclear antigen, AST: Aspartate aminotransferase, CA-125: Cancer antigen-125, CA-19-9: Carbohydrate antigen-19-9, CEA: Carcinoembryonic antigen, CRP: C-reactive protein, hsCRP: CRP, high sensitivity, CK: Creatine kinase, CMV: Cytomegalovirus, DHEA: Dehydroepiandrosterone, THC: Drug of abuse – tetrahydrocannabinol, EBV: Epstein-Barr virus, EBNA: Early nuclear antibody, FSH: Follicle stimulating hormone, GGT: Gamma-glutamyl transpeptidase, CSF: Glucose, body fluid or cerebrospinal fluid, HSV: Herpes simplex virus, HDL: High density lipoprotein, HIV: Human immunodeficiency virus, hCG: Human chorionic gonadotropin, LDH: Lactate dehydrogenase, LDL: Low density lipoprotein, LH: Luteinizing hormone, PTH: Parathyroid hormone, PSA: Prostate specific antigen, SHBG: Sex-hormone binding globulin, T3: Triiodothyronine, UIBC: Unsaturated iron binding capacity, BUN: Urea nitrogen, blood, VZV: Varicella zoster virus, MPO: myeloperoxidase, PR3: proteinase 3

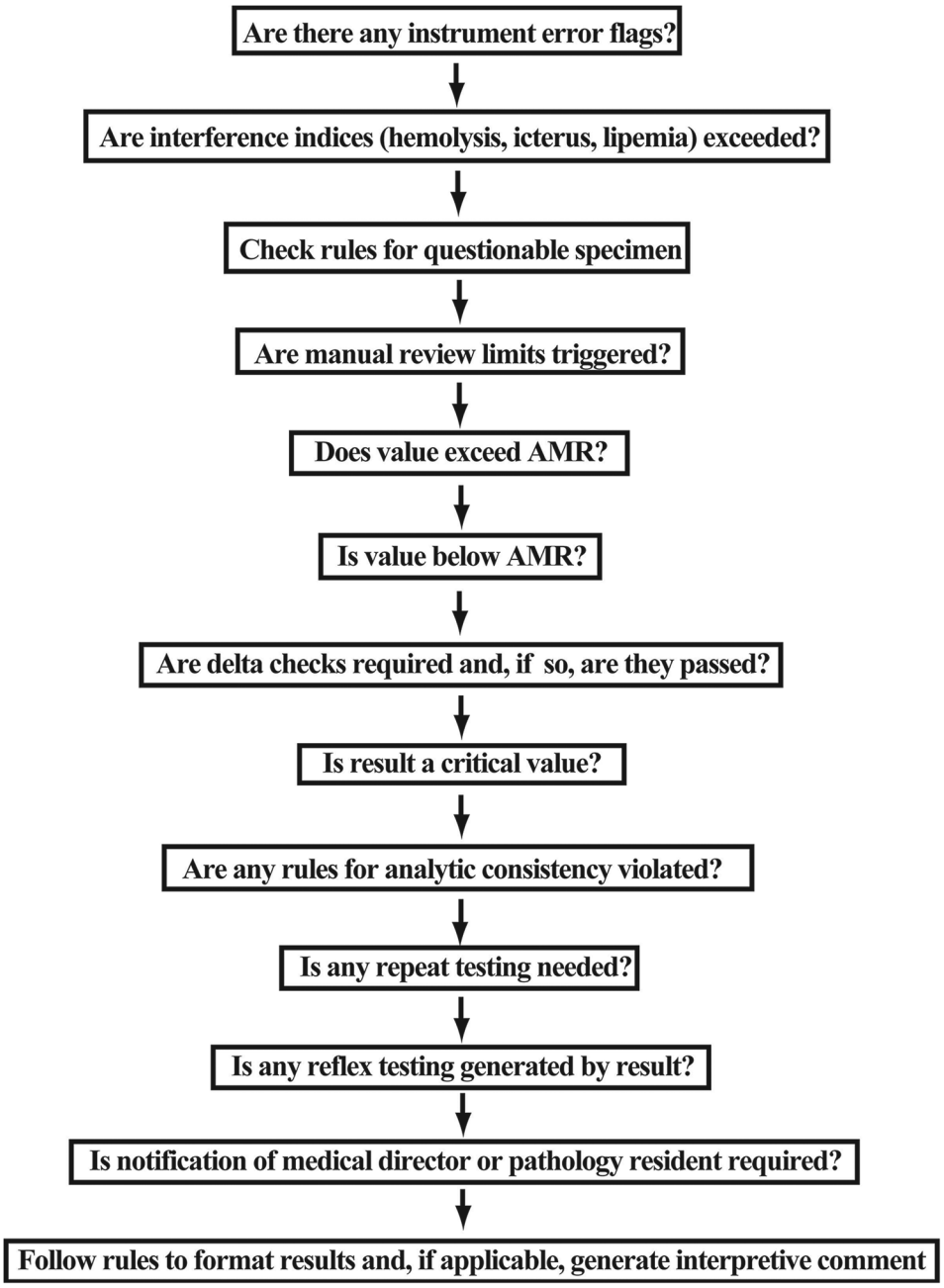

Figure 1: Diagram of main rules impacting autoverification

over a 4-month period in 2013. The highest rates of autoverification occurred with the most frequently ordered tests such as the basic metabolic panel (sodium, potassium, chloride, carbon dioxide, creatinine, blood urea nitrogen (BUN), calcium, glucose; 99.6%), albumin (99.8%), and alanine aminotransferase (99.7%). The lowest rates of autoverification occurred with some therapeutic drug levels (e.g. gentamicin, lithium, and methotrexate) and with serum free light chains (kappa/lambda), mostly due to need for offline dilution and manual filing of results. Table 3 includes the most common reason certain tests or test panels failed to autoverify. For the highest volume tests such as albumin or alanine aminotransferase, problems with specimen (e.g. short sample; possible bubble, or clot) were the most common reason for failure to autoverify.

Several rules were put in place to address specific issues with assays or protocols. The total bilirubin assay used shows rare interference by monoclonal gammopathy (most commonly those with IgM as the heavy chain).[16] This interference can be inferred by a discrepancy between the total bilirubin (in mg/dL) and the numeric icteric index (which usually tracks closely with total bilirubin) by greater than 4. This interference has occurred approximately three to four

Table 2: Autoverification rules and actions

Rules	Action(s)
Quality control	Stop and investigate if QC not passed; no autofile
Error flags on instrument	Stop and investigate if present; no autofile
Interference indices (hemolysis, icterus, and lipemia)	Autofile hemolyzed, icteric, or lipemic as appropriate
	Credit charges
	Notification to clinical areas, if applicable (inpatient units and select outpatient clinics)
Questionable specimen (e.g., possible contamination)	Suppress all results on that specimen; contact clinical area
Result above analytical measurement range	If manual protocol, perform dilution and manually review/verify
	Certain analytes have automated dilution protocol; once completed, proceed to other rules
Result below AMR	Rules dictate how result to be filed (e.g., "<6" or "0"); proceed with other rules
	For certain therapeutic drugs, contact clinical area
Repeat testing	Specified with certain results for some analytes
Delta checks (if applicable)	If violated, do not autofile
Critical value	Printout to notify clinical area (result may proceed to other rules if manual review limit not exceeded)
Analytic inconsistency rules (e.g., albumin>total protein)	Stop and investigate; no autofile
Reflex testing	May be automatically performed (e.g., abnormal thyroid stimulating hormone reflex to free (thyroxine) T4 for TSH reflex panel); reflex tests evaluated by autoverification rules
	With some infectious disease tests, positive results initiate reflex confirmatory testing
Positive infectious disease tests results requiring medical director review (e.g., syphilis; hepatitis B or hepatitis C gray zones)	Medical director notified

QC: Quality control, AMR: Analytical measurement range, TSH: Thyroid stimulating hormone

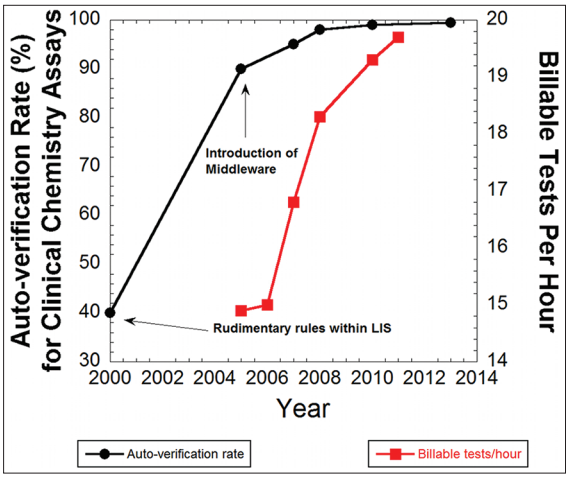

Figure 2: Increases in autoverification rate (black circles) and staff productivity (red squares)

times per year over the course of 3 years. An additional rare problem is hook effect with the myoglobin assay with very high myoglobin concentrations. Dilution protocols were modified following identification of this problem.[17] A protocol for evaluation of possible toxic alcohol or glycol exposure was developed based on osmolal gap.[18,19]

Another rule was put in place to detect weakly positive (gray zone) hepatitis B surface antigen assay results. This assay was originally reported as reactive or nonreactive, but a retrospective analysis determined that a high fraction of reactive specimens with quantitative results barely above the cutoff index were due either to recent hepatitis B vaccination (the vaccine contains surface antigen) or were false positives that did not confirm with hepatitis B surface antigen neutralization assay.[20] Middleware rules print notification to staff to send out specimen for confirmation by neutralization assay and to notify pathology resident or attending pathologist. Following clinician notification, instances where the gray zone result is attributable to recent vaccination can lead to cancellation of test to avoid falsely labeling patient as hepatitis B positive. This avoids downstream problems such as notification of public health authorities.

DISCUSSION

Autoverification of laboratory test results is an essential component of increasing efficiency within the clinical laboratories.[1-6] Despite the importance of autoverification, there is relatively scant literature published on practical application within a clinical laboratory over the course of years.

Table 3: Autoverification rate

Test(s)	Annual test volume	Autoverification rate (%)	Most commons reasons for failure to autoverify
All chemistry tests	3,805,000	99.5	
Basic metabolic panel (sodium, potassium, carbon dioxide, chloride, BUN, calcium, and glucose)	114,140	99.6	Possible contamination flag, specimen errors (e.g., bubble, clot, and short sample), delta check failure
Electrolyte panel (sodium, potassium, carbon dioxide, and chloride)	1,320	98.6	Possible contamination flag, specimen errors (e.g., bubble, clot, and short sample), delta check failure
Lipid panel (total cholesterol, HDL, triglycerides, and calculated LDL)	31,000	98.6	Specimen errors (e.g., bubble, clot, and short sample)
Alanine aminotransferase	137,600	99.7	Specimen errors (e.g., bubble, clot, and short sample)
Albumin	129,650	99.8	Specimen errors (e.g., bubble, clot, and short sample)
ACTH	830	98.6	Specimen errors (e.g., bubble, clot, and short sample)
Alkaline phosphatase	115,700	99.8	Specimen errors (e.g., bubble, clot, and short sample)
Bilirubin, direct	20,560	97.6	High analyte concentration requiring manual dilution
Bilirubin, total	115,200	99.5	Specimen errors (e.g., bubble, clot, and short sample)
Cortisol	4,730	95.0	Specimen errors (e.g., bubble, clot, and short sample)
Free light chains, serum	4,180	88.0	High analyte concentration requiring manual dilution
Gentamicin	2,450	94.0	High analyte concentration requiring manual dilution
Hemoglobin A1C	30,460	99.5	Specimen errors (e.g., bubble, clot, and short sample)
Hepatitis B surface antigen	12,050	97.8	Repeat testing for positives and gray zones
Hepatitic C antibody	14,910	97.0	Repeat testing by alternate method for gray zone or hemolyzed specimens
Lithium	1,500	91.6	High analyte concentration requiring manual dilution
Methotrexate	1,200	89.6	High analyte concentration requiring manual dilution
NT-proBNP	8,630	99.2	Specimen errors (e.g., bubble, clot, and short sample)
Prostate specific antigen	4,050	99.7	Specimen errors (e.g., bubble, clot, and short sample)
SS-A	1,540	100	NA
Tacrolimus	8,310	99.2	Instrument errors
Thyroid stimulating hormone	55,100	99.5	Specimen errors (e.g., bubble, clot, and short sample)
Thyroxine, free	19,990	99.2	Specimen errors (e.g., bubble, clot, and short sample)
Testosterone	1,700	99.1	Specimen errors (e.g., bubble, clot, and short sample)
Troponin T	17,910	99.2	Specimen errors (e.g., bubble, clot, and short sample)
Vancomycin	5,700	98.2	High analyte concentration requiring manual dilution
Vitamin D, 25-hydroxy	18,360	98.4	High analyte concentration requiring manual dilution

BUN: Blood urea nitrogen, HDL: High density lipoprotein, LDL: Low density lipoprotein, ACTH: Adrenocorticotropic hormone, NT-proBNP: N-terminal pro-brain natriuretic peptide, NA: Not available

In this report, we present our experience with autoverification in a busy automated core chemistry laboratory in an academic medical center. The autoverification rules evolved over more than a decade, with a steady increase in autoverification rate to the current rate of 99.5%. The high rate of autoverification is driven in large part by the highest volume tests or test panels (e.g. basic metabolic panel, albumin, alanine aminotransferase, and troponin T), which all have autoverification rates exceeding 99.0%. This frees up staff time to deal with assays such as certain drug levels or endocrinology tests that require offline steps such as manual dilutions, or to investigate questionable test results. Some tests in our study currently have autoverification rates under 90%; however, these tests comprise a small fraction of the total test volume.

To our knowledge, there is very little published data on autoverification of critical values. Our workflows allow for critical value autoverification, provided no other rules are violated. Critical values still require provider notification and subsequent documentation; however, communication of these results by laboratory staff is facilitated by the provider often seeing the autoverified value prior to the call. For example, the emergency treatment center and intensive care units in our medical center use electronic displays or dashboards that continuously display patient data in restricted staff areas. Phone calls to document the critical value proceed more quickly when the laboratory test result has already been seen.

Despite the advantages of autoverification, there are potential negatives that can arise. The validation of autoverification is time-consuming and attention to detail is paramount. Even the most thorough validation plan can miss unexpected instrument error flags or other rare events. It also not possible to test every conceivable combination of rules.

Informatics support is critical to successful implementation and maintenance of autoverification. The most common problems interfering with autoverification would be interruptions of network, LIS, middleware, and/or the interfaces between these systems. In our institution, we have maintained both production and shadow middleware servers in different geographic locations, in addition to using separate test servers for initial testing of middleware rules without compromising the production system. This has reduced period of times the systems are down. The other risk with autoverification, and indeed with increased automation in general, is reduction of staff (both in number of staff and in the mix of level of training and experience) to such a degree that the staff cannot handle downtimes or other challenges without severe compromise of turnaround time.

One benefit of computer rules is to catch rare events that could elude manual verification. Two examples of such rules in our laboratory are plasma albumin exceeding total protein concentration (suggesting an instrument error on one test) and marked discrepancy between total bilirubin and icteric index (possibly caused by monoclonal gammopathy interference).[16] Each of these situations occurs less than 10 times per year in our laboratory, meaning that any particular laboratory staff member may only see such an event once a year or less. Even experienced personnel can miss such combinations of results, especially for patients who have multiple tests ordered on a specimen.

Our experience suggests that successful and continued use of autoverification requires investment in personnel and training over the course of years. Validation of autoverification rules requires high attention to detail. Rules should be based on published evidence and analysis of assays. The use of autoverification also does not obviate need for careful quality control. Lastly, close collaboration between the clinical laboratory and computing services is the key for ongoing success.

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