The Pacific Northwest Laboratory Medicine Sentinel Monitoring Network
Final Report of the Findings of Questionnaire 8
Test Systems with Non-Traditional Mechanisms for Quality Control

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BACKGROUND

The Pacific Northwest Laboratory Sentinel Monitoring Network was created in January 1995 to gather ongoing information about practices in hospital, independent and physician office laboratories. To date, eight questionnaires have been released to the network, exploring issues related to: testing quality; access to testing services; laboratory-related problems and errors; personnel training and changes; proficiency testing participation; and testing systems with non-traditional mechanisms for quality control. The data gathered thus far have provided network participants, interest groups and regulators with information about trends in laboratory medicine, based on actual practices and experiences in testing facilities.

Waived testing

Testing technologies have been rapidly changing with a particular increase in instruments and devices targeted for physician office, point of care and home health care settings. Many of these test systems have been developed to streamline and simplify the testing process and to include non-traditional mechanisms for quality control.

Many manufacturers have developed or refined testing devices in order to meet the criteria set by the Clinical Laboratory Improvement Amendments of 1988 (CLIA) to be approved as a waived test system. In the last year, the Centers for Disease Control and Prevention (CDC) has approved waived testing systems for many new analytes, which are appropriate for physician office laboratories: Group A Strep antigen, Helicobacter pylori antibody, hemoglobin A1C, prothrombin time and mononucleosis testing. As of April 1998, tests for 20 different analytes can be performed using one or more waived test systems. Waived tests are not subject to regulatory oversight through routine inspections or proficiency testing monitoring and accreditation agency standards vary considerably in their oversight of waived testing.

Non-waived test systems with non-traditional mechanisms for quality control

Non-waived, point of care testing technology has recently provided portable testing systems for a variety of routine chemistry, blood gas, electrolyte, cardiac enzyme, drugs of abuse and coagulation tests, in addition to kit tests for the rapid detection of Group A Strep, Chlamydia and mononucleosis, to name only a few. By utilizing "unitized" reagents (i.e., cartridges, cassettes, test packs) and incorporating built-in, procedural or electronic controls, these systems depart from the use of "traditional" liquid controls each day to the use of more innovative quality control mechanisms with each patient test. In some cases, enhanced fail-safe mechanisms, such as internal, electronic self-checks, provide the operator with real-time indicators of the status of the instrument operating conditions. Manufacturers' recommendations for quality control of these systems often do not coincide exactly with CLIA, state, or accreditation agency requirements for daily quality control, resulting in a wide range of interpretations by individual testing sites and laboratory inspectors.

QUESTIONNAIRE 8

Questionnaire 8 was mailed to 431 network laboratories in January 1998. The intent of this questionnaire was to:

•Create an inventory of test systems in use which are waived or are non-waived with mechanisms for non-traditional quality control.
•Evaluate how testing sites assess the quality of patient test results using these systems.
•Determine how laboratories established their quality control policies, when manufacturers' instructions and regulatory standards are vague or at odds with each other for test systems that utilize electronic and/or built-in (procedural) controls.
•Determine the extent to which laboratories are switching between waived test systems and tests of higher complexity and why.
•Evaluate how waived test systems are used (for screening, monitoring or definitive diagnosis).

Two hundred twenty-one laboratories returned a completed questionnaire in time for analysis, a 51% response rate. Data from this questionnaire were analyzed using Microsoft Access ™ and Raosoft SurveyFirst ™. Tests of significance were performed using Student's t-test, at 95% confidence limits (p=0.05). Demographic characteristics of the respondents are summarized in Table 1.

Table 1 - Questionnaire 8 respondents (N=221 laboratories)

Demographic characteristic	**Percent**
STATE	
Alaska	10
Idaho	20
Oregon	21
Washington	49
LABORATORY TYPE	
Physician office laboratory (POL)	58
Hospital	30
Independent	12
CENSUS BUREAU DESIGNATION	
Urban	58
Rural	42
ACCREDITATION STATUS	
Yes	32
No	68

FINDINGS

Waived test systems

Of the 221 respondents, 205 listed a total of 920 waived tests (7 additional tests were listed as "waived" but are currently non-waived test systems or were at the time the questionnaires were returned). Table 2 lists the waived tests performed in hospital, independent and physician office laboratories.

Table 2 - Waived tests

Waived test	**Hospital** N=64 labs	**Independent** N=19 labs	**POL** N=122 labs
	Percent of laboratories performing the test		
Occult blood	81	68	79
Urinalysis	70	63	79
Urine pregnancy	48	47	61
Glucose	58	21	52
Erythrocyte sedimentation rate (ESR)	52	58	43
Hematocrit	23	26	35
pH, qualitative, non-blood	27	21	17
Direct Strep antigen	28	16	32
Helicobacter pylori antibody	22	11	16
Microalbumin	5	16	14
Hemoglobin	6	11	14
Helicobacter pylori, biopsy tissue	25	0	<1
Prothrombin time	2	0	10
Cholesterol, HDL, triglyceride, glucose	3	5	3
Cholesterol	3	0	0
Fructosamine	2	0	0
Hemoglobin A1C	0	5	<1
Other (Not specified)	3	0	<1

Other (Non-waived test systems for H.pylori antibody, Strep antigen, Mononucleosis screen, Bladder tumor antigen, Total eosinophil count, Nasal smear)	2	0	5

How are waived tests used?

Laboratories were asked how they used each of the waived test systems performed in their facility, using the following list of choices:

- Used to **screen** only-abnormal results are confirmed by a non-waived method
- Used for **definitive diagnosis**-results are not confirmed by a non-waived method
- Used only to **monitor** patients already diagnosed by a non-waived method
- Other, briefly describe

Overall, 46% of tests are used for a definitive diagnosis, 42% for screening purposes only and 9% to monitor patients already diagnosed. We found that rural hospitals used waived tests for a definitive diagnosis at a significantly higher rate than POLS, independent laboratories or urban hospitals (Table 3).

Table 3 - How are waived tests used?

How waived tests are used	**POL** 122 labs / 563 tests		**Hospital** 64 labs / 294 tests		**Independent** 19 labs / 70 tests	
	Urban	Rural	Urban	Rural	Urban	Rural
	Number of responses					
	350	192	107	193	50	16
	Percent of responses					
Screen only - Abnormal results are confirmed by a non-waived method	43	50	43	30	44	50
For definitive diagnosis - Results are not confirmed by a non-waived method	47	38	37	55	46	38
Monitor patients already diagnosed by a non-waived method	8	10	14	10	4	0
Other	2	2	5	5	4	13

Table 4 shows how individual waived tests are used in the network laboratories.

Table 4 - How are waived tests used?

Waived test	**Number of responses**	**Percent of responses**				
		screen	**definitive diagnosis**	**monitor**	**multiple uses**	**other***
Occult blood	154	62	30	2	2	3
Urinalysis	146	36	58	1	4	1
Urine pregnancy	112	21	73	1	5	
Glucose	95	42	18	33	7	
ESR	87	23	55	10	4	7
Hematocrit	60	48	37	7	2	7
Direct Strep antigen	56	41	54	2		4
H. pylori antibody	35	37	60			3
pH, qualitative, non-blood	38	45	50		3	3
Hemoglobin	22	68	32			
Microalbumin	22	41	36	18	5	
H. pylori, biopsy	16	56	38			6
Prothrombin time	13	8	46	38		8
Cholesterol, HDL, triglyceride, glucose	6	33	17		17	33
Cholesterol	2		50			50
Fructosamine	1			100		
Hemoglobin A1C	1			100		

* Other responses included: Back up to automated testing for the same analyte; Health fairs; Research; Outpatient self-request; Compare with clinical symptoms before treatment; Adjunct to doctor's evaluation.

Quality control of waived tests

Using the following list of choices, network laboratories were asked "What is the basis of your quality control policy?":

•Manufacturer's recommendations
•CLIA or state regulations
•Accreditation agency standards
•Based on studies we performed to assess reagent, instrument, operator, environmental variables
•Not applicable, quality control is not required
•Do not know
•Other, briefly specify

The responses given most frequently as the basis for quality control (QC) policies were: CLIA or state regulations (36%) and manufacturer's recommendations (35%). Significant differences were not found between laboratories regulated under CLIA and those regulated under CLIA-exempt state programs. Significant differences were noted between the POL and the hospital/independent laboratory groups, with respect to the influence of accreditation standards. This is likely explained by the fact that 16% of POLS are accredited, as opposed to 54% of hospital/independent laboratories. Table 5 summarizes all responses given for various demographic categories of interest.

Table 5 - Basis of quality control policy

Basis of quality control policy	**Percent of responses**					
	Alaska & Idaho*	**Oregon & Washington****	**POL**	**Hospital & Independent**	**Not Accredited**	**Accredited**
Manufacturer's recommendations	37	34	37	32	34	36
CLIA or state regulations	36	36	38	33	40	27
Accreditation agency standards	12	13	6	22	5	27
Based on studies	4	5	5	5	6	5
Not applicable, quality control is not required	7	7	9	5	10	4

Do not know	3	1	2	2	2	1
Other	<1	4	4	2	3	<1

* Laboratories in Alaska and Idaho are regulated under CLIA
** Laboratories in Oregon and Washington are regulated under CLIA-exempt state programs

We found a considerable amount of variation in how laboratories based their quality control protocols for different waived tests and waived test systems. The following tests are examples where the manufacturer's recommendations influenced quality control protocols more than regulations: H.pylori biopsy tissue, hemoglobin, microalbumin, occult blood and glucose. For hematocrit, urinalysis and erythrocyte sedimentation rates, the opposite pattern was found- regulations appeared to have had a greater influence than manufacturer's recommendations as the basis of laboratories' quality control protocols. For pregnancy tests and direct Strep antigen testing, manufacturer's recommendations and regulations had similar influences. Table 6 shows these examples.

Table 6 - Basis of quality control policy

Waived test	**Percent of responses as basis of quality control policy**	
	Manufacturer's recommendations	**CLIA or state regulations**
H.pylori biopsy tissue	47	18
Hemoglobin	52	22
Microalbumin	40	27
Occult blood	53	24
Glucose	40	31
Hematocrit	10	44
Urinalysis	25	48
ESR	13	33
Pregnancy test, urine	35	41
Direct Strep antigen	39	40

Use of external, liquid quality control materials

Participants were asked "Do you run external, liquid quality control materials?" for each of the waived tests that they performed. External liquid controls were tested with 56% of the waived tests that the respondents performed. No significant differences were found when the following groups of laboratories were compared: POLS versus hospital/independent; CLIA versus state

regulations; or accredited versus non-accredited.

We did find that in laboratories where medical technologists or technicians were employed, liquid controls were analyzed with a higher percentage of tests (59%) than in laboratories that did not employ one of these personnel types (39%).

External controls were performed with a significantly higher percentage of tests when they were used for a definitive diagnosis (67%) or to monitor patients already diagnosed (60%), than when used for screening purposes (47%).

We found considerable variation in the proportion of laboratories running liquid controls for individual waived tests and waived test systems. In some instances, liquid controls are not readily available (i.e., ESR, occult blood) which may explain low rates. In addition, the frequencies with which laboratories run liquid controls are variable for one type of waived test or test system. Table 7 summarizes these findings.

Table 7 - Use of external, liquid quality control materials

Waived test	**Number of labs**	**Percent that run liquid QC**	**Frequency that liquid controls are run (Number of labs)**						
			each run or daily	weekly	monthly	each lot or kit	quarterly or semiannually	other	none given
Cholesterol	2	100						2	
Cholesterol, HDL triglyceride, glucose	7	100	4			3			
ESR	96	11	6	1	1		2		1
Fructosamine	1	100	1						
Glucose	104	88	64	9	4	9	2		3
H.pylori antibody	36	78	3	1	5	17	1	1	
H.pylori biopsy	17	41	1			6			
Hematocrit	63	33	12	1	4	1	3		
Hemoglobin	23	48	7	1	1		1	1	
Hemoglobin A1C	2	100	2						
Microalbumin	23	61	7	3	2	2			
Occult blood	161	19	22	1		4	1	1	1
pH	42	57	18	3		1		1	1
Pregnancy	114	82	21	5	12	46	2	2	5
Prothrombin time	13	77	3	1	2	3	1		

Direct Strep antigen	60	73	6	2	7	23	2	1	3
Urinalysis	153	79	78	18	2	12	4	3	4

Other mechanisms to assess accuracy

Using the following list of choices, network laboratories were asked to select any other mechanisms they used to assess the accuracy of each of their waived test systems:

•Validation studies were performed prior to initial use
•Observation of built-in (procedural) control or electronic control results
•Participation in an external proficiency testing program
•Perform correlation studies with another method or another lab using patient samples
•Analyze other reference materials with known results
•Correlate patient test results with presentation or history

The most frequent mechanisms used to assess waived testing accuracy were: observation of built-in, procedural or electronic controls (23% of all responses); participation in proficiency testing (23%) and correlation with patient presentation or history (16%). Correlation studies accounted for 12% of all responses and validation studies accounted for 10%. We found no significant differences in the patterns of these responses when comparing different laboratory types or the accreditation status of respondents.

We again found differences in the mechanisms used to assess accuracy depending on how testing is used. Built-in, procedural controls were used most frequently as mechanisms for assessing test accuracy when tests were used for screening. Proficiency testing was used most frequently when tests were used to diagnose or monitor.

Table 8 - Mechanisms to assess accuracy

Mechanisms to assess accuracy	**How waived test is used** (Percent of responses)		
	screen	**diagnose**	**monitor**
Validation studies	10	9	16
Built-in (procedural) controls	**25**	24	15
Proficiency testing	19	**28**	**23**
Correlation studies	12	10	19
Other reference materials	7	6	3

Correlate patient results with presentation or history	20	12	19
Other mechanism	1	1	1
No mechanisms used	5	9	4

Changes in waived test systems

Laboratories were asked "In the past two years have you changed from one waived test system to another waived test system or to one of higher complexity for a particular test?". Thirty laboratories (14% of respondents) indicated that they had made such a change for 32 different analytes. The majority of these tests (81%) were traded for another waived test system and the remaining 19% were for tests of moderate complexity. The following waived tests were changed in the past two years: glucose (10 laboratories); direct Strep antigen (7); urinalysis (5); H.pylori (3); urine pregnancy (3); hematocrit (2); and ESR (2).

Laboratories gave a wide range of reasons for making this type of change, which are summarized in Table 9.

Table 9 - Changing from a waived test system to another test system

Reason	Percent of all reasons	Analytes
Better cost	17	Glucose, H.pylori, Urine pregnancy, Strep antigen
Better test accuracy	17	Glucose, H.pylori, Strep antigen, Urinalysis
Easier method to perform	17	Glucose, H.pylori, Urine pregnancy, Strep antigen
Better turnaround time for results	15	Glucose, Hematocrit, ESR, Strep antigen
Better correlation with patient history, presentation, diagnosis	6	Glucose, H.pylori
Easier to interpret results	4	Strep antigen, Urinalysis
More definitive test results	4	H.pylori

Other	19	Glucose: Quality control is mandatory; Corporate decision; Provides data management; To be the same as the hospital. Urinalysis: For consistency; Better documentation; Change to a different strip. Urine pregnancy: Trouble with supplier. Hematocrit: Friendlier; Controls available.

We were interested in waived test systems where test accuracy was a concern but did not find any particular test or test system to be singled out.

Labs that changed from a non-waived test system to a waived test system for same analyte

Laboratories were asked "In the past two years, have you changed from a non-waived test system to a waived test system for a particular test?". Seventeen laboratories (8% of the respondents) indicated that they made this type of change for 17 different tests. One laboratory indicated a change to a different arterial blood gas (ABG) test system, however there are no waived test systems for ABGs at this time. The following summarizes these test changes: Direct Strep antigen (9 laboratories); H. pylori antibody (2); Lipids (2); CLO test for H.pylori (1); Glucose (1); HCG (1); Prothrombin time (1).

The highest percent of reasons given for changing to a waived test system (32%) were related to regulations (Different quality control requirements; No proficiency testing requirements; To drop to a lower licensing category; To become a waived site). Table 10 summarizes the wide range of reasons given.

Table 10 - Changing from a non-waived test to a waived test

Reason	**Percent of reasons**	**Analyte**s
Related to regulations	32	H. pylori antibody; Lipids, Strep antigen
Better cost	21	H. pylori (CLO test), Glucose, HCG, Lipids, Strep antigen
Easier method to perform	14	H.pylori antibody, Lipids, Strep antigen
Better turnaround time for results	7	H. pylori (CLO test), Lipids
Better test accuracy	7	H. pylori (CLO test), Strep antigen

Easier to interpret test results	4	Strep antigen
Better storage requirements	4	Lipids
Other	11	H.pylori (CLO test): To give surgeon an on-site answer. Lipids: Can do HDL rapidly. Prothrombin time: Instrument was updated.

Non-waived test systems with non-traditional mechanisms for quality control

Of the 221 respondents, 83 laboratories (38%) listed a total of 184 non-waived tests which utilize built-in controls, procedural controls, electronic control cartridges or devices, control strips or mechanisms other than "traditional" external liquid control materials (Table 11).

Table 11 - Non-waived tests with non-traditional mechanisms for quality control

Analyte	**Percent of tests**
Direct Strep antigen	30
Mononucleosis	15
Serum HCG	15
Drugs of abuse	8
Chlamydia	7
Arterial blood gases + electrolytes	5
Prothrombin time or Activated partial thromboplastin time	5
Activated clotting time	3
H. pylori antibody	2
Respiratory syncytial virus	2

Other: Clostridium difficle; Automated ESR; Rheumatoid arthritis; Automated urinalysis; Group B Strep; Influenza; CK-MB; Troponin; Centrifugal hematology; Antibody identification.	8

Quality control of non-waived test systems

The responses given most frequently as the basis of quality control policies were: CLIA or state regulations (46% of all reasons) and manufacturers' recommendations (32%). There were no significant differences between laboratories that are regulated under CLIA and laboratories regulated under CLIA-exempt state programs. Significant differences were found between POLs and hospital/independent laboratories, but these are attributed to the significant differences in the percentages of laboratories that are accredited between these two groups (Table 12).

Table 12 - Basis of quality control policies for non-waived test systems

Basis of QC policy	**Percent of responses**			
	CLIA regulations Alaska/Idaho	**State regulations Oregon/Washington**	**POL**	**Hospital & Independent**
Manufacturer	33	34	35	32
CLIA or state regulations	50	47	53	44
Accreditation standards	16	14	9	20
Based on studies performed	1	4	3	2

We found that for any one test system, there was a wide range of responses by laboratories for the basis of their quality control protocol. For example, 12 laboratories used one particular test system for drugs of abuse testing (i.e., same manufacturer and device). Five based their quality control policy on manufacturer's recommendations, 3 on regulations, 2 on accrediting standards

and 2 on combinations of these. Other similar examples were found for: an ABG device; a kit for Chlamydia; a kit for mononucleosis; and kits for direct Strep antigen testing.

Use of external, liquid quality control materials

External controls were performed with 85% of the tests in this category. Liquid controls were run with a significantly higher percentage of tests in CLIA-exempt states (91%) than in CLIA-regulated states (72%). The majority of tests were checked with external controls with each kit or lot of reagents (64%), followed by a frequency of each run or day of testing (15%) and monthly (13%).

Other mechanisms used to assess accuracy

The most frequent mechanisms used to assess the accuracy of these non-waived test systems were: proficiency testing (32% of all reasons given); built-in, procedural or electronic controls (31%) and validation studies (17%). We found no significant differences in the patterns of these responses when comparing different laboratory types or the accreditation status of respondents.

One hundred forty-eight of these tests were regulated analytes (where proficiency testing is required). Proficiency testing was performed for 78% of these tests.

DISCUSSION

A total of 920 waived tests were evaluated for 17 different analytes. The majority of these tests are used for a definitive diagnosis (46%) or for screening purposes (42%). We determined that "traditional" quality control (external liquid controls) was performed with 56% of the waived tests overall, but this varied significantly depending on the individual test, how the test was used and the type of testing personnel employed. In addition, for any waived test or for the same waived test there was a wide variation in the frequency with which these controls were performed. Built-in, procedural or electronic controls were used at a rate equal to proficiency testing participation as additional mechanisms to assess the accuracy of waived tests. These rates also fluctuated depending on how the waived tests were used.

Respondents indicated that their quality control protocols for waived tests were based most frequently on either regulations (36%) or manufacturer's recommendations (35%), but this varied significantly depending on the particular waived test.

A total of 184 non-waived tests, with non-traditional quality control mechanisms, were evaluated for 20 different analytes. Thirty-eight percent of respondents indicated that they used these types of methods. Traditional quality control (external liquid controls) was performed with 85% of these tests overall, but we did observe a significant difference in this rate between CLIA-regulated and state-regulated laboratories. We noted a wide variability in the frequency with which traditional controls were performed, with most tests being checked with liquid controls with each kit or lot of reagents (64%). Respondents indicated their quality control protocols for these tests

were based most frequently on regulations (46%) or manufacturer's recommendations (32%). Again, built-in, procedural or electronic controls were used at a nearly equal rate to proficiency testing participation to assess testing accuracy.

Only 14% of the respondents indicated that, in the past two years, they had changed from a waived test system to another test system for the same analyte. A wide range of reasons was given for these changes and no particular test or test system stood out as having an accuracy concern. Eight percent of the respondents made a change from a moderately complex test system to a waived test system for the same analyte during this time period. The majority of these laboratories changed to reduce regulatory oversight, but costs and ease of use were also shared as reasons for this type of change.

CONCLUSIONS

Whether it is due to the recent advances in point of care testing technology, legislation by physician groups or pressure from manufacturers, we recognize an expanding number of test systems being added to the waived test list. We observe that network laboratories are taking advantage of these waived tests, which offer testing sites access to a wide range of analytes with minimal regulatory oversight.

There also appears to be a blurring of lines between waived and non-waived tests systems with respect to the testing principles and quality control mechanisms. We found that there are differing perceptions about what quality control should be performed for these point of care test systems, whether waived or non-waived. For any particular test system, laboratories were divided on running external controls or using any other mechanism to assess testing accuracy. For these testing systems, manufacturers' guidelines and regulations are open for interpretation and accreditation standards vary with each agency. Not surprisingly, network laboratories demonstrated that their various quality control approaches are driven not only by their interpretation of regulations, accreditation standards or manufacturer's information but also by the intended use of the test and whether quality control materials are readily available.

We found that most respondents were performing "traditional" quality control on waived tests, even though laboratories are not required to do anything other than "follow manufacturer's instructions for performing the test," as stated in the CLIA regulations. This may be because the network is composed of laboratories that perform moderate and high complexity testing, and

consequently have a higher propensity to perform traditional quality control than laboratories that perform only waived testing.

Network laboratories did not demonstrate much dissatisfaction with waived testing accuracy - very few laboratories switched to other waived tests or to tests of higher complexity. This type of technology may represent a clear improvement in ease of use and fail-safe operation while meeting expectations for testing accuracy.