

The History of the pSMILE Contract

- Original Contract awarded on November 16, 2004 (through 2011)
 - · Robert Miller, MD Principal Investigator
 - Johns Hopkins Medical Laboratory Continuous Quality Improvement (JHML CQI) Division

"This contract will provide a critically needed comprehensive, uniform program to evaluate the capability of laboratories in developing countries, advise and train when deficiencies are identified, and ensure the ongoing quality of study test results and ultimately the outcome of clinical research performed in these countries. It will address gaps in the area of laboratory-based patient safety monitoring."

- Period of Performance was extended (Mod 7) through 2012.
- November 15, 2012, new seven-year contract awarded (severable, through 2019).
- November 15, 2019, new seven-year contract awarded (severable, through 2026).
 - · Lori Sokoll, PhD Principal Investigator
 - · Johns Hopkins University School of Medicine, Department of Pathology

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The original RFP, drafted in 2004, called for 6 US trained technologists living onsite at DAIDS funded labs on a 1-year rotational basis. That model quickly evolved into the current staffing plan with International QA/QC coordinators based in Baltimore providing support to labs via email, teleconference and occasional site visits.

In 2012 JHU answered the RFP for the next 7 year period with a model very similar to what we have today. 11.7 FTE, including a project manager, 8 QA/QC coordinators, a programmer analyst for the psmile website and a financial officer. Additional IT support is managed using consultants.

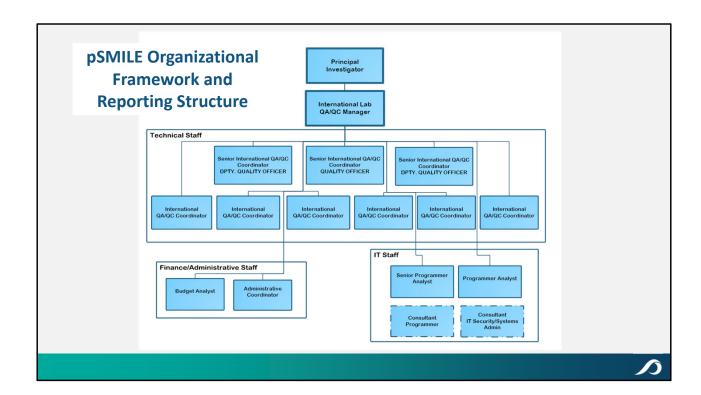
Johns Hopkins University Overview and Organization

Founded in 1876 as America's first research university, the mission of JH Medicine is to improve the health of the community and the world by setting the standard of excellence in medical education, research, and clinical care. The JHU School of Medicine (SOM) ranks as one of the top graduate schools in the country. Johns Hopkins University researchers continuously lead the nation in federal research and development funding.

Johns Hopkins University Overview and Organization

The pSMILE contract is administered through the JHUSOM Department of Pathology. JHU Pathology, in service since the opening of Johns Hopkins Hospital in 1889, is preeminent nationally and globally in the study and treatment of human disease and in professional training for all areas of pathology and laboratory science.

In fiscal year 2018, the Pathology Department of the JHUSOM (JHU Pathology) faculty had over \$63 million in sponsored research expenditures, ranking first in NIH-funding for the ninth time in ten years.



Johns Hopkins University Overview and Organization

Regulatory Inspection History: pSMILE

- FISMA Moderate Certification/Inspection October 2017
 - SAR prepared by MBL Technologies
 - · Submitted to NIH
- ISO 9001: 2015 certification awarded in July 2020.
 - Most recent inspection in May 2025, zero non-conformances

Regulatory Inspection History: JHH/JHU Pathology Laboratories

- CAP Accredited since 2009, most recent inspection in 2023 (due in June of 2025)
- CLIA Licensed, most recent inspection in 2023 (due in August of 2025)

pSMILE FOUR CORE FUNCTIONS

- Review and monitor labs compliance with Good Clinical Laboratory Practices (GCLP)
- Monitor ability of Labs to perform Protocol-specified tests
- Assist, guide and train Labs
- Develop, maintain and host computerized software systems



Review and monitor labs compliance with Good Clinical Laboratory Practices (GCLP)

- As directed by the Contract Office Representative (COR), JHU staff will review audit reports and prepare action plans within 10 business days of receipt. The JHU approach will include a multifaceted strategy for carefully reviewing each audit report, identifying GCLP deficiencies and providing recommendations for corrective and preventive actions (CAPA).
- A systematic approach will be used to develop each action plan document using an internally developed and customized Microsoft Excel spreadsheet and by following internal procedure AP_ 1110, Action Plan Procedure.



Audits and Action Plans

- Laboratory audits conducted by PPD based on the standards of Good Clinical Laboratory Practice (GCLP)
- Audit report sent to SMILE within 30 days of completion of audit
- Action Plan is prepared by SMILE and sent to DCLOT POC
- Networks/DCLOT designate critical/major/minor items
- Action Plan and audit sent to lab by DCLOT POC
- pSMILE works with the laboratory to remediate action items

| | | Key | ₽ pSMILE | | | | | |
|----|---|--|---|---|-------------------------------|-----------------------|-----------------------|--|
| | tion Recomme | nded; Follow-up Not | Enter Lab | Name (Enter Mnemonic) I Country where lab is located. | | | STATUS | |
| Со | mplete | | Enter the Networks involved with the site | | | | | |
| In | Progress | | SMILE comments in BLUE | Enter the type of visit (PP | | | | |
| St | atus Unknown | | Site comments in RED | Created: Enter date and | | | | |
| Сс | ntingent or Cri | tical Items | Network comments in GREEN | Revised: Enter Date and | | | | |
| # | Audit SUB- SECTION | OBSERVATION / FINDING | SUGGESTED ACTION | HISTORY | REVIEWER COMMENTS | NETWORK COMMENTS | STATUS & DATE | |
| | | | SECTION I- EXTERNAL QUALITY AS | | | | | |
| 1 | Enter the subsection of the Audit report where finding is listed. | Short description of items arranged by Audit assessment outline. One or two key word heading in bold for each item. Follow with link to audit source. | Color codes can be used on # column and the Date column. # column can be colored if deemed critical to study start, and then never changes. Date column is color coded as to current status. | SMLE comments should be written in blue (initial). Jun: Site comments should be entered in red. O2 August: Network comments should be entered in green. | | | | |
| 2 | | Example section below | | | | | | |
| | | | SECTION II- ORGANIZATION AND | PERSONNEL | | | | |
| 3 | II. 1. A-C | Organization chart Organogram verified, but did not include the XXX Study. | Modify Laboratory Organogram to include XXX study. Send copy to SMILE. | 19 Jun: Complete and on file with SMILE (JS). | | Complete 19 Jun 12 | | |
| 4 | II. 3. G. | Competency training Competency form in personnel files for direct observation. No SOP available. | See listed SOPs above. Do they address this item? Send example of completed XXXL/1001FR-23 Personnel Competence Assessment Form. Conduct audit of personnel folders to verify the frequency of competency assessment for each employee. | 16 Jun: Competency form and in- use forms on file with SMILE. SOP reviewed and approved (JS). | forms on file with SMILE. SOP | | Complete 16 Jun 12 | |
| | | | SECTION III- TESTING FACILITIES A | AND OPERATION | | | | |
| 5 | | | | | | | | |
| 6 | | | SECTION IV- VERIFICATION OF PERFORM | ANCE EDECIFICATIONS | | | | |
| 7 | Г | | SECTION IV- VERIFICATION OF PERFORM | ANCE SPECIFICATIONS | | | | |
| 8 | | | | | | | | |
| 9 | | | | | | | | |
| 10 | | | SECTION V- LABORATORY INFORMAT | ION SYSTEMS (LIS) | | | | |
| 11 | | | | | | | | |
| | | | SECTION VI- LABORATORY DATA MANAG | EMENT SYSTEM (LDMS) | | | | |
| 12 | | | | | | | | |

The Action Plans are "Keyed" to the audit shell. Lab can cross-reference original audit report.

SMILE suggests an action for remediation and provides resources/training.

and we track the history of that action item.

The AP is color coded. Can see at a glance where the lab stands.

Generates feedback and interaction --between the lab and SMILE to resolve items.

SMILE is able to provide guidance and training based on our SMILE resources and experience of SMILE staff to address specific problems in the lab.

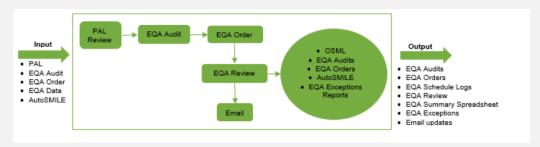
Used by networks and DAIDS as a tool to assess lab readiness for opening of new studies.

Also used as a tool to assess the readiness of a brand new lab to open it's first study.

Goal is to close the Action Plan before the next audit.

Monitor ability of laboratories to perform Protocolspecified tests

As directed by the COR, Johns Hopkins University will monitor the capability of laboratories to perform protocol-specified tests by sourcing, providing and monitoring proficiency testing (PT) also known as external quality assurance (EQA).



| | | | | | / Name: XYZ Labor event Vascular Ev | • | • | 11401 | | | |
|---|--------------------------|-----------------------------------|-------------------------|---|---|---|--|---|---|-------------------------|---------------------|
| | | | | | | | | 1127 | | | |
| Completed by: Alexandra Apollon | | is tr | e Protocoi an in | vestigati | onal New Drug (IN | J) Study? (Y) //v | D number. 118 | 1121 | | | |
| Date Completed: 13 February 2017 Updated: 11 May 2017 | | | | | | | | | | | |
| CKD: Sam Ghanta, 30 May 2017 | | | | | | | | | | | |
| Assav | P) | ease fill in as much | | as you can | provide. Do not add o | r delete analytes as imaru Method/Beac | | specific. | | | |
| | Instrument Name | Instrument Manufacturer | Instrument Model Number | FDA Approve d (Yes/No/ Don't Know) | Method/Kit Name | Method/Kit Manufacturer | Method/Kit Product Number or Product Code | FDA Approve d (Yes/No/ Don't Know) | Primary laboratory performing testing for this protocol | External QA provider | Frequence of EQA |
| Chemistry | Vitros 250 | Ortho Clinical | SN-27001710 | | Slide/Vitros ALT | Ortho Clinical | Side/Vitros | YES | IMSI Chemistry Lab | Accutest | 3 X/vear |
| ALT (SGPT) | | Diagnostics/J&J | | Yes | | Diagnostics/J&J | ALT,Ref#1655281 | | | | , |
| AST (SGOT) | Vitros 250 | Ortho Clinical Diagnostics/J&J | SN:27001710 | Yes | Slide/Vitros AST | Ortho Clinical Diagnostics/J&J | Stide/Vitros AST, Ref#8433815 | YES | IMISII Chemistry Lab | Acoutest | 3 X /year |
| LDL cholesterol (calculated) (Fasting) | Vitros 250 | Ortho Clinical Diagnostics/J&J | SN:27001710 | Yes | N/A | Ortho Clinical Diagnostics/J&J | N/A | YES | IMISII Chemistry Lab | Acoutest | 3 X /year |
| Direct LDL cholesterol (Fasting) | AU-series | BECKMAN | AU-series | YES | Liquid Selective LDL- Reagent | BECKMAN | 05R6296 | YES | QUEST LAB | CAP | 3 X /year |
| HDL cholesterol (Fasting) | Vitros 250 | Ortho Clinical Diagnostics/J&J | SN:27001710 | Yes | Slide/Vitros HDL | Ortho Clinical Diagnostics/J&J | Slide/Vitros HDL,Ref#6801895 | YES | IMISII Chemistry Lab | Acoutest | 3 X /year |
| Triglycerides (Fasting) | Vitros 250 | Ortho Clinical Diagnostics/J&J | SN:27001710 | Yes | Slide/Vitros TRIG | Ortho Clinical Diagnostics/J&J | Slide/Vitros TRIG Ref#1336544 | YES | IMISII Chemistry Lab | Acoutest | 3 X /year |
| Total cholesterol (Fasting) | Vitros 250 | Ortho Clinical Diagnostics/J&J | SN:27001710 | Yes | Slide/Vitros CHOL | Ortho Clinical Diagnostics/J&J | Slide/Vitros CHDL_Ref#166982 | YES | IMSII Chemistry Lab | Acoutest | 3 X /year |
| Creatrine | Vitros 250 | Ottho Clinical Diagnostics/J&J | SN:27001710 | Yes | Slide/Vitros CREAT | Ortho Clinical Diagnostics/J&J | Slide/Vitros CREAT, Ref#6802584 | YES | IMISII Chemistry Lab | Acoutest | 3 X /year |
| Creatinine clearance (measured or estmated using Cockcroft-Gault equation) | N/A | N/A | N/A | N/A | N/A | NIA | N/A | N/A | N/A | N/A | N/A |
| Urinalysis | | | | | | | | | | | |
| HCG (test must have a sensitivity of 15-25 mlUlmL) | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Hematology Hgb, Hor, Pir, WBC | Cell Dyn 3200 | ABBOTT | SN:62792AF | Yes | ABBOTT, CellDyn 3200 | ABBOTT | 03H80-02/03H78- | YES | IMISII Hematology Lab | Acoutest | 3x/year |
| Serology HCG | NA NA | NA NA | NA NA | Yes | StanbioQupid PlusER | Stanbio | Preg. Test #1251- | YES | GHESKIOChemistruLab | Accutest | 3X/year |
| HIV Rapid Test | N/A | N/A | N/A | N/A | Determine HIV 1/2 | Alere | 7D2343 | NO | GHESKIOSerologyLab | Acoutest | 3x/year |
| HIV EIA/ELISA(Chemiluminescence) HIV Western Blot | ArArchitect I 1000 NA | ABBOTT NA | I 1000 SR NA | Yes Yes | HIVAq/Ab Combo Cambridge Biotech HIV-1 | ABBOTT Maxim Biomedical | #4J27-27 98002 | NO YES | IMIS Serology GHESKIOSerologyLab | CAP CAP | 3x/year 3x/year |
| Other | | | | | | | | | | | |
| CD4/CD8 Absolute count and percentages | BD Facscount | Becton Dickenson | D850001279 | YES | FACSCount | 80 | 340167 | YES | MISII Imunology Lab | UKNEGAS | 6x/year |

This form was originally developed jointly by the networks/DAIDS and SMILE and it has become a critical tool for SMILE.

Specific to a particular protocol.

It shows the details of analytes are needed for a protocol—and how and where they will be tested.

It also shows how we intend to cover those analytes with EQA—who the provider is and how frequently the panels will be delivered.

It is a way to communicate what the specific needs of a protocol are.

How does SMILE use proficiency testing?

Monthly review and monitoring of EQA results

- Direct data feed of provider data into the pSMILE AutoSMILE database
- pSMILE coordinators review all data, comparing it to the provider survey pdf reports
- EQA review is generated from the database, ensuring consistency and accuracy
- EQA summary and schedule are updated by the database



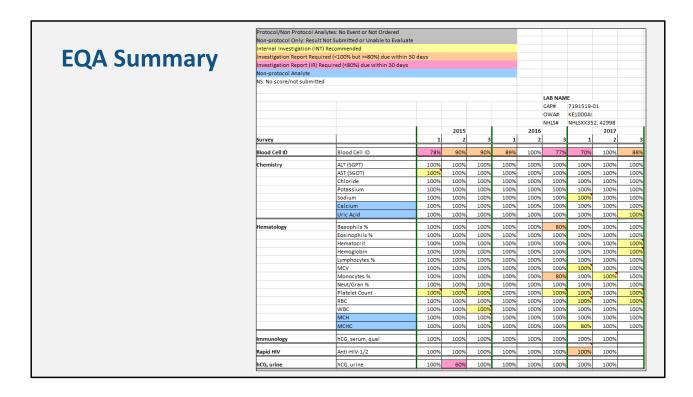
| EC | QA S | Scha | S 6 1 1 1 | | | | | |
|----------------------------------|--------------|----------|------------------|---|------------------------|------------------------|----------------------|--------------------------------------|
| | | | | | | | | |
| | | | _ u u | | | | | |
| | | | | | | | | |
| Investigation | Report Requi | red | | | | | | |
| | | | | | | | | |
| 2017 | | | | LAB NAME | | | | |
| Ship | EQA | Survey | Module | | SMILE Reviewed | | Investigation | |
| Date 1 23-Jan-17 | Provider | Sequence | Code | Test Group Name Viral Markers | (Date) | (Date) | Complete (Date) | Comment 100% Successful |
| 1 23-Jan-1/ | CAP | Α | VM | Viral Markers | 19-Apr-17 | N/A | N/A | |
| 2 30-Jan-17 | CAP | A | FH10 | Ulamatala m | 40.4 47 | 04 4 47 | 4.14 47 | Acceptable IR received- PNL approved |
| 3 30-Jan-17 3 30-Jan-17 | CAP | A | BP BP | Hematology Blood Parasite | 19-Apr-17 19-Apr-17 | 21-Apr-17 28-Apr-17 | 4-May-17 4-May-17 | approved 100% Successful |
| 3 30-Jan-17 | CAP | A | DP | DIOUG Parasité | 13-Apr-17 | 20-Apr-17 | 4-may-11 | Acceptable IR received - sent |
| 4 13-Feb-17 | CAP | A | С | Chemistry | 19-Apr-17 | 17-May-17 | 30-Jun-17 | for PNL approval |
| 5 21-Feb-17 | CAP | A | F1 | Mycology | 28-Jun-17 | 20-Jul-17 | 26-Sep-17 | IR received - approved |
| 6 21-Feb-17 | CAP | A | CM | Urinalysis | 19-Apr-17 | 20-Jul-17 | 20 000 11 | IR received - under review |
| 7 21-Feb-17 | CAP | Ä | CRYP | Cryptococcal Antigen | 19-Apr-17 | N/A | N/A | 100% Successful |
| 8 6-Mar-17 | CAP | A | GH5I | HgbA1C International | 19-Apr-17 | N/A | N/A | 100% Successful |
| 9 8-Mar-17 | OWA | 1 | UHCG435 | Urine hCG | 28-Jun-17 | N/A | N/A | 100% Successful |
| 10 3-Apr-17 | CAP | A | AHIV | Rapid HIV | 28-Jun-17 | N/A | N/A | 100% Successful |
| 11 17-Apr-17 | CAP | A | М | CSF Chemistry | 28-Jun-17 | N/A | N/A | 100% Successful |
| 12 18-Apr-17 | CAP | A | G | Syphilis Serology | 28-Jun-17 | N/A | N/A | 100% Successful |
| 13 8-May-17 | CAP | В | FH10 | Hematology | 28-Jun-17 | 20-Jul-17 | | IR received - under review |
| 14 15-May-17 | | A | IND | India Ink | 28-Jun-17 | N/A | N/A | 100% Successful |
| 15 15-May-17 | | В | VM | Viral Markers | 21-Jul-17 | N/A | N/A | 100% Successful |
| 16 22-May-17 | CAP | В | BP | Blood Parasite | 20-Jul-17 | N/A | N/A | 100% Successful |
| 17 30-May-17 | | A | RMAL | Rapid malaria | 21-Jul-17 | N/A | N/A | |
| 18 30-May-17 | | В | F1 | Mycology | | | | |
| 19 30-May-17 | CAP | В | CRYP | Cryptococcal Antigen | 2-Nov-17 | N/A | N/A | 100% Successful |
| | | _ | _ | | | | | IR Required For: Chloride, |
| 20 5-Jun-17 | CAP | В | C | Chemistry | 2-Nov-17 | | | Creatinine |
| 21 14-Jun-17 | AWO | 2 | UHCG435 | Urine hCG | 2-Nov-17 | N/A | N/A | 100% Successful |
| 22 19-Jun-17 23 31-Jul-17 | CAP | B | GH5I G | HgbA1C International Syphilis Serology | 2-Nov-17 | N/A | N/A | 100% Successful |
| 23 31-Jul-17 24 14-Aug-17 | CAP | B | AHIV | Rapid HIV | 2-Nov-17 2-Nov-17 | N/A N/A | N/A | 100% Successful 100% Successful |
| 24 14-Aug-17 25 28-Aug-17 | CAP | C | VM | Viral Markers | 2-Nov-17 2-Nov-17 | N/A N/A | N/A | 100% Successful |
| 26 5-Sep-17 | CAP | В | M | CSF Chemistry | 2-Nov-17 | N/A | N/A | 100% Successful |
| 20 3-Sep-17 | CAP | _ D | IVI | COI CHEMISTRY | 21101-11 | INDA | IWA | Investigation Required For: |
| 27 11-Sep-17 | CAP | В | СМ | Urinalysis | 29-Nov-17 | | | Ketones, urine |
| 28 18-Sep-17 | CAP | A | HECI | Hemocytometer Fluid Count | | N/A | N/A | 100% Successful |
| 20 10-Sep-17 | O/AF | _^_ | 111 C1 | remocytometer Fluid Count | 2-1407-17 | 140 | THE CO. | Investigation Required For: |
| 29 18-Sep-17 | CAP | С | F1 | Mycology | 29-Nov-17 | | | Yeast ID |
| 30 18-Sep-17 | CAP | C | CRYP | Cryptococcal Antigen | 29-Nov-17 | N/A | N/A | 100% Successful |
| | 0.0 | , i | | | | | | Investigation Required For: |
| 31 25-Sep-17 | CAP | С | FH10 | Hematology | 29-Nov-17 | | | Blood Cell ID |
| 32 25-Sep-17 | CAP | C | BP | Blood Parasite | 2-Nov-17 | N/A | N/A | 100% Successful |
| 33 2-Oct-17 | CAP | C | C | Chemistry | 29-Nov-17 | N/A | N/A | 100% Successful |

On this first page of the spreadsheet is the year's schedule for EQA shipments.

Lab knows a year in advance when to expect their survey shipments

This page also summarizes the laboratory's status at a quick glace.

By color coding we can quickly see that there is an outstanding investigation required for Gram stain.



The second page of the EQA spreadsheet gives detailed information about each analyte tested in the lab.

The EQA history for 3 years is maintained on this sheet.

Color coding also gives a quick picture of how well the lab is performing.

Investigations

- Required for EQA failures (any score <100% for protocol analytes)
- SMILE provides assistance, tools and resources
- Root cause and prevention of future failure
- Documentation of corrective action is end product

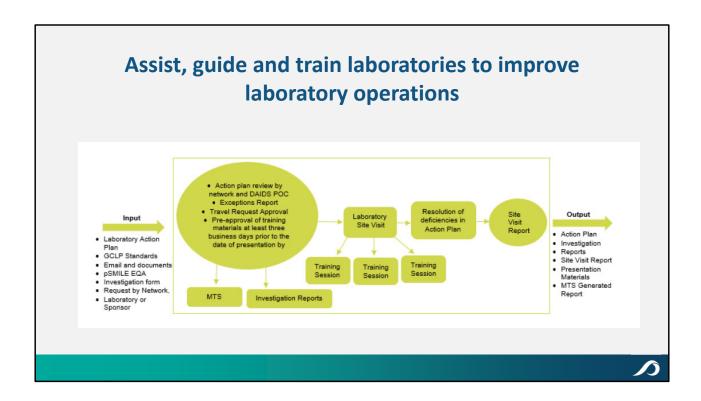
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SMILE assists with investigations of EQA failure and provides labs with tools and resources for **corrective action**.

The process of troubleshooting the cause of EQA failure is another example of how important our extensive experience in the laboratory is.

The process often involves a lot of back and forth email and research and discussion of possible causes.

Our goal is to **teach the labs how to investigate** problems and prevent them in the future by the use of good laboratory practices.



pSMILE Site Assistance and Training

- Email
- Phone
- Web conference
- At annual network conferences
- On site
- International Regional Training



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The Action Plan often leads to opportunities to help our labs by teaching or training.

Many times this takes place in email or telephone conversations.

Our computer expertise and support has also allowed us to use web tools and create computer based training programs.

•We utilize the Adobe Connect software which allows us to connect with our sites via the web and show them any presentations or walk them through any trainings that we have.

We have also presented trainings at conferences. TB Safety training was given at the last ACTG meeting and will be presented in Thailand in January.

We also are occasionally asked to visit a lab to provide specific training or assistance. Accomplish a specific goal or need—focused visit.

Our goal is to empower the labs through training. By doing this the knowledge and the experience stays with the lab even after the DAIDS study is finished.

Develop, maintain and host computerized software systems

pSMILE operations are managed by the use of three interconnected databases

- Oversight Masterlist Database (OSML)
- pSMILE.org Database
- AutoSMILE Database



Oversight Masterlist (OSML) Database

- Listing of all pSMILE supported laboratories including contact information, primary and backup coordinator, PNL status, DCLOT POC
- Contact information for each lab including shipping address details, EQA provider numbers
- EQA order for each laboratory including bulk shipping arrangements and email tracking list for notification of shipments
- EQA details by provider, including ship dates, cost, events per year
- EQA Performance Review—a review of each EQA event across all pSMILE labs with documentation of corrective action
- Action Plan tracking, including detailed information on the lab accreditation status
- pSMILE office equipment inventory



AutoSMILE Database

- EQA review
- Generate EQA summary and schedule
- EQA email notification to labs
- EQA data loaded directly from provider data feeds
- EQA Exceptions List
- QA functions—Turnaround Time

pSMILE Website: www.psmile.org

- Document Repository
 - EQA surveys, reviews and investigations on www.psmile.org
 - Available to site labs (privately by log-in)
 - Available to DAIDS and the Networks
 - Also on www.psmile.org
 - Audits and Action Plans
 - Site visit reports
 - Protocols and Protocol Analyte Lists (PAL)
- Resources on www.psmile.org
- EQA Exceptions list on www.psmile.org

pSMILE Internal Standard Operating Procedures

- Currently stored on the MediaLab Document management portal
- Searchable and protected database
- Reviewed biennially