SCRI LabKey Server

Using existing LabKey modules to build a platform for immunotherapy clinical trials

Olivia Finney, PhD

Seattle Children's
HOSPITAL · RESEARCH · FOUNDATION

CSL
Correlative Studies Lab
Seattle Children's Research Institute

The Immunotherapy Integration Hub

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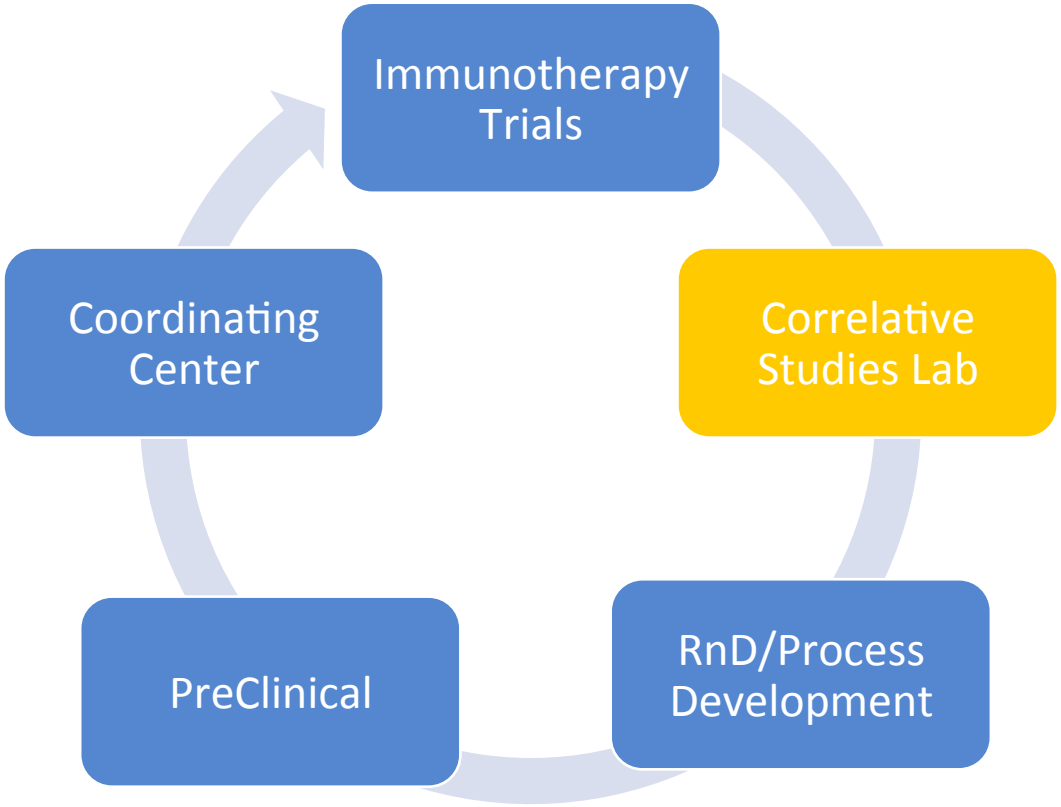
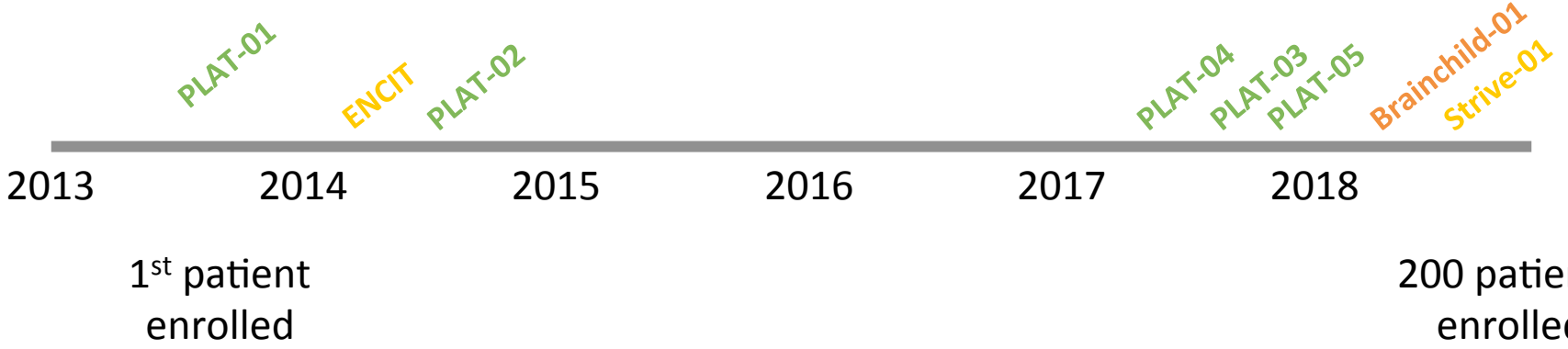
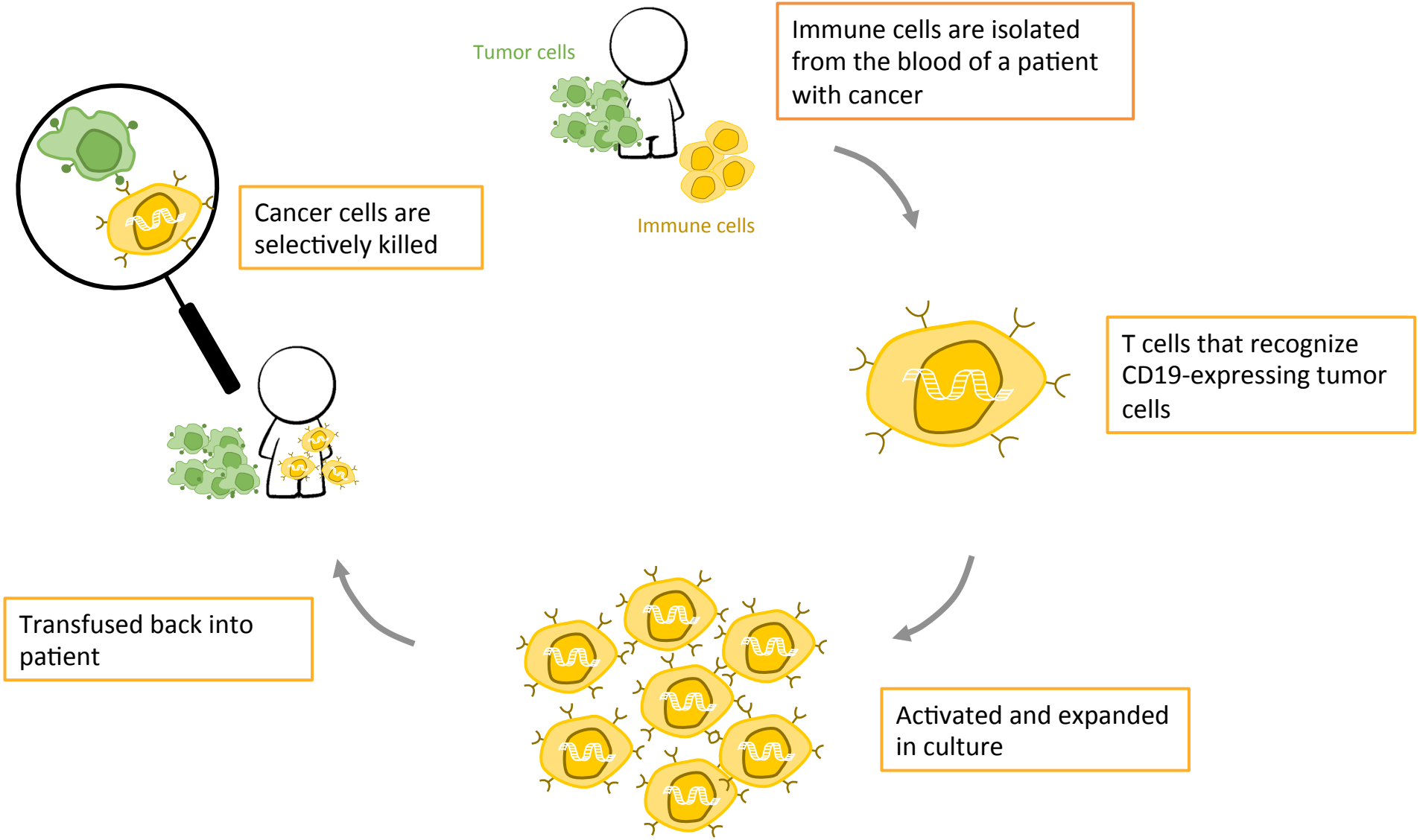
Research Institute



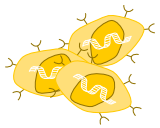


Cellular Immunotherapy in Cancer



What makes a successful engineered T cell

- Cell characteristics pre-modification
  - Last chemotherapy treatment
  - Type of drug
  - Cells before and after transplant

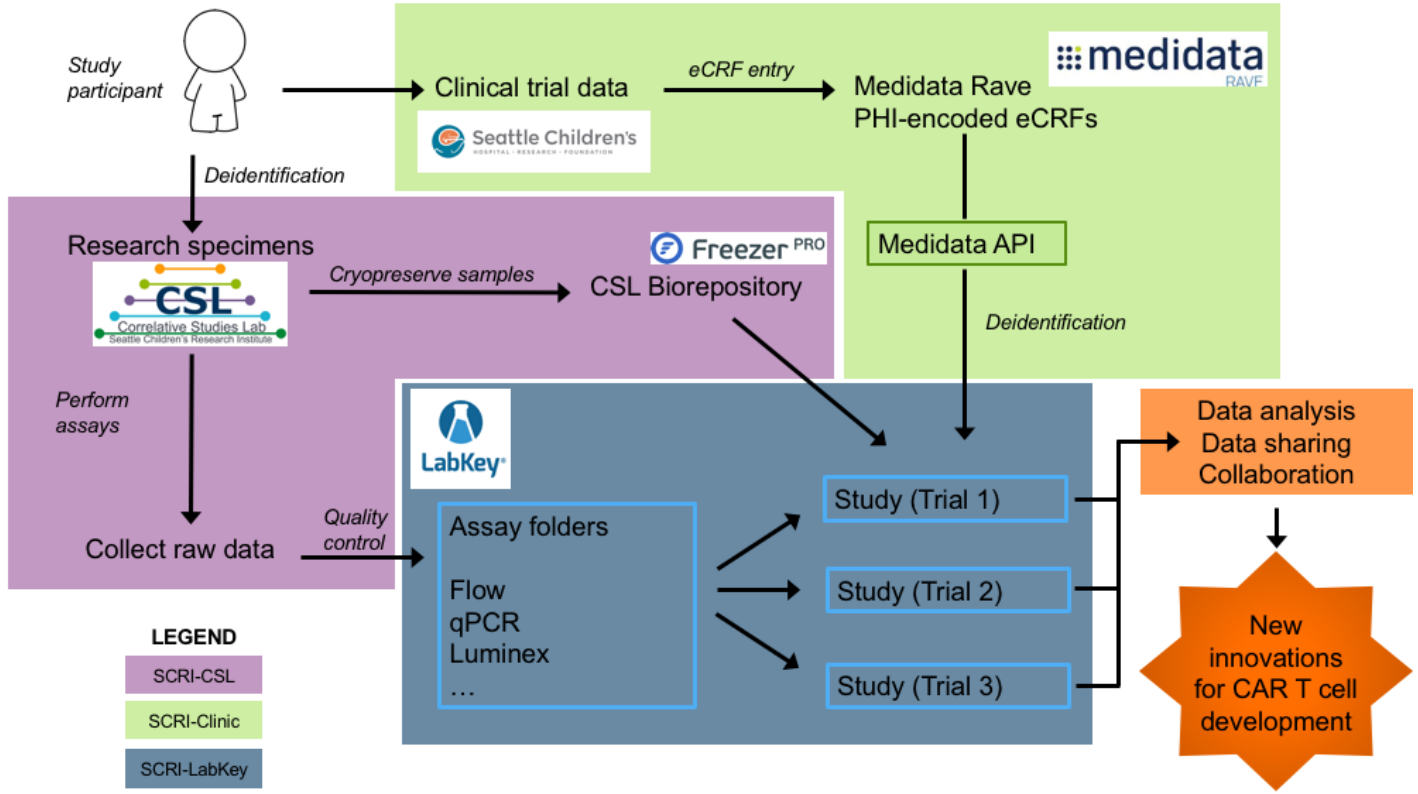


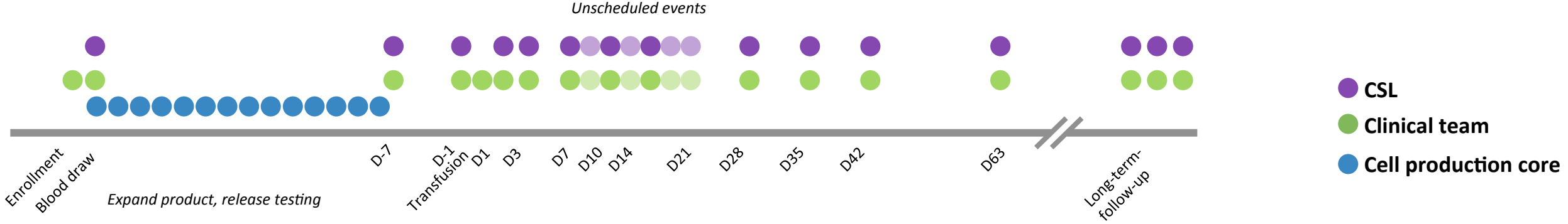
- Characteristics of genetically modified cells
  - Cell markers that make them better “killers”
    - Differentiation
    - Memory phenotype
    - Proliferative potential
    - Function

- Persistence of engineered T cells
  - How long is long enough to gain complete long term remission?

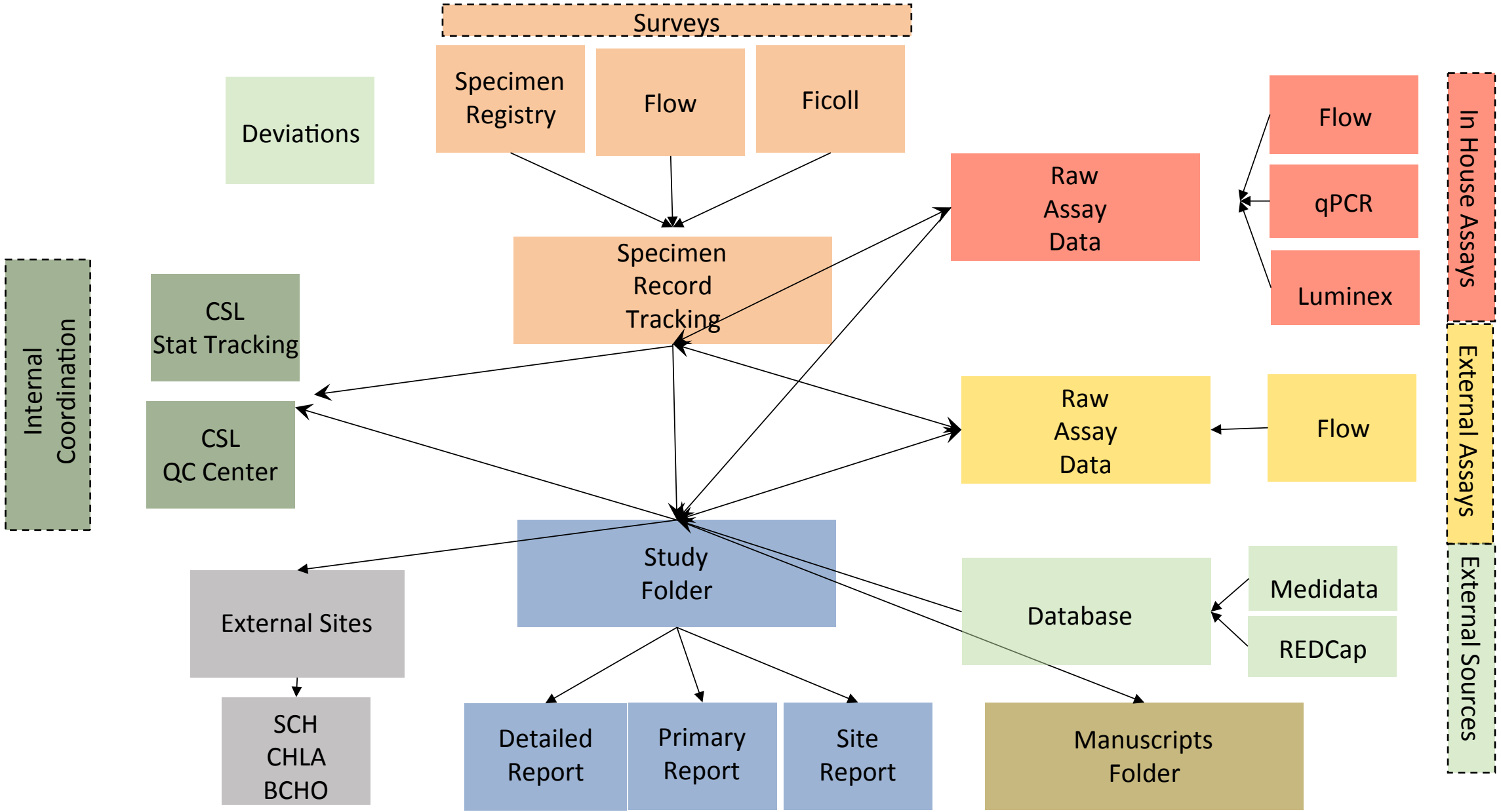
- Toxicity
  - Cytokine release syndrome
  - Neurotoxicity

Multidisciplinary Data Collection





The SCRI Server at a Glance



Landing Page – Key Facts and Stats

Welcome to the SCRI-CSL LabKey Server!

Active Clinical Trials

CSL currently have six active phase I and II clinical trials. Click study titles to access the dedicated study sites. Click trial info and clinical PI to learn more about the studies and PIs.

ENCIT-01

Official Title:	Engineered Neuroblastoma Cellular Immunotherapy (ENCIT)-01
Target:	L1-CAM+ Recurrent / Refractory Neuroblastoma
Trial Info:	NCT02311621
Institution:	Seattle Children's
Clinical PI:	Navin R. Pinto, MD

PLAT-02

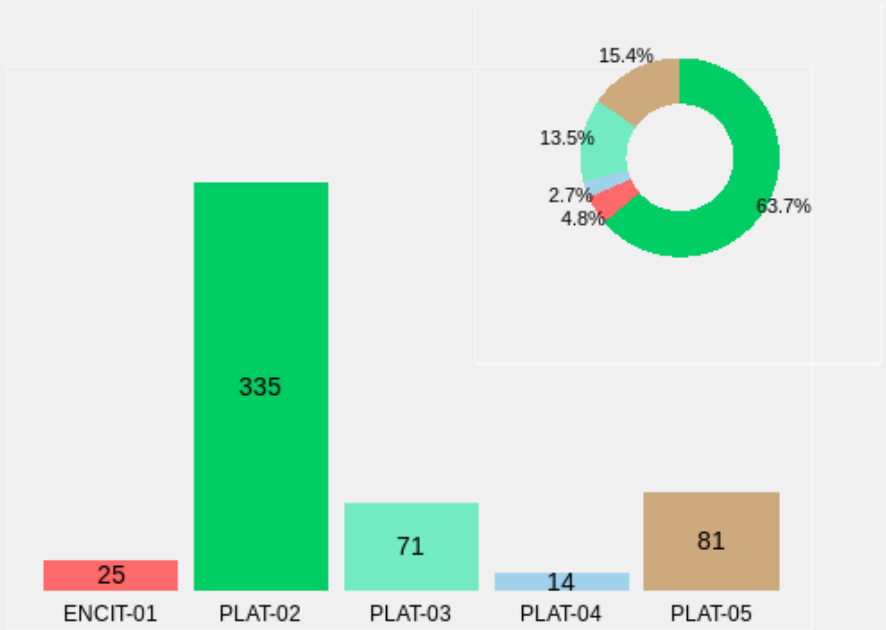
Official Title:	Pediatric and Young Adult Leukemia Adoptive Therapy (PLAT)-02: A Phase 1/2 Feasibility and Safety Study of CD19-CAR T Cell Immunotherapy for CD19+ Leukemia
Target:	CD19+ Acute Leukemia
Trial Info:	NCT02028455
Institution:	Seattle Children's
Clinical PI:	Rebecca A. Gardner, MD

PLAT-03

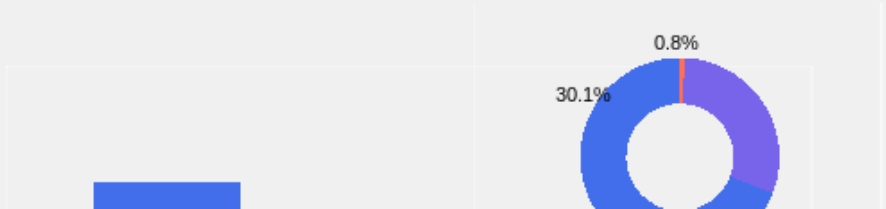
Official Title:	PLAT-03: A Pilot Feasibility and Safety Study of CD19t T-Antigen Presenting Cells (T-APCs) Following CAR T Cell Immunotherapy for CD19+ Leukemia
Target:	CD19+ Acute Leukemia
Trial Info:	NCT03186118
Institution:	Seattle Children's
Clinical PI:	Colleen E. Annesley, MD

CSL Statistics

Correlative Studies Lab (CSL) processes research samples from hospitals across the nation and around the global for all active clinical trials. Below are some key statistics.



Number of Specimen Sample Processed Year to Date by Trial



Specimen Receipt
Using Surveys to Track Specimens

specimenRegistry (18)

Participant ID*	14602_CS_S1097
Visit*	C1.D63
Specimen Type*	BMA
Specimen ID	14602_CS_S1097 C1.D63 BMA
Was the sample drawn?	Yes
Date of draw at origin	2018-10-02
Time of draw at origin (Military Time, HH:MM)	10:55
Country at origin	USA
City at origin	Fontana
State at origin (U.S. Only)	California
Date of draw in Seattle Time*	2018-10-02
Time of draw in Seattle Time (Military Time, HH:MM)	10:55
Was the sample received by CSL?	Yes
Did specimen meet Acceptability Criteria?	Yes
Date received into CSL	2018-10-03
Aliquots received/created (select all that apply):	☑ Flow ☐ Whole Specimen DNA ☑ Ficoll ☐ None
Submitted by (initials)*	SS
Has the survey been verified?	Yes
Verified by (initials)*	tb
What's the sample status?	Leave this blank

Reducing errors: using generated specimen ID for other surveys and assays

FicollReport

Specimen Id

Was Ficoll performed? Select...

Submitted by (initials)*

Has the survey been verified? Select...

Verified by (initials)*

Status Code (DO NOT MODIFY)

Save | Submit Completed Form

Note: The following fields must be before you can submit the form:
-submittedby
-verifiedby

flowStaining

Specimen Id

Did specimen meet Acceptability Criteria? Select...

Was the sample stained? Select...

Submitted by (initials)*

Has the survey been verified? Select...

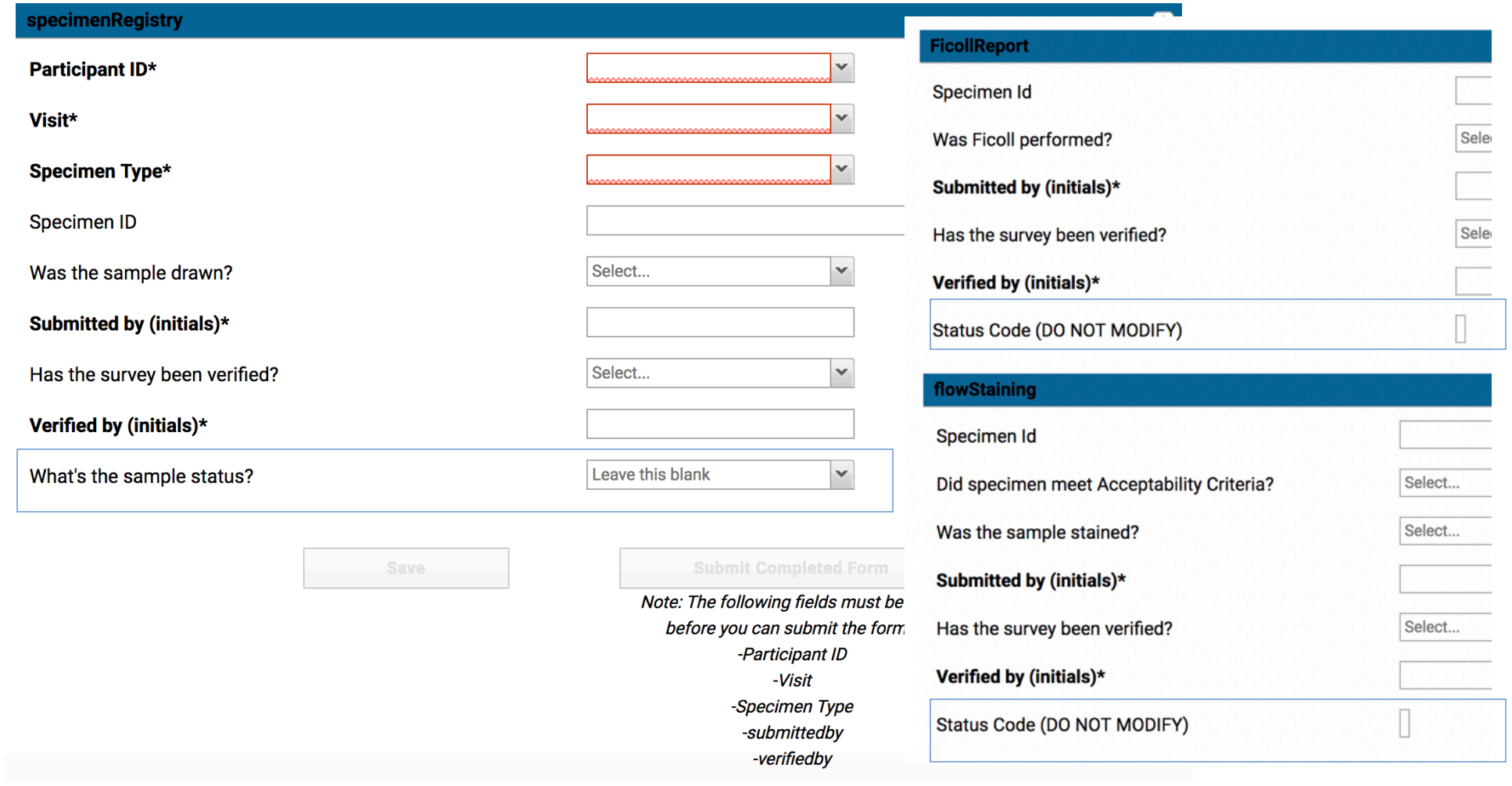
Verified by (initials)*

Status Code (DO NOT MODIFY)

Save | Submit Completed Form

Note: The following fields must be valid before you can submit the form:*
-submittedby
-verifiedby

Recalling Samples



QC - programmatic checks

Specimen Record QC (Multiple Entries):

Specimen Registry:

1 - 9 of 9

Specimen ID	Sample Status	Received Date	Verified	Survey Key
15125_CS_S16 C1.AE4 TUMOR				196
15125_CS_S16 C1.AE4 TUMOR		2018-01-09		195
15125_CS_S16 C1.AE4 TUMOR		2018-01-09		194

Flow Staining Registry:

1 - 10 of 10

Specimen ID	Sample Status	Date Stained	Run Number	Verified	Survey Key
152_CS_S004 C1.T1.D1 PB	Normal	2018-07-02	1	Yes	721
152_CS_S004 C1.T1.D1 PB	Normal	2018-07-03	2	Yes	717
14602_CS_S1089 C1.PreA PB	Recalled	2018-05-04		Yes	517

Ficoll Registry:

Specimen ID	Sample Status	Ficoll Date	Verified	Survey Key
14602_CS_S1065 6M PB	Recalled		Yes	85
14602_CS_S1065 6M PB	Normal	2018-07-19	Yes	150
14602_CS_S1063 6M PB	Normal	2018-06-20	Yes	35

Study Report QC (Multiple Entries and/or Missing Information):

1 - 100 of 112

Participant ID	Visit Description	Sample Type	Potential Reason
15125_CS_S01	PreP	PB	Missing Infusion Date
15125_CS_S02	6M	PB	Missing Info
15125_CS_S04	PreP	PB	Missing Infusion Date
15125_CS_S06	12M	PB	Missing Info
15125_CS_S06	D126	BMA	Missing Info

Tracking our deviations for patterns

Correlative Studies | Studies | Start Page | Deviation Survey V00 | Deviation Survey V01 | +

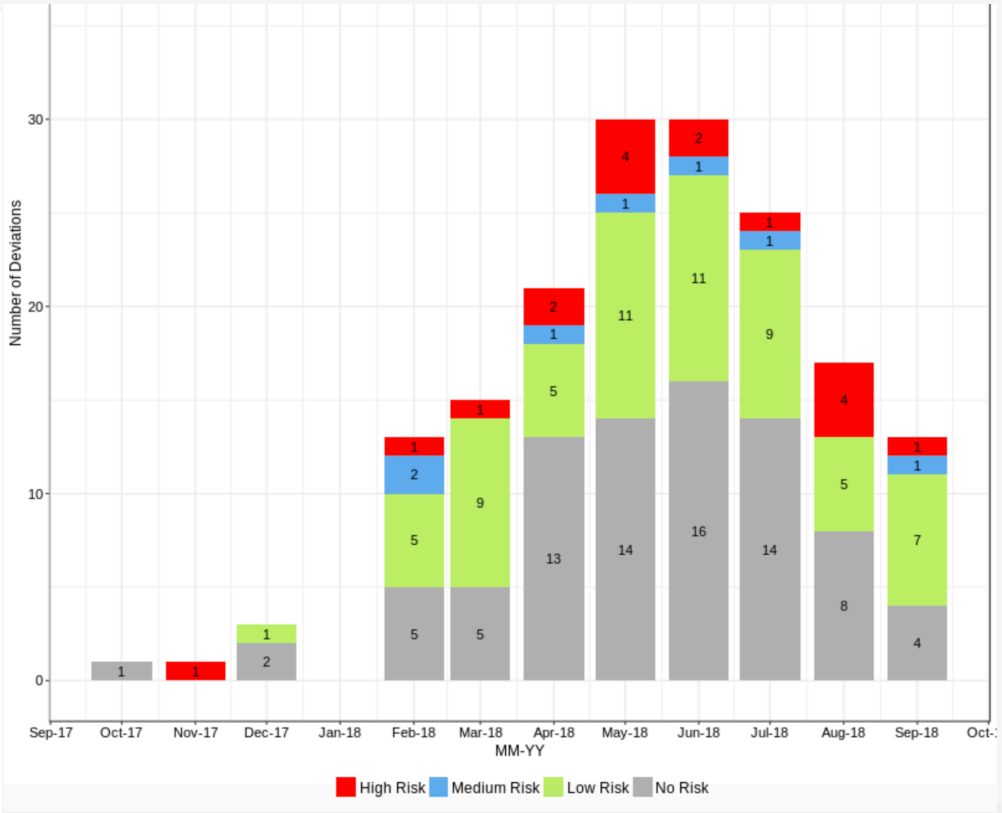
Deviation survey

Deviation Tracking by Category

CSL Deviation Record Tracking by Month, Generated for olivia finney

1 - 11 of 11

Month	0.No Risk	1.Low Risk	2.Medium Risk	3.High Risk
2017-10	1			
2017-11				1
2017-12	2	1		
2018-2	5	5	2	1
2018-3	5	9		1
2018-4	13	5	1	2
2018-5	14	11	1	4
2018-6	16	11	1	2
2018-7	14	9	1	1
2018-8	8	5		4
2018-9	4	7	1	1



Using Labkey as a Visual Board

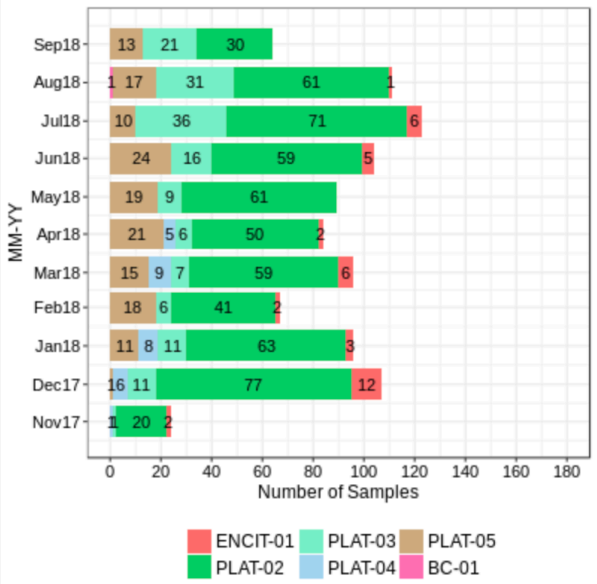
SCRI-CSL SDI Board

CSL Goals:

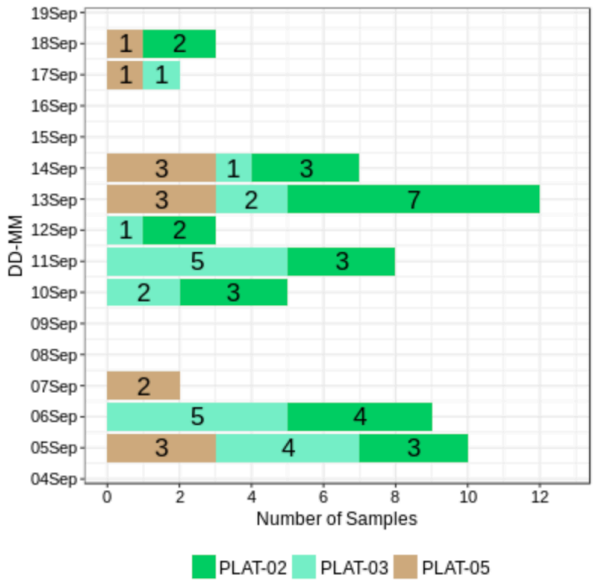
1. Greater Impact: CLIA			
Task	Status	Expected Date	Path to Green
Assay Validation	May 2018	May 2018	
Procedure Manual	Jul 2018	Jul 2018	
CLIA Licence		Jul 2018	Not in Progress

Processing Capacity Tracking

Sample Processed By Month

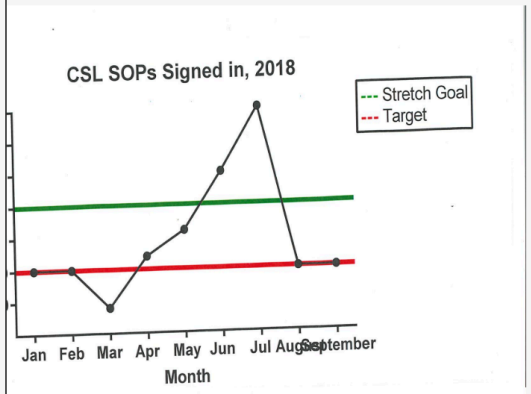


Sample Processed In Past 14 Days



2. Better Outcomes: SOP Compliance				Current SOPs Open: 16
	Status This Month	Status For 2018	Target	Path to Green
SOP Tracking	100%	100%	100%	
%SOP Closed ≤ 31 Days	0%	50%	80%	Only one SOP closed in August, close more SOPs!
Average Days Open	44	41	31	

Per Month Performance:



SDI Dashboard

Trial Pipeline (Demand)

Trial	Phase	Multi-Site	Start	Lab Manual	Study Plan	Assays	Labkey	Status	Path to Green
BC-01	1	No	15Jun18	Yes	Yes	Yes	Yes		
STRIvE-01	1	No	05Aug18	No	No	Yes	No		Waiting for BDM to finish eCRF build
PLAT-06	2	Yes	Nov18	No	No	Yes	No		
BC-02	1	No	Oct18	No	No	Yes	No		
ENLIGHTen-01	1	No	May19	No	No	No	No		

Issue + Risks

Description	Action	Owner	Due Date
SCCA Not Cooperating for Sample Collection	Continue to Monitor	Margo	Complete, in Monitoring

LTFU Updates

Study	Status	Study	Status	Study	Status
ENCIT-01		PLAT-01		PLAT-02	
PLAT-03		PLAT-04		PLAT-05	
PLAT-06		BC-01		STRIvE-01	

Kaizan:

Issue	Action	Measurement	Owner	Status
More than 70% of the SOPs close ≥ 31 Days	• Move work flow to SharePoint • Create automatic document control	Percentage of SOPs closed less than 31 Days	• Travis • SharePoint Team	Dec18
Incorrect packaging from the sites	• Test picture-based packaging instruction	Deviation resulted from packaging error per month	• Shayne • Travis • Alanna	Oct18

Kaizen of the Month

Marilyn has successfully completed precessing capacity test to increase Ficoll limit per operator. Great job Marilyn! (Picture goes here)

Kaizen Tracker

Huddle Training:	100%
Kaizan ideas (Marilyn):	5/22
Kaizan ideas (Olivia):	22/22

Submit you Kaizan Idea!

Submit Ideas!

How to edit the board when most members don’t code

2. Better Outcomes: SOP Compliance			Current SOPs Open: 16	
	Status This Month	Status For 2018	Target	Path to Green
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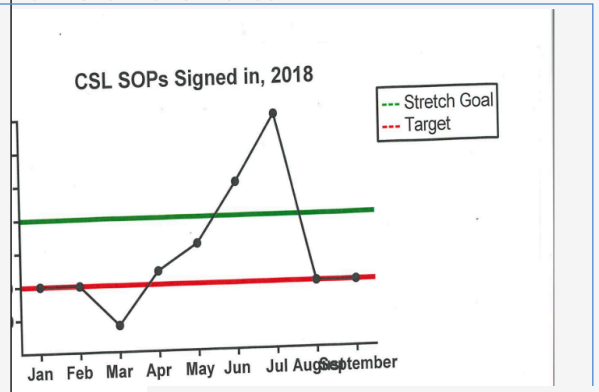
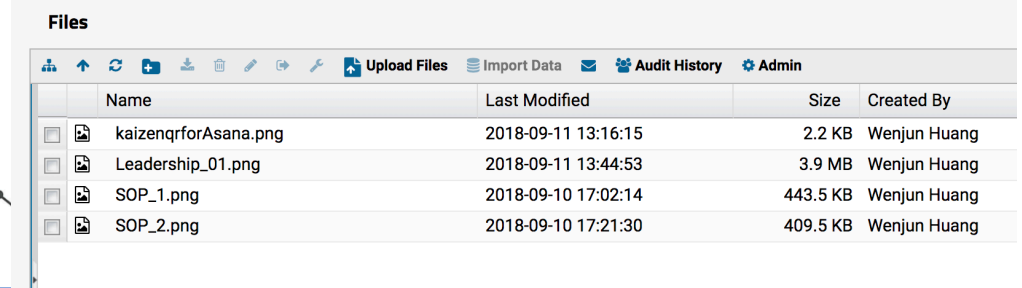
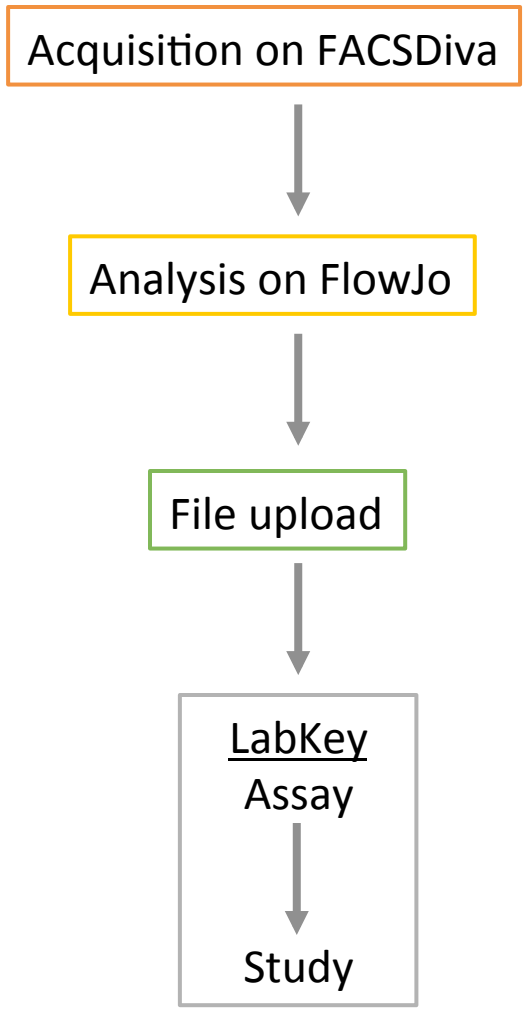
Per Month Performance:				






```
        <td>
            <font size="3">SOP Tracking</font>
        </td>
        <td bgcolor="green">
            <font size="3">100%</font>
        </td>
        <td bgcolor="green">
            <font size="3">100%</font>
        </td>
        <td>
            <font size="3">100%</font>
        </td>
        <td>
            <font size="2"></font>
        </td>
    </tr>
    <tr>
        <td>
            <font size="3">%SOP Closed &#8804; 31 Days</font>
        </td>
        <td bgcolor="red">
            <font size="3">0%</font>
        </td>
        <td bgcolor="Yellow">
            <font size="3">50%</font>
```

Assay Data – Flow Cytometry



- Compensate sample .fcs files
- Done three times a week
- Use drag and drop feature of in assay folder
- Manually direct files to appropriate folder - Get sample descriptions from specimen survey through ETL - Quality control - Push to study

Flow Cytometry – QC is an essential step

- Quality control is a requirement
  - FlowJo user errors
  - FlowJo bugs- 10.0.6
  - Erroneous file transfer

- Thumbnail view is a helpful tool
- QC review in Flow survey, reviewer pushes to study

flowStaining

Specimen Id

Did specimen meet Acceptability Criteria? Select...

Was the sample stained? Select...

Submitted by (initials)*

Has the survey been verified? Select...

Verified by (initials)*

Status Code (DO NOT MODIFY)

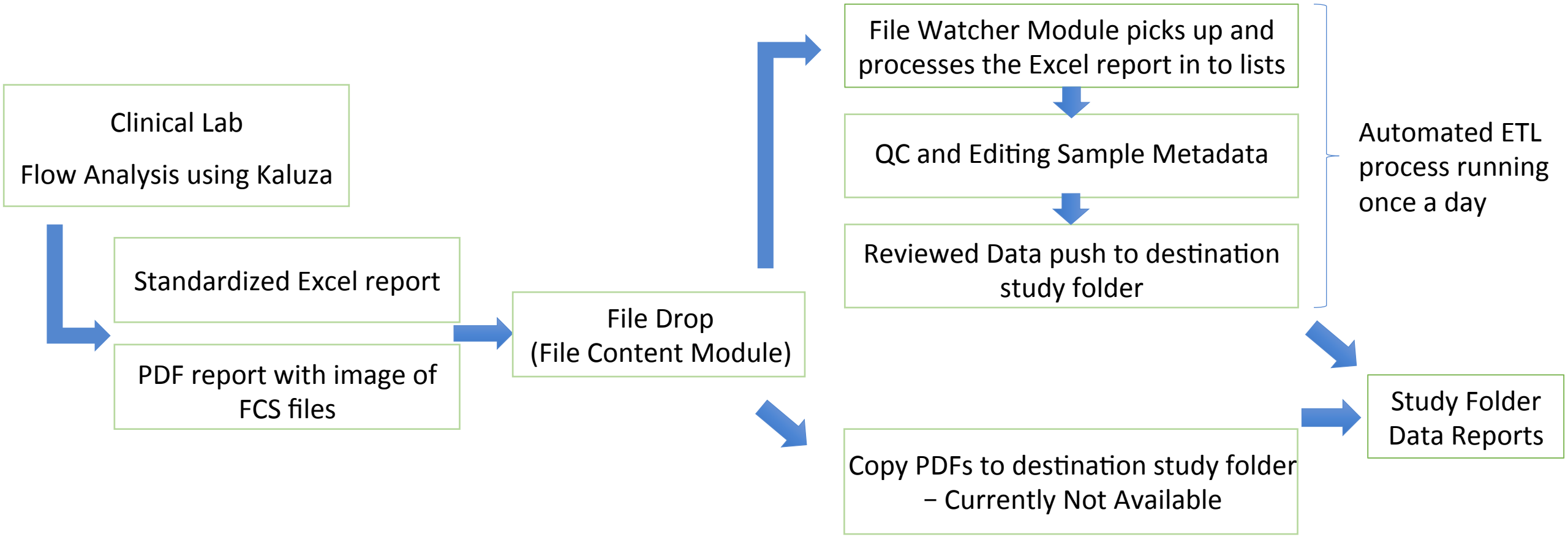
Save | Submit Completed Form

Note: The following fields must be valid before you can submit the form:*
-submittedby
-verifiedby

Name	Participant ID	Visit Description	Visit ID	Sample Type	Lymphocytes:%P	Lymphocytes(Comp-Blue 530_30-A:Comp-Blue 695_40-A)	CD3:%P	B cells:%P	B cells:Median(Comp-Blue 530_30-A)	NKT cells:%G
Samples_S01 D-1 PB_003.fcs	13835_CS_S01	D-1	400	PB	92.691		88.983	0.032	220.446	2.703
Samples_S01 D21 BM_008.fcs	13835_CS_S01	D21	1100	BM	86.659		53.4	0.125	240.843	6.002
Samples_S01 D7 PB_004.fcs	13835_CS_S01	D7	800	PB	95.166		92.687	0.006	291.497	14.845
Samples_S01 D42 BM_011.fcs	13835_CS_S01	D42	1400	BM	94.536		41.145	17.603	438.268	1.856
Samples_S01 cCS0001_012.fcs	13835_CS_S01	cCS0001			73.866		77.43	4.198	580.397	3.918

Assay transfer to clinical lab: how to recreate workflow?

Cannot use assay folder as too complex and would require access to main server
→ File Share



Assay Management within the Group: how to track and streamline workflow?

CSL:
Sample received,
Aliquot for DNA generated and stored
Shipped to Hutch

Fred Hutch:
DNA Extracted
Sample sent to CSL

CSL:
Sample received in freezer inventory
Manually generate list for assays

CSL:
Assays run
Data stored on shared drive

Issues:

Hard to know where a sample is in the process
Hard to retrieve data (need run date)

Assay Management within the Group: how to track and streamline workflow?

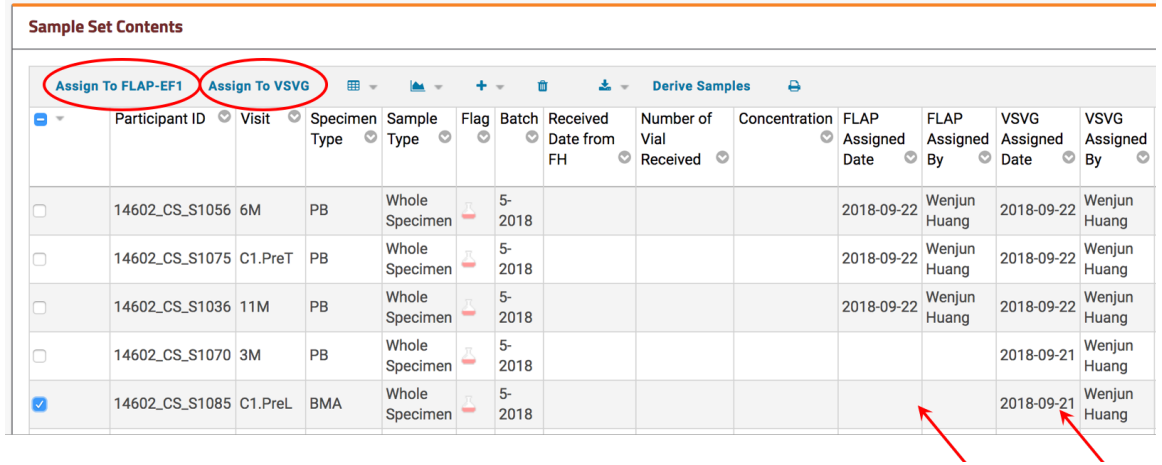
CSL:
DNA Sample Record Tracking

File Watcher Module picks up files from Fred Hutch and integrate the internal and external records

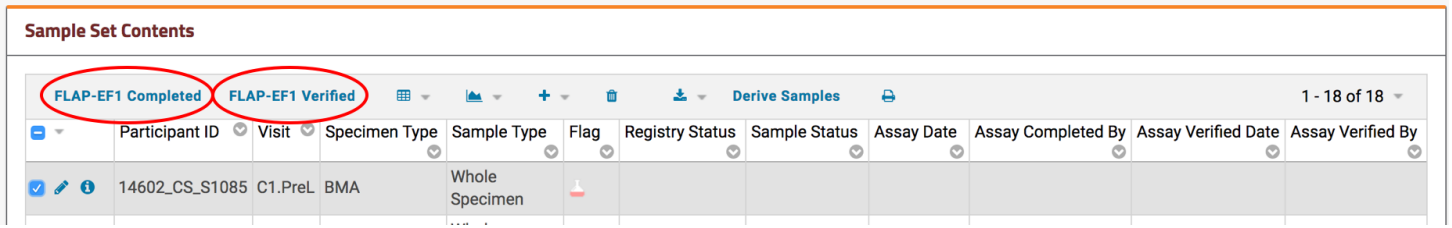
File Drop
(File Content Module)

Fred Hutch:
DNA Sample Process Record

Assign sample to various assay queues (Sample Sets)



Date, complete, and verify assay results from assay queues



Study Folder Data Reports

Study Folders – Sharing Assay Data

Correlative Studies | Studies

Overview | Primary Report | Detailed Report | Participants | Clinical and Assay Data | Manage

PLAT-03

PLAT-03 general information

Links to Standard Reports

IND/DSMB

PLAT-02 D10/D14 ratio

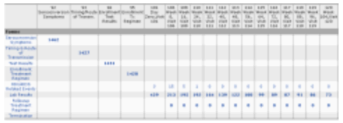
Limit of detection for EGFRt-CD19 CAR T cells

Panel	PB	BMA	CSF	Percent EGFRt+ of
HEL V01	0.02	0.02	0.83	Lymph

Study Overview

Investigator: Colleen Annesley

PLAT-03 tracks data in 53 datasets over 310 visits. Data is present for 50 Participants.

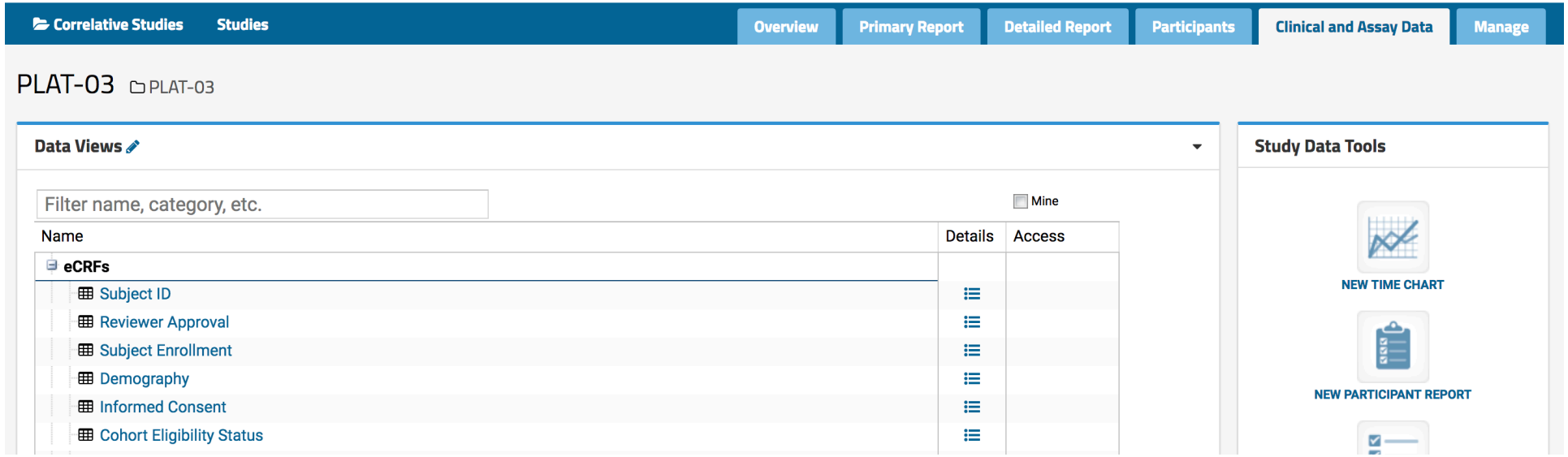


STUDY NAVIGATOR

MANAGE STUDY

MANAGE FILES

Study Folders – Sharing Assay Data
Using APIs to integrate eCRFS into datasets



Achievements:

Labkey developed integration for Medidata and REDCap

Addition of UI for field selection for each CRF

Lessons learned:

Devil is in the detail – design of eCRF is critical

Data entry can be an issue (missing data)

QC needed

DATSTAT

REDCap
Research Electronic Data Capture

medidata

Study Folders – Sharing Assay Data
Custom Reports to Highlight Key Information

Primary Report

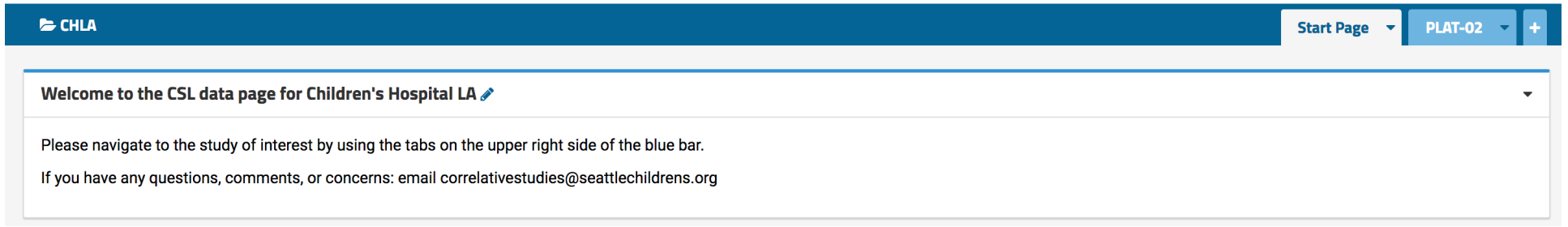
1 - 100 of 133

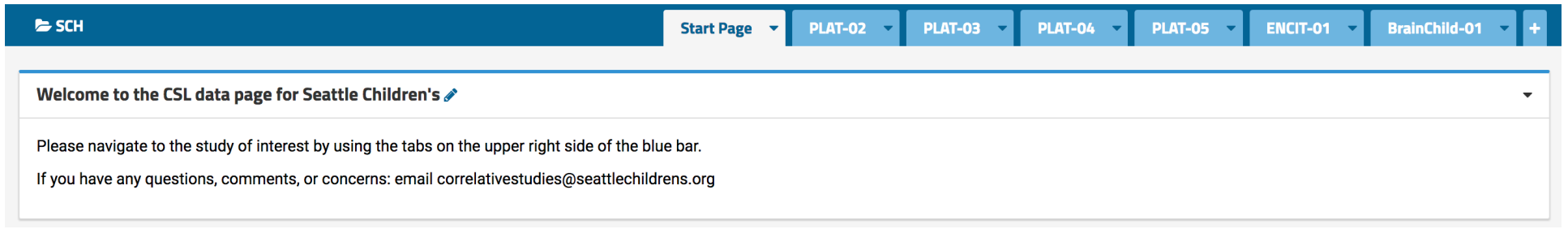
Participant Id	Visit Description	PB CD3/EGFRt+%	BMA CD3/EGFRt+%	CSF CD3/EGFRt+%	PB CD3/TAPC+%	BMA CD3/TAPC+%	CSF CD3/TAPC+%	PB Lymph/CD19+%	BMA Lymph/CD19+%	CSF Lymph/CD19+%	EGFRt detected in PB/BMA	CD19 detected in PB/BMA	Sample Quality Flag
152_CS_S004	C1.T4.D0	0.16			0.0			0.0			Yes	No	
152_CS_S006	C1.T2.D3	0.01			0.85			0.24			No	No	
152_CS_S005	C1.T2.D21	0.3			0.0			0.0			Yes	No	
152_CS_S001	9M	0.03			0.01			0.0			Yes	No	
152_CS_S006	C1.T2.D1	0.03			0.25			0.09			Yes	No	
152_CS_S006	C1.D63	0.01	0.0		0.02	0.0		0.05	38.23		No	Yes	

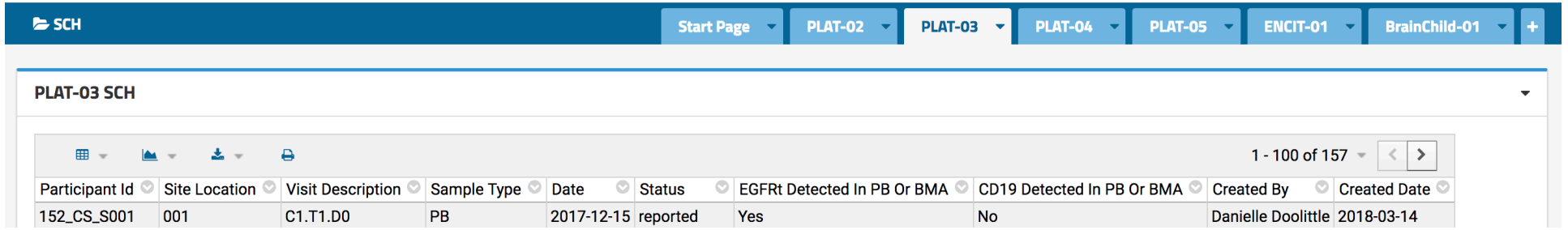
EGFRt and CD19 Detected at Scheduled Visits After Most Recent T-Cell Infusion

			PreL		PreT		D10		D14		D21		D63		T1.D-2		T1.D0		T1.D1		T1.D3		T1.D7		
Patient ID	Site Location	Cohort	EGFRt	CD19+	EGFRt	CD19+	EGFRt	CD19+	EGFRt	CD19+	EGFRt	CD19+	EGFRt	CD19+	EGFRt	CD19+	EGFRt	CD19+	EGFRt	CD19+	EGFRt	CD19+	EGFRt	CD19+	
152_CS_S001	001	A			No	Yes	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Y
152_CS_S002	001	B	Unknown	Unknown	No	No	No	Yes																	
152_CS_S003	001	A			No	No	Yes	No	Yes	No	Yes	No	Yes	Yes			Yes	No	Yes	No	Yes	No	No	No	Y
152_CS_S004	001	A			No	Yes	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Y
152_CS_S005	001	A			No	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Y
152_CS_S006	001	A			No	Yes	Yes	No	Yes	No	Yes	No	No	Yes	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	N
152_CS_S007	001	B									Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	N

Site Reports: Giving clinical sites access to site-specific information







Manuscript “studies”: a playground for analysis

Correlative Studies Studies

Immunobiology manuscript Immunobiolo

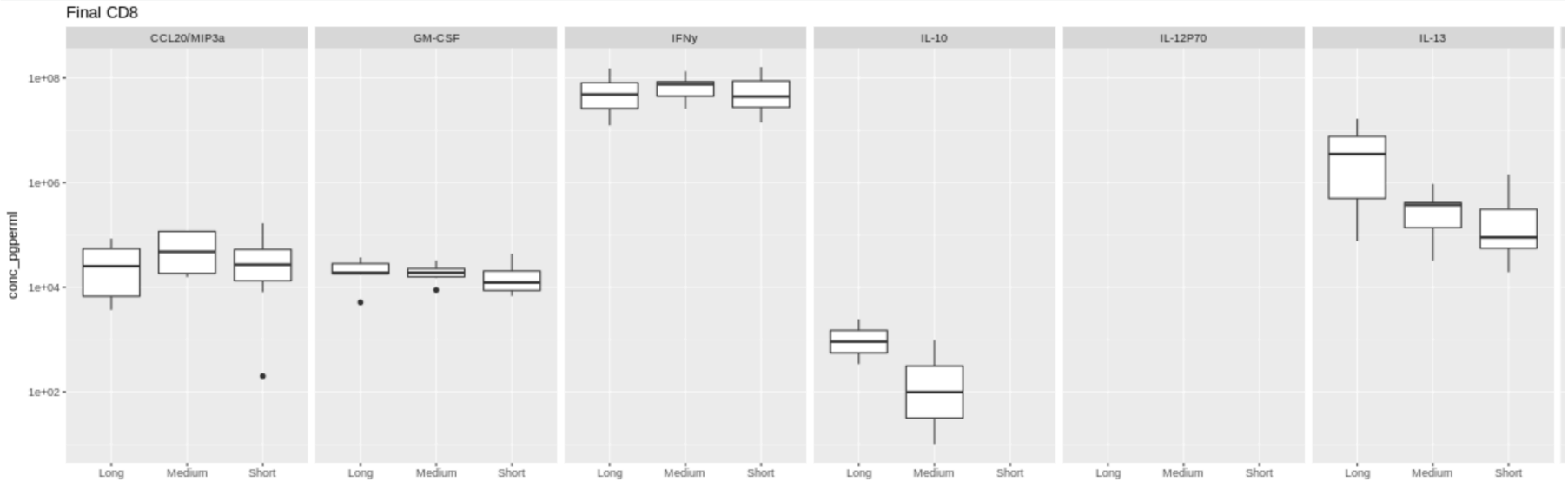
Data Views

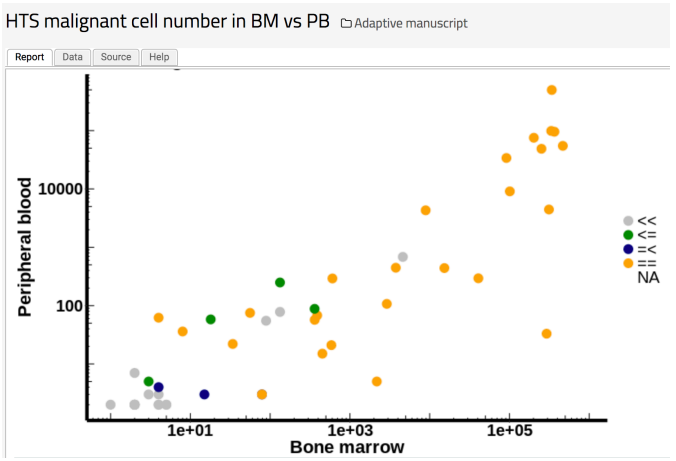
Filter name, category, etc.

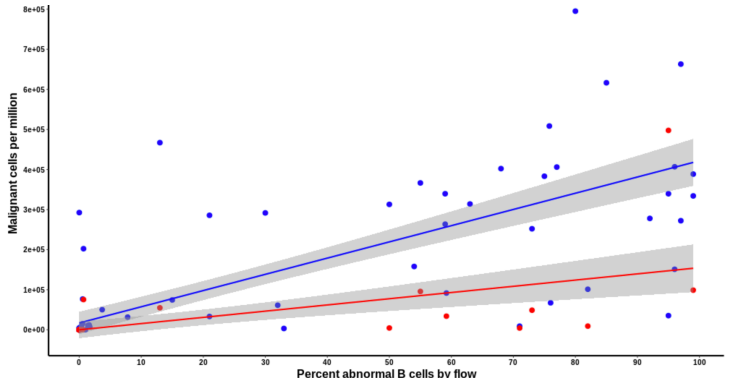
Name

- Uncategorized
  - CR/NoCR Cytokines
  - Final Product Staining
  - Ex vivo basics
  - Ex Vivo D10/D14
  - Th17 luminex BG
  - Ex vivo CD8
  - Cytokines by subject group
  - Ex vivo CD4
  - Stem V01
  - Exh V01
  - Exh V00
  - Stem V00
  - Th V01
  - TcL V00 V01
  - ICCS V01
  - ICCS V00
  - CRA
  - Jule_CSF

Image output







Conclusions

What we've learnt

- Design data with LabKey in mind
- Quality control is an essential step of the process
- Out-of-the-box does not mean ready to use
- You get out what you put in

Moving forward

- Expand use of sample sets for other assays
- Find a way to move files other than excel
- Develop our SDI board
- Create more user-friendly pages for people to explore data

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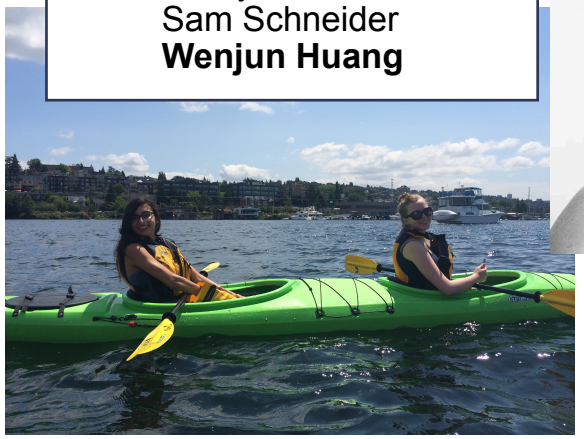
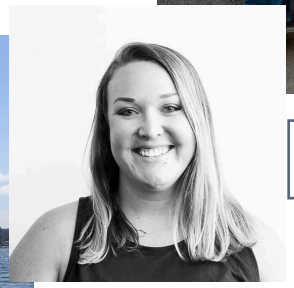




Immunotherapy Integration Hub

Michael Jensen
Julie Park
Rebecca Gardner

Labkey

Avital Sadot
Jon Yoon
Karl Lum
Kevin Krouse
Brad Holland

Patients and Families

ben towne foundation
pediatric cancer research

Life Sciences
DISCOVERY FUND

STRONG AGAINST CANCER

St. Baldrick's FOUNDATION

STAND UP TO CANCER

Questions?

Why Immunotherapy?

Chemotherapy

- Long treatment (2-3 years)
- High risk of off-target side effects
- High toxicity
- Cannot always eliminate minimal residual disease (MRD)
- Risk of relapse

Immunotherapy

- Short treatment
- More targeted approach
- Less toxic?
- May eliminate MRD
- Reduced risk of relapse?

QC - programmatic checks

Research reports

SpecimenRegistryDashboard

Hello olivia finney, Welcome to the CSL Specimen Registry Dashboard!

Run this ETL job to update this dashboard

Name	Source Module	Schedule	Enabled	Last Status	Last Successful Run	Last Checked	Run	Reset	Last Transform Run Log Error
Sample Status List Generator	SpecimenRegistry	0 0 12 ? * MON-FRI	☑	COMPLETE	2018-09-19	2018-09-19	Run Now	Reset State...	

View Processed Jobs

Specimen record from the past day:

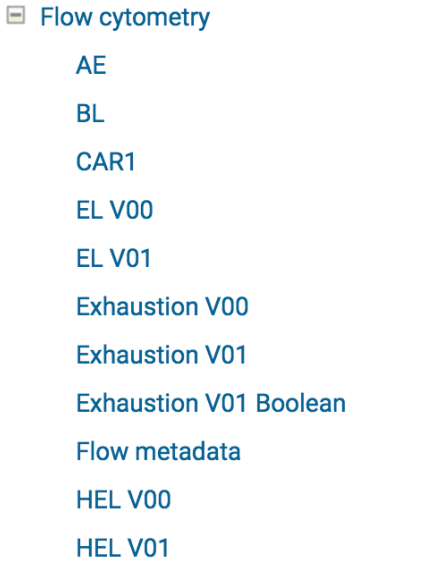
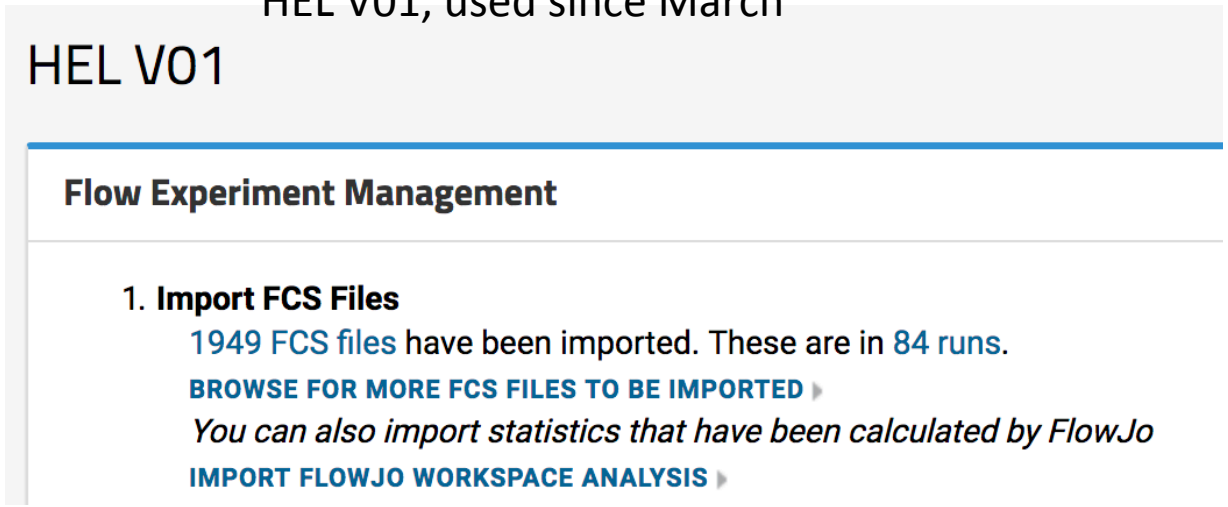
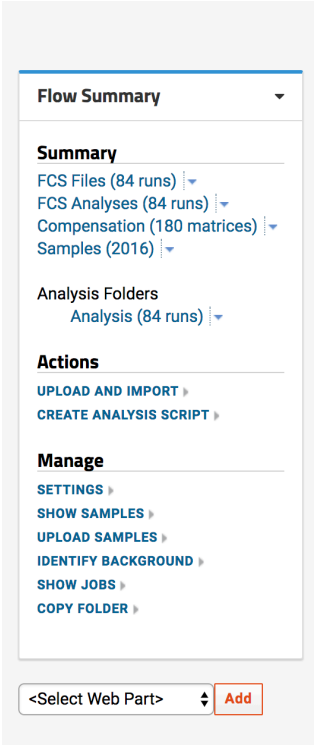
1 - 5 of 5

CoordinateCenterView

Participant ID	Visit Description	Specimen Type	Draw Date Origin	Draw Time Origin	Draw City Origin	Draw State Origin	Draw Country Origin
00961_CS_S003	C1.6M	PB	2018-09-18				
14602_CS_S1101	C1.PreL	BMA	2018-09-19				
152_CS_S004	C1.T4.D1	PB	2018-09-18				
00680_CS_S001	AC1	CSF	2018-09-18				
14602_CS_S1101	C1.PreL	CSF	2018-09-18				

Organizing FCS files is a bottleneck

- Import data to individual folders
  - One panel per folder
  - 3 analyses a week – 3 workspaces and corresponding files/weel
- Use ETL to push sample descriptions from specimen survey



HEL V01, used since March