

THAMES AUDIT GROUP

Audit of Fluids

13 Jan 2023

Danni Fan

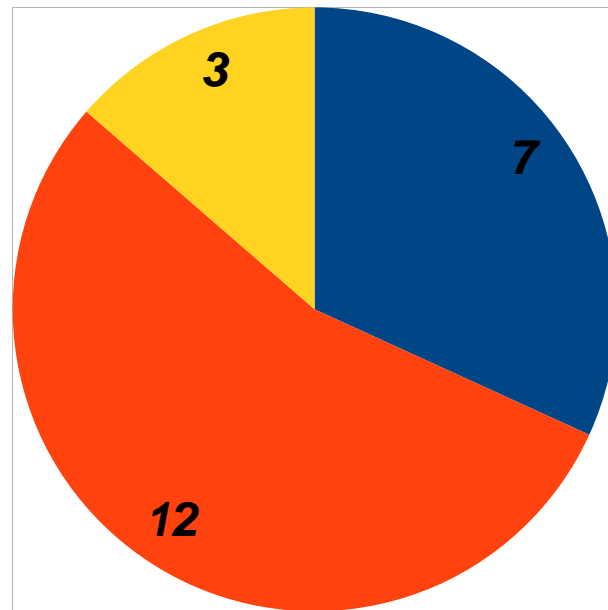
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Fluid Audit 2022

Participants n=14



■ Teaching Hospital

■ DGH

■ Specialist

Part 3. General questions on fluids

Section A - Requesting

- **[Q1] Trust guidelines for fluid testing available:** 3 labs

One of the guidelines was written by the clinical teams, which recommended inappropriate tests on particular types of fluid.

- **[Q2a] CSF test codes:**

12 labs have separate CSF test codes in LIMS

- **[Q2b] Fluid test codes:**

Most labs have a set of fluid test codes which can be used for any non-CSF fluid.

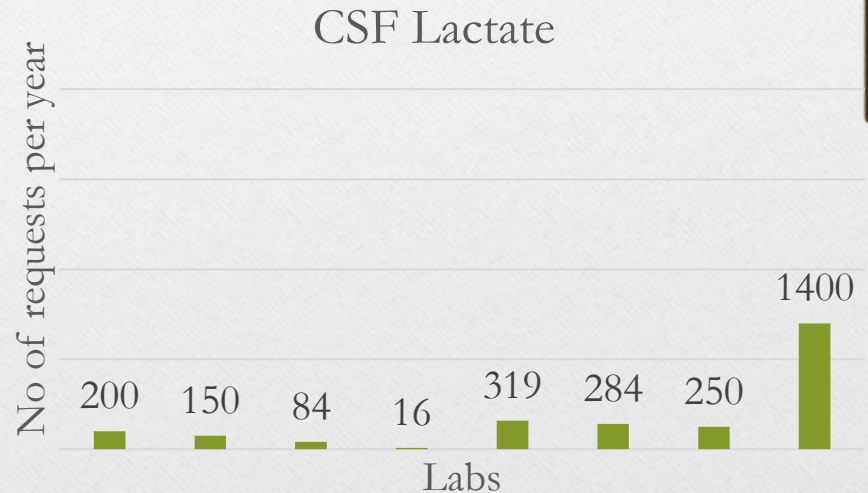
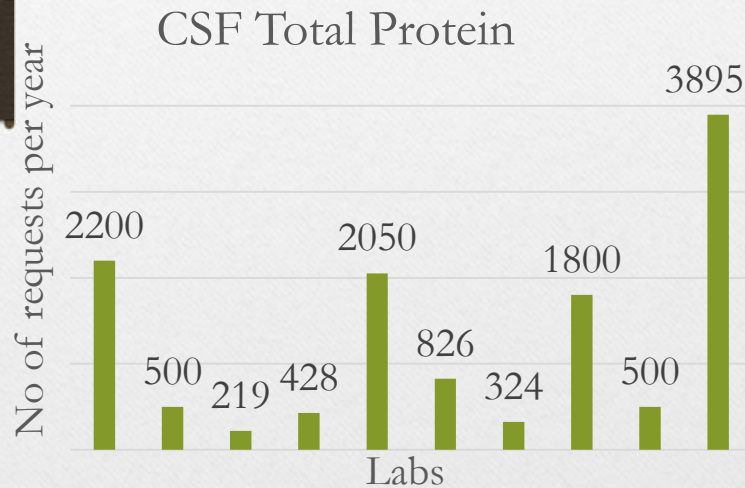
1 lab has some specific test codes for

- ascitic fluid (PROT,LDH,GLU)
- dialysis fluid, pancreatic cyst fluid (CEA, CA199,CA153)
- pleural fluid (CHOL,PROT,LDH,GLU,TRIG).

• [Q3] Tests available and workload

CSF routine test:

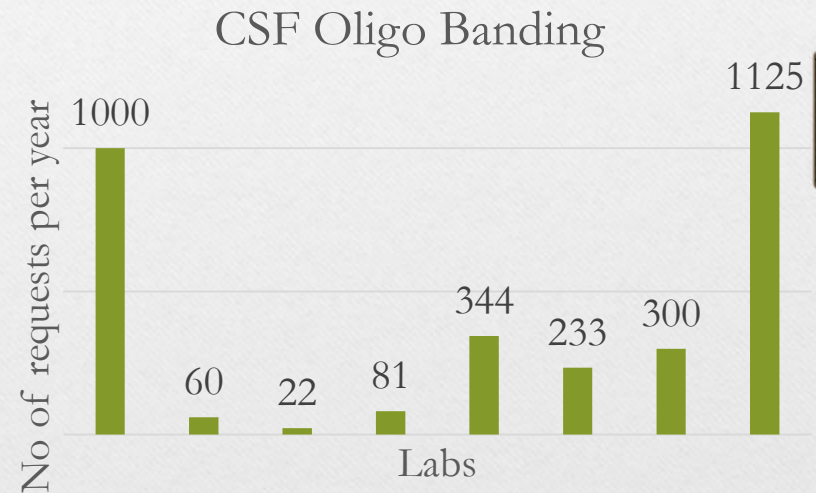
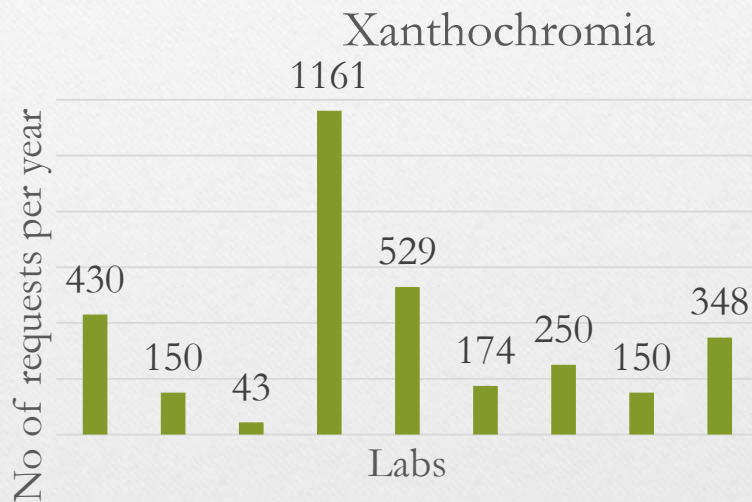
- CSF Protein & Glucose (14 labs)
- CSF Lactate (12 labs, of which 1 lab referring)



• [Q3] Tests available and workload

CSF special test:

- CSF Xanthochromia: (14 labs, of which 5 labs referring)
- CSF Oligo Banding: (11 labs, of which 8 labs referring)

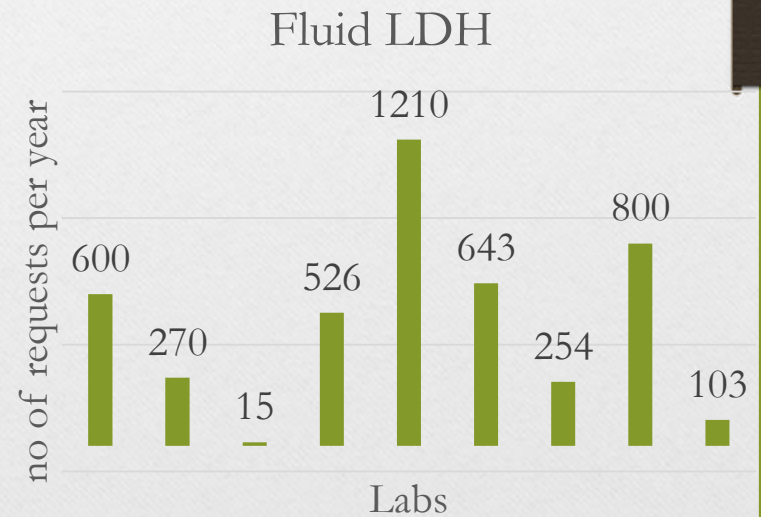
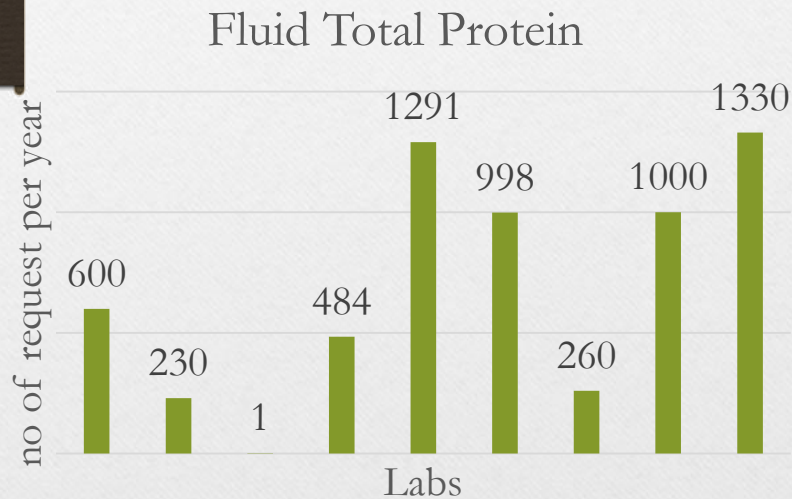


- L-CSF Tumour Markers (AFP, CEA, hCG), LDH, Ferritin : 2 labs
- Other CSF special tests are not covered here

• [Q3] Tests available and workload

Available non-CSF fluid routine tests:

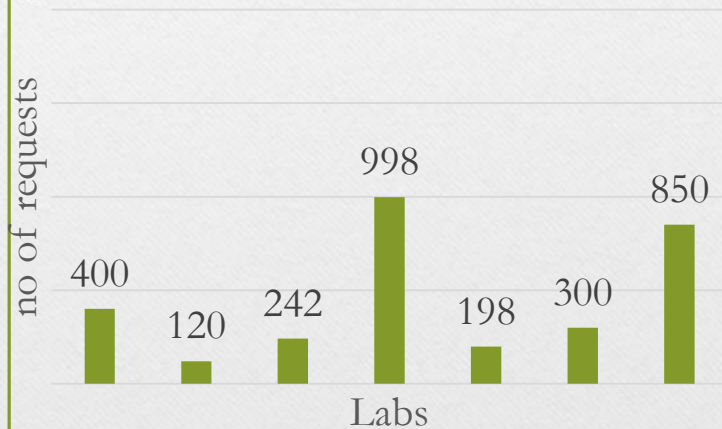
- Fluid Total protein (13 labs)
- Fluid LDH (13 labs)



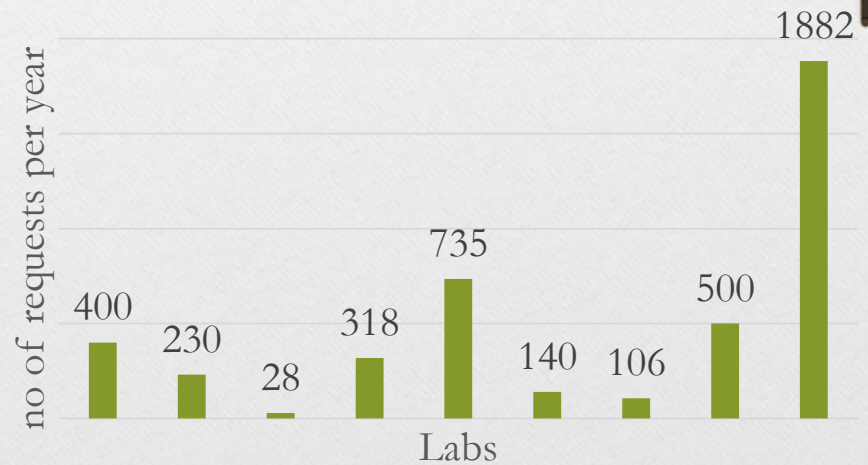
• [Q3] Tests available and workload

- Fluid Albumin (9 labs); serum-ascites albumin gradient(SAAG) (3 labs)
- Fluid Glucose (14 labs)
- Fluid Lactate (7 labs, up to 7 requests per year)

Fluid Albumin

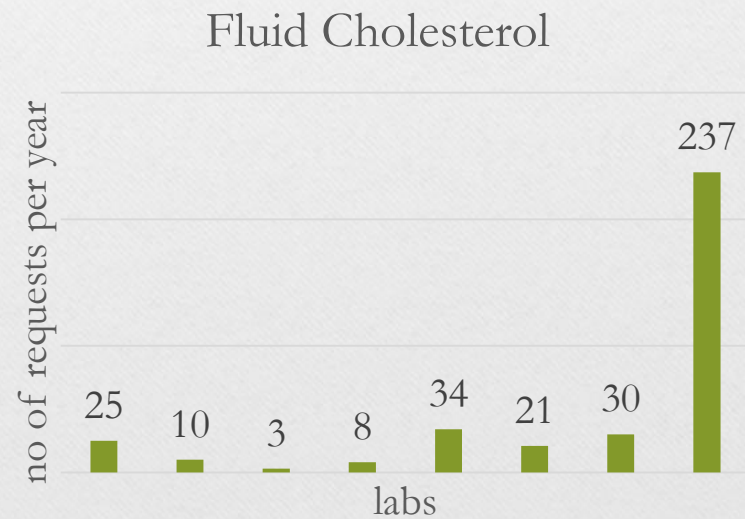
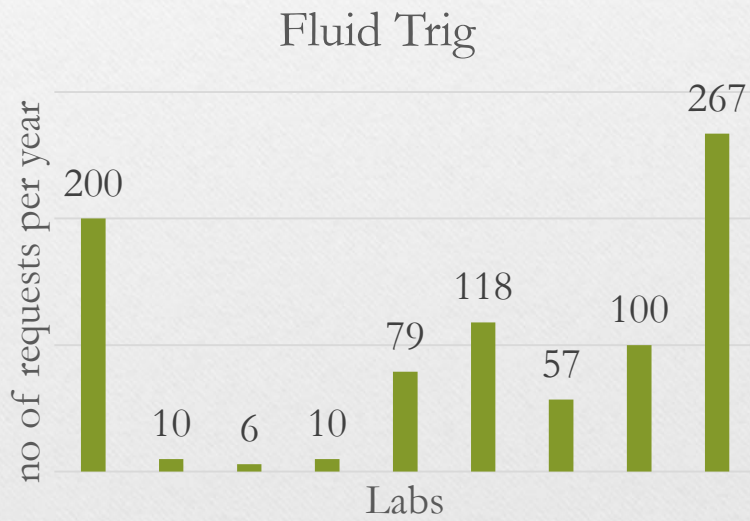


Fluid Glucose



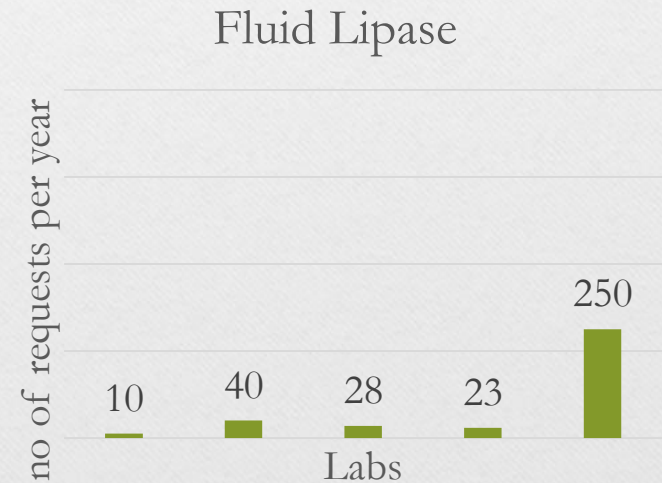
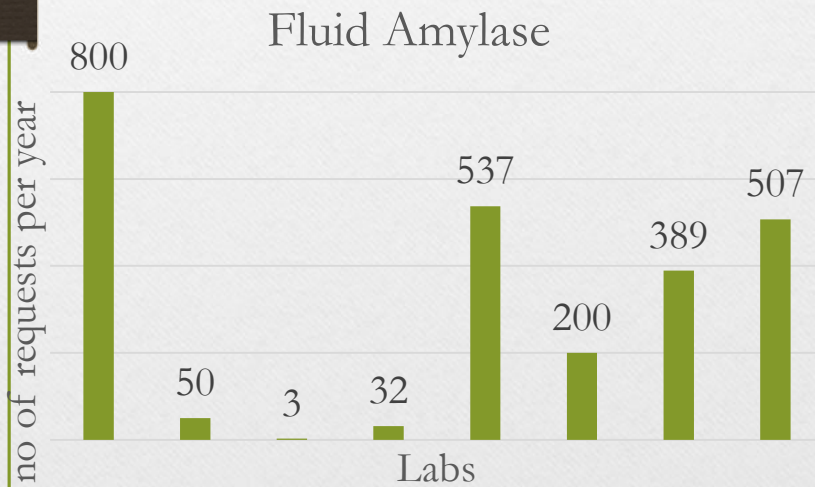
- [Q3] Tests available and workload

- Triglyceride (13 labs)
- Cholesterol (11 labs)
- Chylomicra (2 labs, up to 51 requests per year)



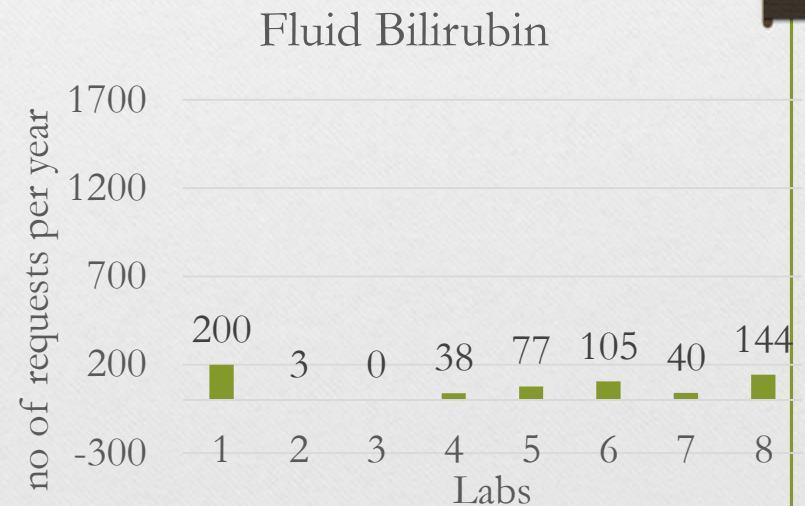
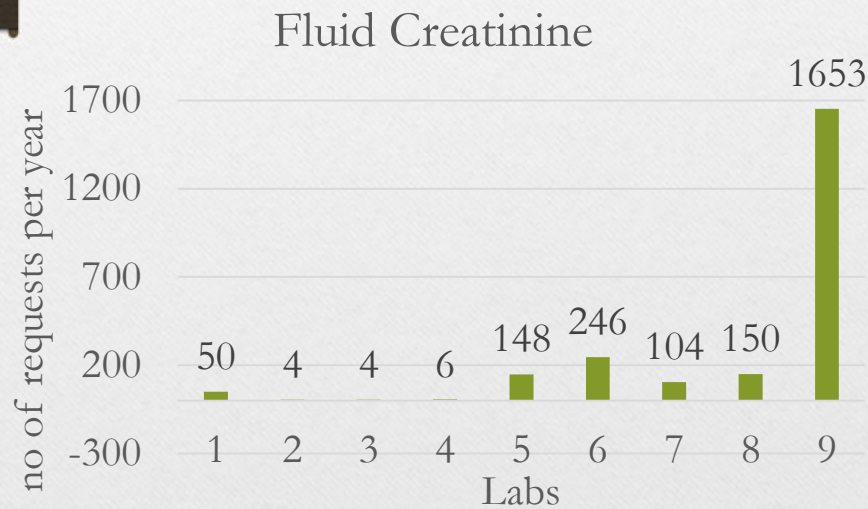
- [Q3] Tests available and workload

- Fluid Amylase (12 labs, of which 1 lab referral)
(1 lab mentioned offer to salivary fluid))
- Fluid Lipase (5 labs)



• [Q3] Tests available and workload

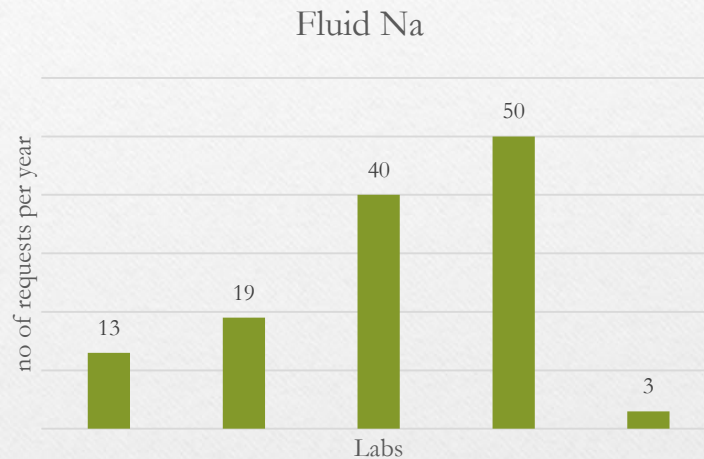
- Fluid Creatinine (14 labs)
- Fluid Urea (14 labs)
- Fluid Bilirubin (13 labs)



• [Q3] Tests available and workload

Available non-CSF fluid electrolytes:

- Fluid Na (5 labs)



- Fluid K (4 labs, up to 38 requests per year)
- Fluid Ca (3 labs, up to 51 requests per year)
- Fluid Osmolality (2 labs, up to 9 requests per year)
- Fluid P (1 lab, up to 3 requests per year)
- Fluid Cl (1 lab, up to 3 requests per year)

- [Q3] Tests available and workload

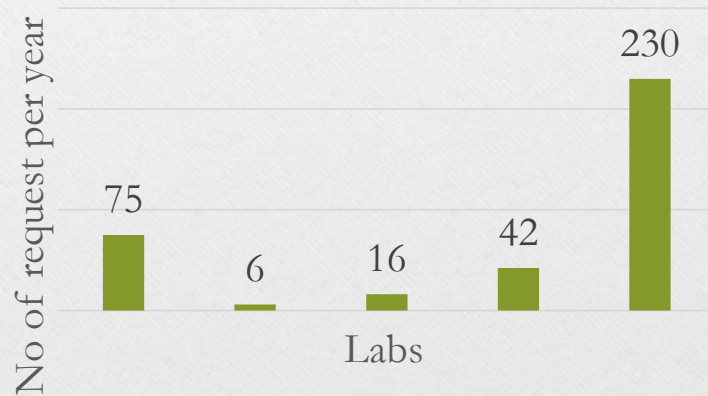
- Fluid PH (5 labs, up to 212 requests per year)
- Fluid Urate (4 labs, up to 22 requests per year)
- Fluid Adenosine deaminase (4 labs, up to 20 requests per year, referring)
- Fluid ALT (2 lab, up to 51 requests per year)
- Fluid ALP (1 lab)
- Fluid Chromium, Cobalt & Titanium (1 lab)

• [Q3] Tests available and workload

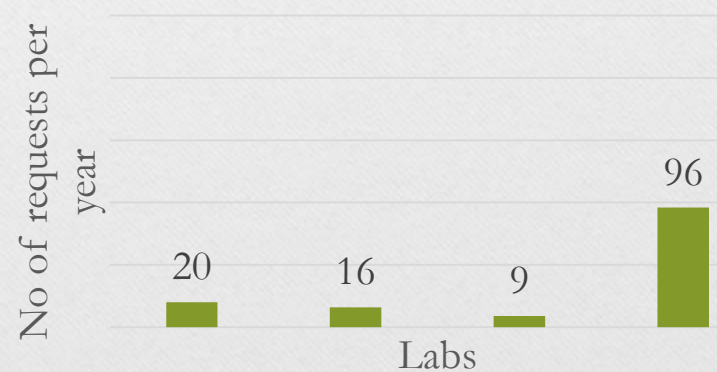
Available non-CSF fluid tumour markers

- CEA (7 labs)
- CA199 (6 labs)
- AFP (6 labs, up to 130 requests per year)
- CA125 (3 labs, up to 10 requests per year)
- CA153 (2 labs, up to 8 requests per year),
- PSA & hCG (2 labs, up to 51 requests per year)

Fluid CEA



Fluid CA199



Section B - Operation and Analysis

- **[Q4] Fluid samples spun prior to analysis** - All labs
- **[Q5] Haemolysis, Icteric and Lipaemic (HIL) index**
 - 2 labs use HIL indices for CSF and 5 labs use HIL indices for non-CSF fluids, based on manufacturer's guidelines (if the fluid test does not have its specific cut-offs, use the one for its corresponding serum test)

- 8 labs visually inspect the samples

If samples are visually grossly haemolysed/lipaemic

- a) For CSF protein, glucose or lactate

6 labs would not run.

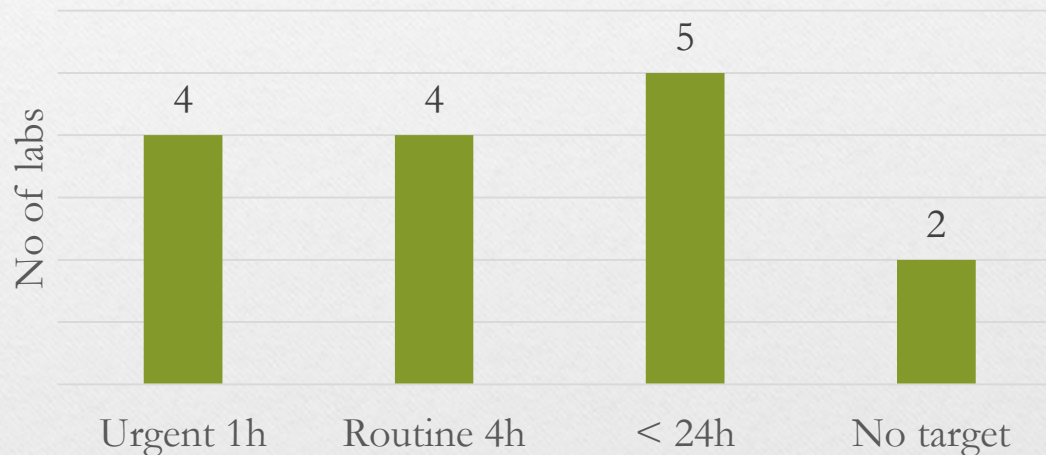
2 lab would always analyse but would add caveat comment to report.

- b) For CSF Xanthochromia, all labs would always analyse the sample

Section B - Operation and Analysis

- **[Q6] How frequent is the fluid analysis run?** All labs run fluid tests as required through the day, expect specialised CSF testing, such as oligo tested in batches
- **[Q7] Target Turnaround time (TAT)**
 - For CSF Glucose, Protein and LDH

TAT for CSF Glu, Protein and LDH



- For CSF Xanth: 1-2 days
- For CSF referred test such as Oligo: 10-16 days

Section B - Operation and Analysis

- **[Q8] Calculation setup in LIMS for any type of fluid analysis**
 - 2 labs: SAAG
- **[Q9] Analytical Platforms**
 - 8 labs : the serum version of the assays are used for all other fluid types, apart from
 - 4 labs use urine protein assay for CSF protein
 - 2 labs use total protein urine/CSF assay with a specific CSF application.
 - 1 lab use CSF protein & glucose that are specific CSF assays
 - 13 labs: use assays provided by the same manufacture of the platform

Section B - Operation and Analysis

- [Q10 & Q21] IQC

CSF routine biochem tests	3 labs confirmed the use of dedicated CSF IQC
CSF Xanth	All labs use in house self-made IQC Most protocols are complicated, involving diluting and mixing multiple QCs. The most simple protocol: Technopath Multichem S Level 1 diluted 1:1 with H ₂ O
Fluid non-CSF routine biochem tests	12 labs confirmed the use of > 2 levels of IQC

Section B - Operation and Analysis

- [Q11] EQA

CSF	13 labs: UKNEQAS (IMMQAS) CSF Proteins and Biochemistry Scheme 7 labs: UKNEQAS (IMMQAS) CSF haem pigments 3 labs: UKNEQAS (IMMQAS) CSF for oligo bands 1 lab: UKNEQAS (IMMQAS) CSF beta 2 transferrin
Fluid routine biochem	12 labs: UKNEQAS fluids

- [Q12] In scope for UKAS

CSF Protein 11 labs CSF Glu : 10 labs CSF Lactate: 9 labs
Xanth: 3 labs

Fluid routine biochem tests: 4 labs
(3 labs are planning/in the process of applying)

Section C - Interpretation and Reporting

- **[Q13] Reporting:**

4 labs report appearance for CSF

3 labs report appearance for other fluids

Inc. colour, turbidity & if blood stained pre- and post- centrifugation, pellet appearance e.g dark yellow clear fluid with small cell pellet post-centrifugation

- **[Q14] Auto-validation :**

8 labs auto-validate CSF routine biochem

9 labs auto-validate other fluids

Section C - Interpretation and Reporting

- **[Q15] Samples sent to a referral lab for confirmation in suspicion of interference**

1 lab occasionally send CSF xanthochromia samples to referral laboratory if abnormal chromatogram

- **[Q16] Test verification:**

11 labs did verification studies for routine biochem CSF tests, including precision, method comparison, EQA

4 labs did verification studies on routine tests on fluids, 2 of which did full validation, including linearity, spiking, comparison with other labs & manufacturers

Part 4. CSF

Section A – CSF Requesting

- [Q18] Sample requirement

CSF protein	9 labs: plain 2 labs: plain; not blood stained 1 lab : plain; not blood stained; must be received within 2 h
CSF Glucose & Lactate	8 labs: fluoride oxalate, 3 labs: fluoride oxalate, but plain tubes also accepted (1 lab stated plain needs to be analysed immediately) 1 lab offers lactate to paediatric patients only
Xanthochromia	2 labs: plain 5 labs: plain, protected from light 3 labs: plain, protected from light + paired serum
CSF oligoclonal bands	10 labs: plain universal + paired serum 2 labs: plain

Section A - CSF Requesting

- [Q18] Vetting

4 labs would vet send away CSF tests e.g. CSF Oligo

Vetting criteria e.g.

- a) Xanth: Only for ?, SAH, if CT head neg and LP >12h post onset of symptoms.
- b) Oligo banding: routinely available for ? MS and neurology requests.

Scenario 1: If the sample for xanthochromia test is not protected from light, would your laboratory still run the sample?

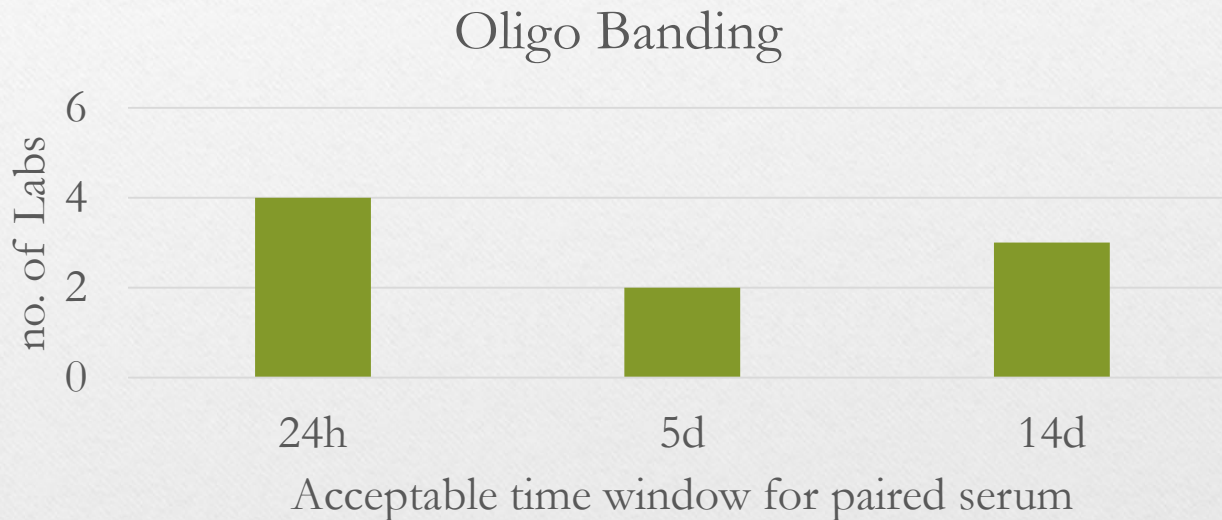
All labs said yes and most labs would report with a comment 'not protected from light. Interpret results with caution.'

BUT only 2 labs specified if the result negative, state: '**SAH not excluded**'

Section A - CSF Requesting

Scenario 2: If there is no paired serum sample for the test for CSF oligoclonal bands, how would your laboratory proceed?

11 labs would still send the oligo test.



Section A - Requesting

- [Q19] Trust guidelines for the collection of CSF for xanthochromia

7 labs have trust guidelines to cover

- when to collect (e.g. time scale in relation to headache, CT negative)
- how to collect (e.g. the 4th tube and least blood stained)
- how to transport the sample to lab (e.g. in foil wrap or brown envelope)

Section B - Operation and Analysis

- [Q22] Special precautions for handling CSF given the Covid guidelines

10 labs: CSF is considered low risk, process as normal with appropriate PPE
2 of which stated that initially not accepting CSF right at the start of the pandemic

3 labs: CSF is prepared in local microbiological safety cabinet

If samples which have a high index of suspicion or known for Covid-19:

All labs will proceed except 1 lab who would hold the tests – DB to discuss with the requesting clinician and only proceed if clinically indicated.

Section C - Interpretation and Reporting

- [Q23] Reference ranges

Fluid Test	Lab no.	RR in use	Analyser Platform	
CSF Protein	0.25 - 0.45	g/L	2 labs Roche	
	0 - 0.44	g/L	3 labs Roche	
	150-450	mg/L	Adults	1 lab Roche (<u>Kit insert</u>)
	400-1200	mg/L	Newborn	
	200-800	mg/L	<1month	
	0.4 - 1.2	g/L	Neonate:	1 lab Roche & Siemens (Tietz)
	0.15 - 0.45	g/L	>1 month:	
	0.15 - 0.40	g/L		1 lab Abbott Alinity (<u>Kit insert</u>)
	0.15- 0.45	g/L	>10 years	1 lab Abbott Alinity
	0.15- 0.80	g/L	<10 years	(<u>NWLP harmonisation</u>)
0.15- 0.45	g/L		1 lab Abbott Architect (kit insert)	
0.12- 0.60	g/L		1 lab Ortho Clinical Diagnostics Vitros 5600 (<u>Source IFU</u>)	

Section C - Interpretation and Reporting

- [Q23] Reference ranges

Fluid Test	Lab no. RR in use	Analyser Platform
CSF	No range quoted	4 labs Roche
Glucose	3.3-4.4 mmol/L Child	2 labs Roche (Manufacturer)
	2.2-3.9 mmol/L Adult	(Only 1 lab specified child is defined as < 16y)
	3.3-4.4 mmol/L Child	1 lab Abbott Alinity (Kit insert)
	2.2-3.9 mmol/L Adult	(definition for child - unclear)
	1.5-4.7 mmol/L < 4 weeks	1 lab Abbott Alinity
	2.2-3.9 mmol/L > 4 weeks	<u>(NWLP harmonisation)</u>
	2.2- 3.3 mmol/L (or 60% of plasma glucose)	1 lab Abbott Architect (Kit insert)
	2.2-3.9 mmol/L	1 lab Ortho Clinical Diagnostics Vitros 5600 <u>(Source IFU)</u>

Liturautre

The study by W Leen et al 2012 concluded that lower limit of RR for CSF glucose is down to 1.9 mmol/L in infant up to 6 month

Section C - Interpretation and Reporting

- [Q23] Reference ranges

Fluid Test	Lab no. RR in use	Analyser Platform
CSF Lactate	1.1 - 2.4 mmol/L	3 labs Roche
	1.00-2.00 mmol/L	1 lab Roche
	0.7 -2.00 mmol/L	1 lab Roche
	1.1 - 2.8 mmol/L	1 lab Roche (Kit insert)
	1.1 - 6.7 mmol/L < 3 days	1 lab Roche & Siemens (Manufacturer)
	1.1 - 4.4 mmol/L < 11 days	
	1.1 – 2.8 mmol/L < 16 years	
	1.2 - 2.4 mmol/L Adults	
	0.9 - 2.5 mmol/L < 4 weeks	1 lab Abbott Alinity (W Leen et al 2012)
	0.9 - 2.2 mmol/L 4 weeks-1 year	
	1.0 - 2.1 mmol/L 1-10 years	
	1.2 - 2.7 mmol/L > 10 years	
	1.0 - 2.9 mmol/L	1 lab Abbott Alinity (<u>NWLP harmonisation</u>)
	<2.8 mmol/L	1 lab Abbott Architect (Historical)

Section C - Interpretation and Reporting

- [Q24] Interpretation comments :

8 labs auto-validate CSF routine biochem

Test	Some example of auto-comments
CSF glucose	In Adults, CSF Glucose is typically 60 - 80% of that in a paired serum sample. In bacterial meningitis, decreased CSF glucose may be seen
	Please interpret CSF glucose in association with a paired plasma glucose

Some lab hold certain abnormal results for manual authorisation

e.g. CSF total protein <0.15 or >0.45 g/L. CSF glucose <2.2 or >16 mmol/L

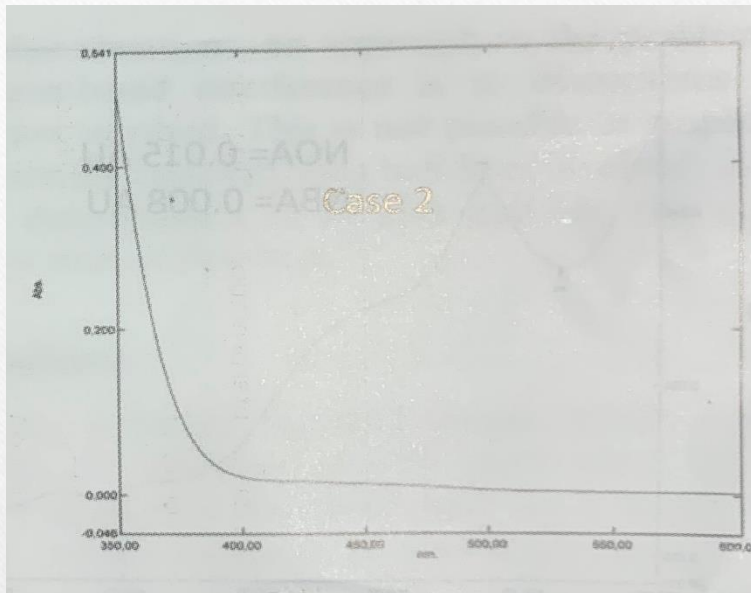
Section C - Interpretation and Reporting

- [Q25] Interpretation software to analyse the Xanthochromia trace automatically
 - All labs have (i.e. 9 labs who perform this test in-house)

- [Q26] a set of coded comments in your LIMS to automatically input the interpretation of Xanthochromia trace to the final reports:
 - 8 labs have
 - 1 lab need manually typing

Section C - Interpretation and Reporting

Scenario 3: How would you report the Xanthochromia trace below ?



6 labs reported as:

‘No evidence to support SAH’

Of which 4 labs mentioned would re-run to confirm the trace either in a quartz cuvette or with a fresh blank solution

1 lab: ‘strong absorbance in the UV range masking ability to detect oxyhaemoglobin and bilirubin. ?patient undergone procedure using **contrast dye** or similar.’

2 labs: ‘cannot interpret the scan due to possible **antibiotic interference.**’

Section C - Interpretation and Reporting

- **[Q27] Document date and time since the start of the onset symptom**
 - 5 labs: info required to be entered on the test ordering page
- **[Q28] comment on the time window for the Xanth results to be valid:**
 - 7 labs have
(6 of which have auto-comments:
all have >12 h but <14 d, except 1 lab stated >12 h but <10 d)
- **[Q29] potential net bilirubin absorbance lowering effect of some antibiotics such as tetracyclines and doxycycline**
 - 9 labs: not aware
 - 2 labs: validate results with a comment ‘ possible false negative in light of antibiotic use (i.e. tetracycline, doxycycline)’
 - 2 labs: updating the SOP with above information
 - 1 lab: aware , but no procedures in place yet.

Part 4. Pleural Fluid

Section A - Requesting

- [Q30] Sample requirement

Fluid glucose	6 labs: fluoride oxalate 2 labs: plain universal + paired serum
Fluid protein and other routine tests	5 labs: plain universal 2 labs: plain universal + paired serum 2 labs: lithium heparin (green)
Chromium, Cobalt & Titanium	1 lab: K2-EDTA Vacutainer (dark blue)

Section A - Requesting

- **[Q30] Vetting**
2 labs mentioned procedures in place for vetting
- **[Q31] Procedures in place to prevent an inappropriate test on fluid**
1 lab - through vetting
- **[Q32] Pleural fluid total protein and LDH**
12 labs do both tests together
1 lab do cascade testing
- **[Q33] Tumour markers**
7 labs have tumour markers available
 - 4 labs CEA, CA199, AFP
 - 1 lab CEA
 - 1 lab CEA, CA199, CA125, CA153, hCG, AFP
 - 1 lab CEA, CA199, CA125, CA153, hCG, PSA
- **[Q34] Platforms** (similar to those mentioned in CSF section)

Section B - Operation and Analysis

- [Q35] Special precautions for handling pleural fluids given the Covid guidelines

8 labs: pleural fluid is considered high risk, of which

5 labs not accepted on known COVID

3 labs process samples in microbiological safety cabinet

1 lab: will only accept serum tubes with pleural fluid

3 labs confirmed the same rules applies to other non-CSF fluids

3 labs mentioned that the guidance has now been relaxed

Section C - Interpretation and Reporting

- **[Q36] Reference ranges**

All labs: no reference ranges are provided for fluids test except CSF

- **[Q37] Interpretive comments**

7 labs: auto-validated and up to requestors to interpret. Some labs attach an auto-comment 'assay not validated for fluid, interpret with caution'

1 lab: BMS/Clin Scient would write interpretive comments for all fluid tests

- **[Q38] Rules/tools in place to aid the interpretation of a transudate and exudate for pleural fluid**

No lab has anything set up in the LIMS.

- **[Q39] Need a paired serum sample for distinguishing a transudate and exudate for pleural fluid**

All labs do not need

1 lab would request this when needed.

Section C - Interpretation and Reporting

- [Q38] Cut-offs to distinguish between transudate and exudate for pleural fluid and what are the

3 lab mentioned **Light's criteria**:

1 lab uses cascade testing :

run total protein initially and only reflect LDH if total protein is in equivocal range (i.e. 25-35g/L)

PF < 25 g/L	transudative
PF > 35 g/L	exudative
PF 25-35 g/L & LDH U/L < 147	transudative
PF 25-35 g/L & LDH U/L > 147	exudative

Section C - Interpretation and Reporting

Scenario 4: In patients with raised fluid triglycerides and suspected chylothorax, would you add a fluid cholesterol to rule out pseudochylothorax?

10 lab: Up to requestor to interpret
(of which 1 lab: do not offer fluid cholesterol in the trust)

3 labs: would add a fluid cholesterol

Comments include:

'Pleural fluid triglyceride levels >1.24 mmol/L with a cholesterol <5.18 mmol/L is diagnostic of chylothorax.'

If triglycerides = <0.56 mmol/L, chylothorax is excluded.

Part 4. Ascitic Fluid/Peritoneal Fluid

Section A - Requesting

- [Q41] Sample requirement
- [Q42] Procedures in place to prevent an inappropriate test on fluid
- [Q43] platform/analytical method
- [Q44] Reference ranges
- [Q45] Interpretive comments

– (similar to pleural fluid)

Section C - Interpretation and Reporting

- [Q46] Rules/tools in place to aid the interpretation of serum ascites albumin gradient (SAAG) analysis

2 labs have calculation set up in the LIMS, using $SAAG = (ALB) - (FALB)$

- [Q47] time window for the paired serum sample for SAAG

3 labs mentioned < 24h

- [Q47] Cut-offs for interpretation

Interpretation	Cut-offs SAAG
SAAG consistent with ascites caused by portal hypertension due to cirrhosis	2 lab: $\geq 11\text{g/L}$ (recommended)
	1 lab: $> 11\text{g/L}$
	1 lab: $> 12\text{g/L}$

Section C - Interpretation and Reporting

Scenario 5: If the SAAG calculation gives a negative value, how the result would be reported?

Most labs: do not provide calculation for SAAG

1 lab would reported as 0 g/L.

2 labs would reported as a negative value and comment appended

Scenario 6: What would your laboratory do if no paired serum sample was sent with the ascitic fluid for the SAAG analysis? What if no paired serum sample could be obtained?

Most labs: do not provide calculation for SAAG

4 labs would look up for serum samples 1 day old

If not sample obtained, would report 'unable to calculate SAAG due to lack of paired serum'

Part 4. Other type of fluids

Section A - Requesting

- **[Q49] Sample requirement and test available**

8 labs provide pericardial fluid, knee aspiration & drain fluid

Tests available on individual basis e.g.

- creatinine for drain fluids
- urea for drain fluids
- urine triglycerides for ?chyluria

1 lab mentioned would vet tests

- **[Q50] Fluid pH in your Trust**

6 labs provide fluid pH analysis in the trust, of which 4 in lab and 2 in wards on blood gas analysers.

Section C - Interpretation and Reporting

Scenario 7: If your laboratory receives a tumour marker request on any type of fluids, would the sample be rejected?

5 labs would bring attention to Duty Biochemist

2 labs certain tumour marker tests run automatically

1 lab (specialist cancer hospital) would perform any requests

2 labs: providing CSF tumour markers (e.g hCG, CEA, CA153, CA199, CA125, SCC, NSE and PSA), in one of which tests are vetted by the consultant chemical pathologist; analysed by an external laboratory and are reported with reference ranges and interpretative comments provided by the external laboratory.

Section C - Interpretation and Reporting

Scenario 8: If your laboratory received a fluid sample with unknown source, how would you book it in, what tests to be run and how to report the results?

4 labs would try to contact the requestor and find the source

8 labs would book in as unknown source reported and the specified tests would get done as requested

If no test requested, 2 labs would save the sample and 1 lab mentioned to add an albumin

Scenario 9: If your laboratory received a fluid sample with a deep brown colour, how would you proceed and would you still analyse the sample?

9 labs proceed to run the sample post centrifugation; reaction failures-not reported.

1 lab would reject

1 lab would run HIL and then decide

1 lab if the colour remains post spun -case by case decision

Conclusion

- Only 14 TAG laboratories that responded to the survey for fluid testing, with some laboratories collecting samples and sending them to referral laboratories for testing.
- Despite having a limited number of testing sites, the survey results reveal considerable variation in the pre-analytical, analytical, and post-analytical practices being used for these tests.
- The audit results may help individual laboratories determine how their processes differ from their peers and how they can adjust processes to align with the current best laboratory practices for fluid testing.
- The information revealed by this audit could provide insight into the practices in need of standardization. There is an need for reaching an agreement of best practices among the TAG laboratories.

Recommendations – draft only

- All laboratories should consider to introduce trust guidelines available for requesting biochemistry tests on fluids to avoid inappropriate requests. All laboratories should liaise with the clinical team and ensure trust clinical guidelines and clinical practice are in line with the laboratories guidelines.
- All laboratories should have protocols in place for both clinical and laboratory staff indicating sample requirement and handling procedures.
- Available fluid tests should be reviewed. The ones which are obsolete or not routinely available within clinical biochemistry should be removed from PAS and from LIMS, so that they are not requestable to avoid confusion to the service user and laboratory staff.

Recommendations – draft only

- Laboratories should ensure that appropriate internal quality control (IQC) and external quality assessment (EQA) procedures are in place.
- Laboratories should verify their fluid tests. Otherwise, test results must be reported with a comment stating test not verified and interpret with caution.
- Laboratories should be aware of their test's susceptibility to interference.

For instance:

- for xanthochromia test, strong absorbance of certain contrast dye or antibiotics in the UV range can mask the ability to detect oxyhaemoglobin and bilirubin, leading false negatives. Laboratories should be able to identify these cases and discuss the results with the clinician.
- Laboratories should use manufacturer-specific, gender-related reference ranges if available.
- All laboratories should provide interpretation for the results where if possible. Interpretation should be in line with guidelines available.

Questions for you:
Clinical use for fluid tests below

CSF	Tumour markers (2 labs) (AFP,CEA,hCG)
	LDH, Ferritin (2 labs)
Non-CSF	Bilirubin (13 labs)
	Electrolytes (up to 5 labs) (Na, K, Ca, Osmo, P, Cl)
	ALT (2 labs) ALP (1 lab) Urate (4 labs)
	Chromium, Cobalt & Titanium (1 lab)
	Tumour markers (up to 7 labs) (CEA, CA199,AFP,CA125,CA153,PSA,hCG)

Thank you for your attention

Any questions?

Macrolactin Audit 2020

22 labs participated

Feedback received from 12 labs

Out of which:

- 3 labs implemented changes
- 2 labs in the process of implementing changes