The Royal College of Pathologists
Pathology: the science behind the cure

PART 2 PRACTICAL EXAMINATION IN CLINICAL BIOCHEMISTRY

Module 1: Paper 1 (OSPE)

This is a three-hour objective structured practical examination (OSPE) where candidates are required to answer a series of 19 questions using a selection of material provided. The selection of material will include:

- analytical outputs (e.g. electrophoretic strips, chromatography scans)
- clinical scenarios (e.g. sample requirements, investigation protocol questions)
- internal quality control and/or external quality assessment data
- analytical, physiological or pharmacological calculations
- One question will test communication skills using responses made in writing.

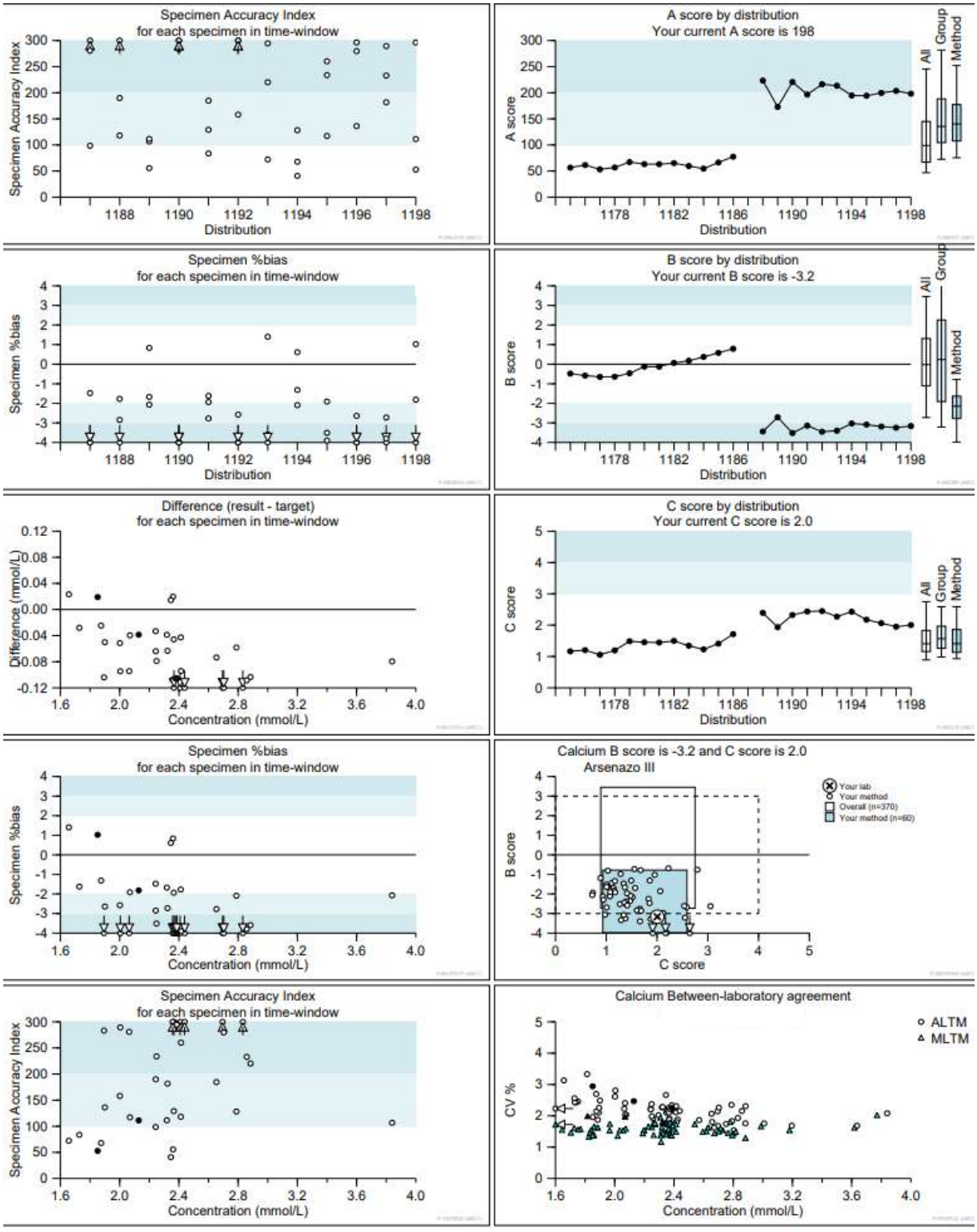
Candidates should aim to spend approximately 9 minutes on each question with an additional 9 minutes at the end. This makes a total of 3 hours. Candidates can attempt the questions in any order and can decide how much time they wish to spend on specific questions within the 3 hour time window. Each question is marked out of 20, making a total of 380 marks, which is then proportionally reduced to give an overall percentage mark.

The following questions have been retired from the OSPE question bank and will not appear again in their exact current format. The topic areas remain very much in scope for future exams.

Dr Kevin Deans – FRCPath Clinical Biochemistry Panel Chair June 2026

QUESTION 1

You have recently changed reagent for your calcium assay, followed swiftly by an equipment refresh with a new type of analyser. The external quality assessment report is below:



a) What is the difference between ALTM and MLTM? [2 marks]

ALTM (All Laboratory Trimmed Mean) and **MLTM (Method Laboratory Trimmed Mean)** (1)
The difference lies in the data used for calculation: ALTM includes all participants, while MLTM is restricted to laboratories using the same method or instrument (1) **[2 marks]**

b) Comment on the external quality assessment results. [10 marks]

At distribution 1187 there was a significant shift in results [2 marks]

The accuracy deteriorates [2 marks]

There is significant negative bias across the concentration range [2 marks]

The method group is overall negatively biased cf other methods [2 marks]

Your lab is negative within the method group in addition [2 marks]

c) What actions would you consider? [8 marks]

Check you had been assigned to the correct method group [2 marks]

Check you had set up the analyser correctly [2 marks]

Check the values for calibrators, QC, units etc for any mistakes in set up [2 marks]

Look at your method verification, was the negative bias identified? [2 marks]

Discuss with manufacturer is no obvious set up errors discovered [2 marks]

Look at patient means to confirm shift exists etc [2 marks]

Assess clinical impact of shift [2 marks]

(Max 8 marks)

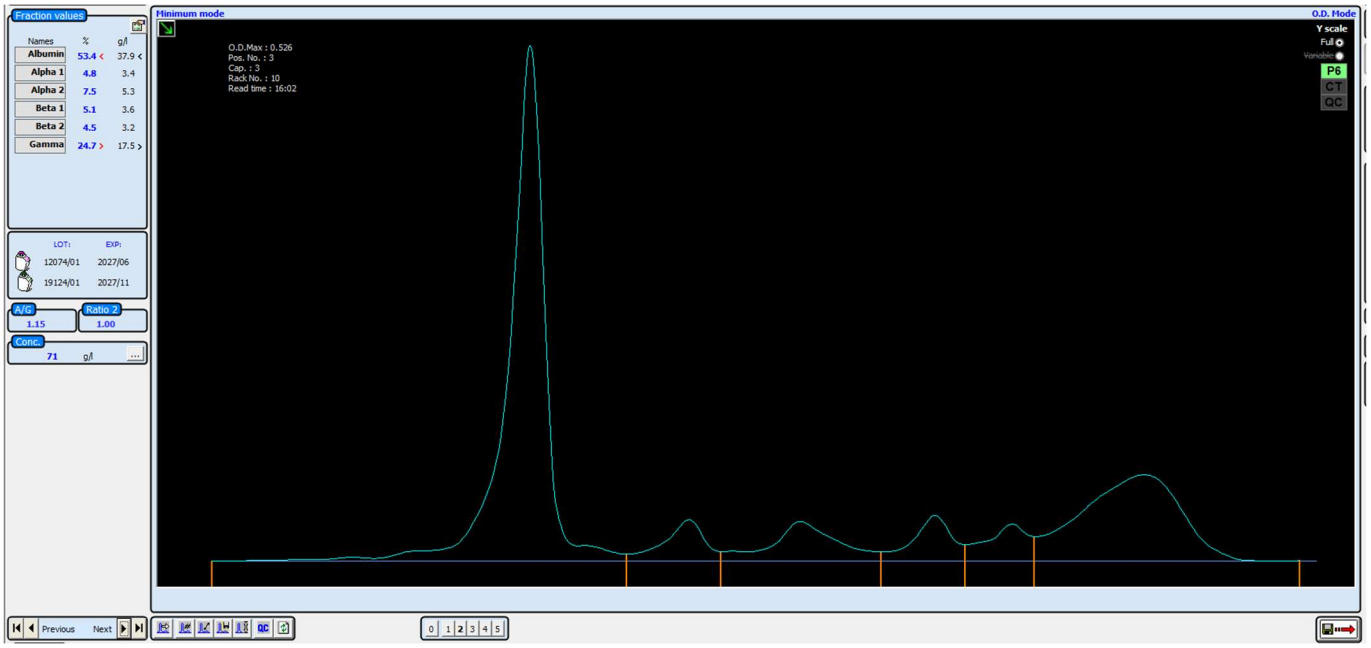
QUESTION 2

a. The CRAB criteria are sometimes used in the diagnosis of active multiple myeloma. Outline the CRAB criteria, including the cut offs used in each. [8 marks]

- **C**alcium – hypercalcaemia (1) serum calcium >0.25mmol/L higher than ULN OR >2.75 mmol/l (1)
- **R**enal insufficiency (1) creatinine clearance <40ml/min OR serum creatinine >177 umol/L (1)
- **A**naemia (1) Hb <100g/L OR >20g/L below LLN (1)
- **B**one lesions (1) >/= 1 osteolytic lesion (on x-ray, CT or PET/CT) (1)

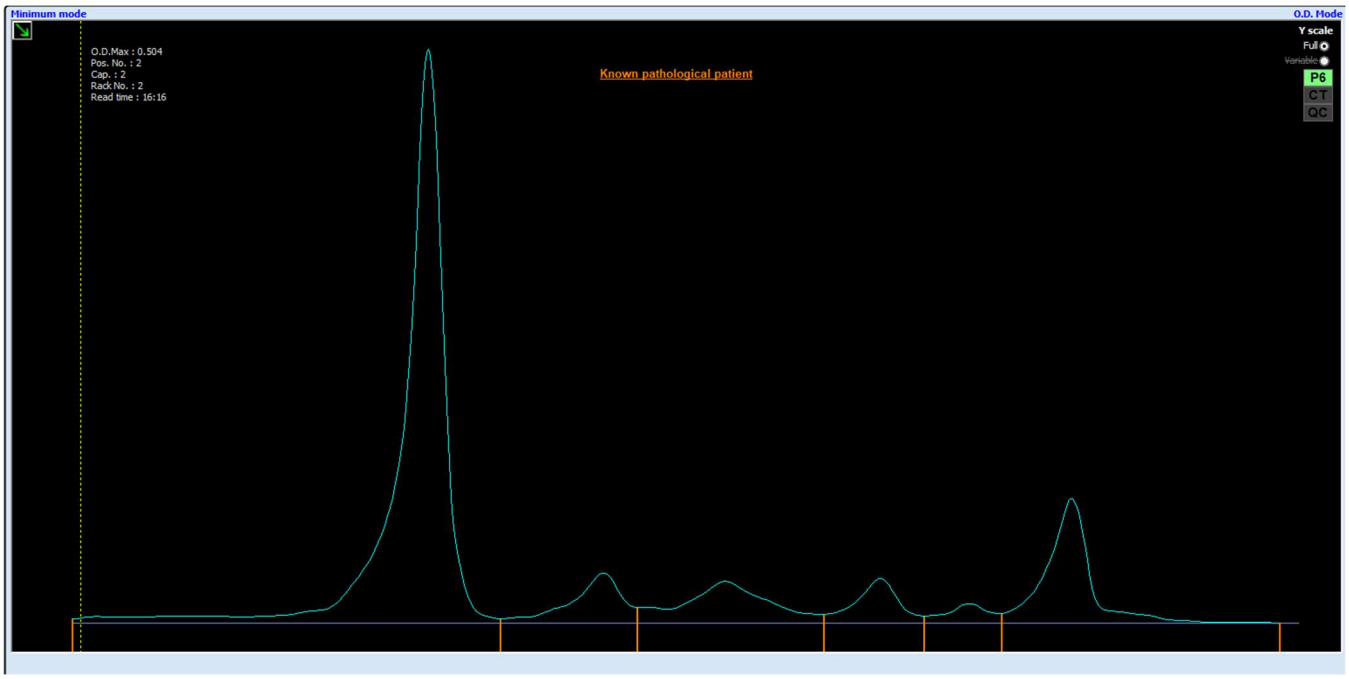
b. How would you report the following protein electrophoresis trace? [2 marks]

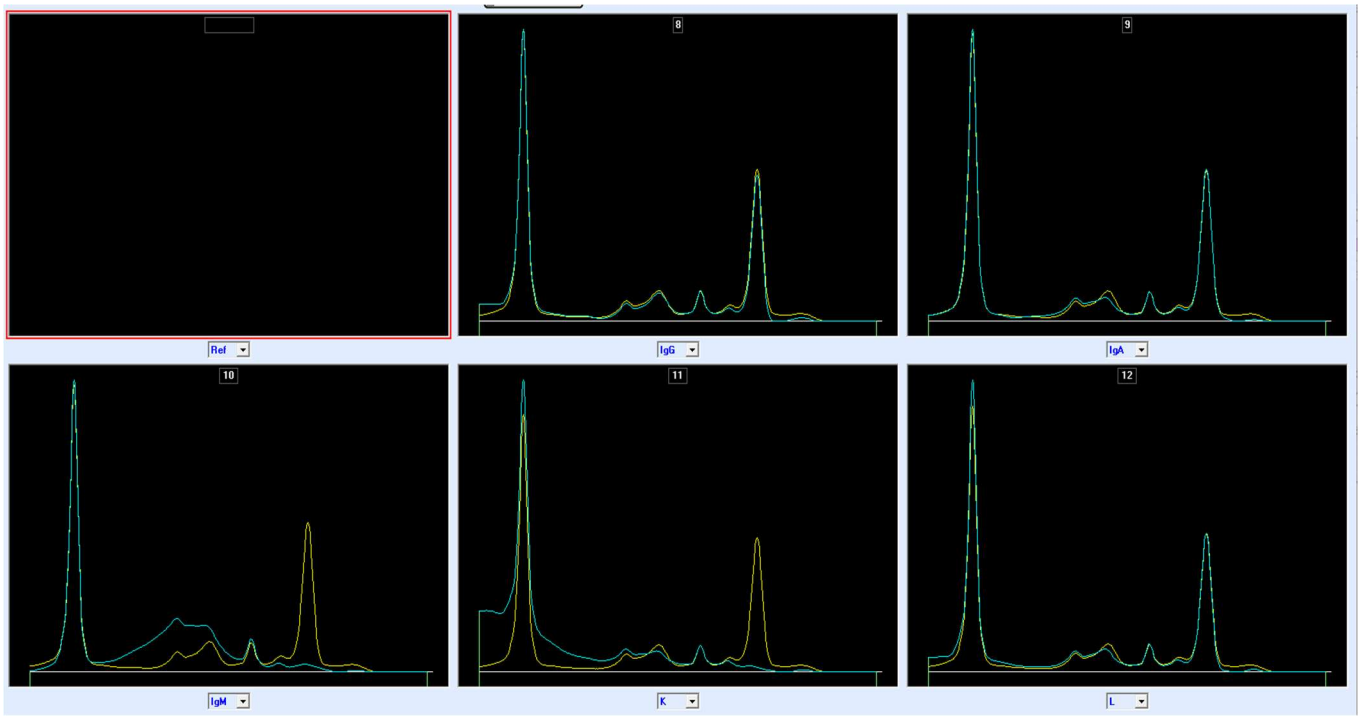
- No evident paraprotein [2]



c. How would you report the following protein electrophoresis trace with associated immunotyping? [2 marks]

- Paraprotein detected [1]
- IgM kappa [1]





d. Comment on the following serum free light chain results.

i.	Serum Kappa Free Light Chain	34.22	mg/L	(3.30 - 19.40)
	Serum Lambda Free Light Chain	31.17	mg/L	(5.71 - 26.30)
	Serum Kappa/Lambda Light Chain Ratio	1.10		(0.26 - 1.65)

[3 marks]

- Raised kappa and/or lambda with normal ratio, monoclonal free light-chains NOT detected. (1)
- Can occur with increased immunoglobulin production/inflammation (1) or reduced excretion/abnormal renal function. (1)

ii.	Serum Kappa Free Light Chain	51.75	mg/L	(3.30 - 19.40)
	Serum Lambda Free Light Chain	16.70	mg/L	(5.71 - 26.30)
	Serum Kappa/Lambda Light Chain Ratio	3.10		(0.26 - 1.65)

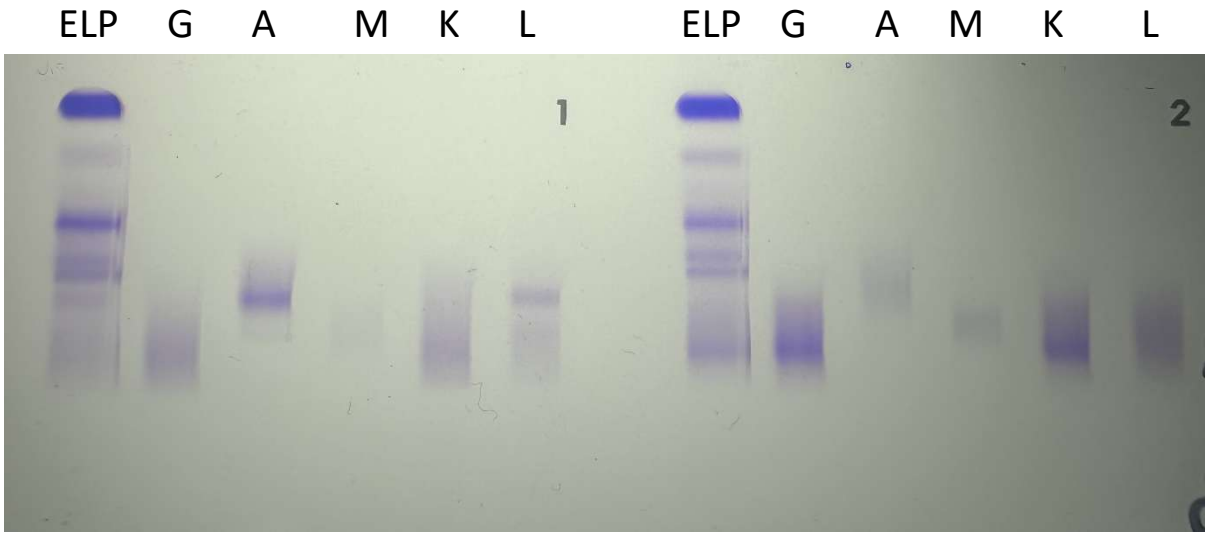
[3 marks]

- Mildly abnormal ratio up to 3.1 commonly occurs with renal impairment/CKD. (1)
- If not explained by renal function consider MGUS, myeloma or amyloidosis (1) – must mention exclusion of renal impairment/CKD to get the point.
- If absence of other features of myeloma, repeat at interval around 3-6 months (1)

e. Interpret the following samples on the serum immunofixation gel: [2 marks]

i. Patient 1 – IgA lambda paraprotein (1)

ii. Patient 2 – IgG kappa paraprotein (1)



QUESTION 3

A consultant gastroenterologist contacts you about an outpatient with chronically increased serum amylase with no symptoms of pancreatitis, and for further interpretation of a urine amylase.

	Result (IU/L)
Serum amylase	312 (<100)
Serum lipase	31 (13-60)
Random Urine amylase	415

Further tests were performed 2 weeks later:

	Result
Serum creatinine	64 umol/L
Serum amylase	241 IU/L
24 hr Urine Creatinine	11.0 mmol/L
24 hr Urine amylase	350 IU/L

(a) Explain the limitations of the initial urine amylase result and what assumptions are made. [4 marks]

Difficult to interpret random urine without creatinine concentration (1)

24 hour urine amylase clearance is optimal (1)

Assumes normal renal function (1)

Urine should be alkaline (1)

(b) Calculate the amylase/creatinine clearance ratio [6 marks]

Equation : $\frac{\text{Urine Amylase x serum creat (mmol/l)}}{\text{Serum Amylase x urine creatinine (mmol)}} \times 100$

(need to ensure creatinine is in the same units umol/l or mmol/l)

Result= (350*0.064mmol/l /241*11mmol/l)*100

= (22.4/2651)*100

=0.84 %

(c) The reference interval for the amylase/creatinine clearance ratio is 2-4%. Interpret the result in the context of this. [8 marks]

Low urine amylase excretion in the context of raised plasma amylase and normal lipase excludes pancreatitis as cause of raised amylase. (2)

Low urinary excretion may be due to poor renal function but this is excluded by normal serum creatinine. (2)

Low urinary excretion may be due to macroamylase as macroamylase (amylase- Ig complex) is not filtered by the kidney due to size. (2)

Other non-pancreatic (e.g. salivary) sources may contribute but these should be freely filtered by the kidney so unlikely to be significant in this case. (2)

(d) What further analytical techniques could be performed to support the diagnosis? [2 marks]

PEG precipitation measure amylase pre and post PEG precipitation (1)

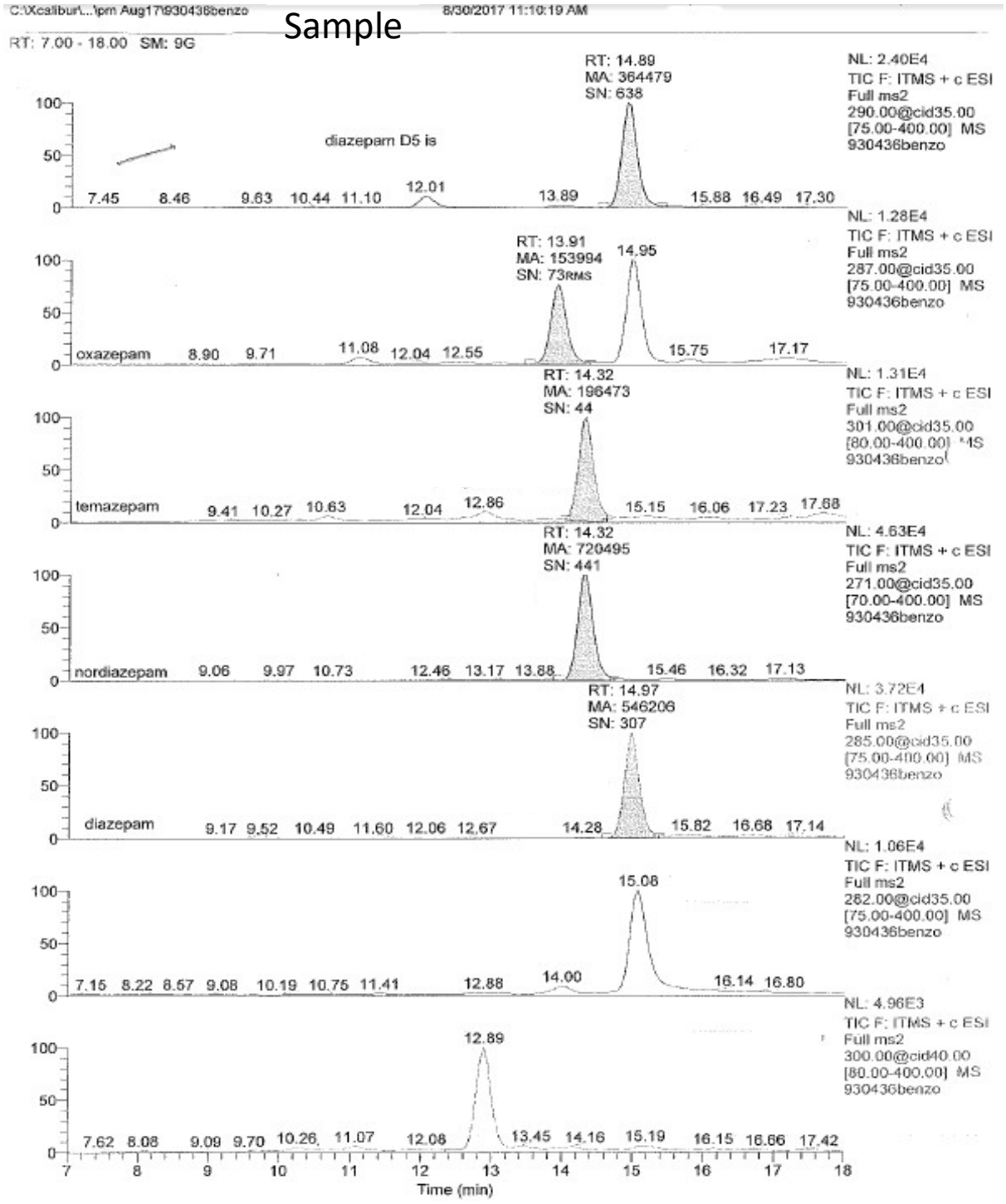
Amylase isoenzyme electrophoresis, to evaluate non-pancreatic sources and confirm the presence of macroamylase. (1)

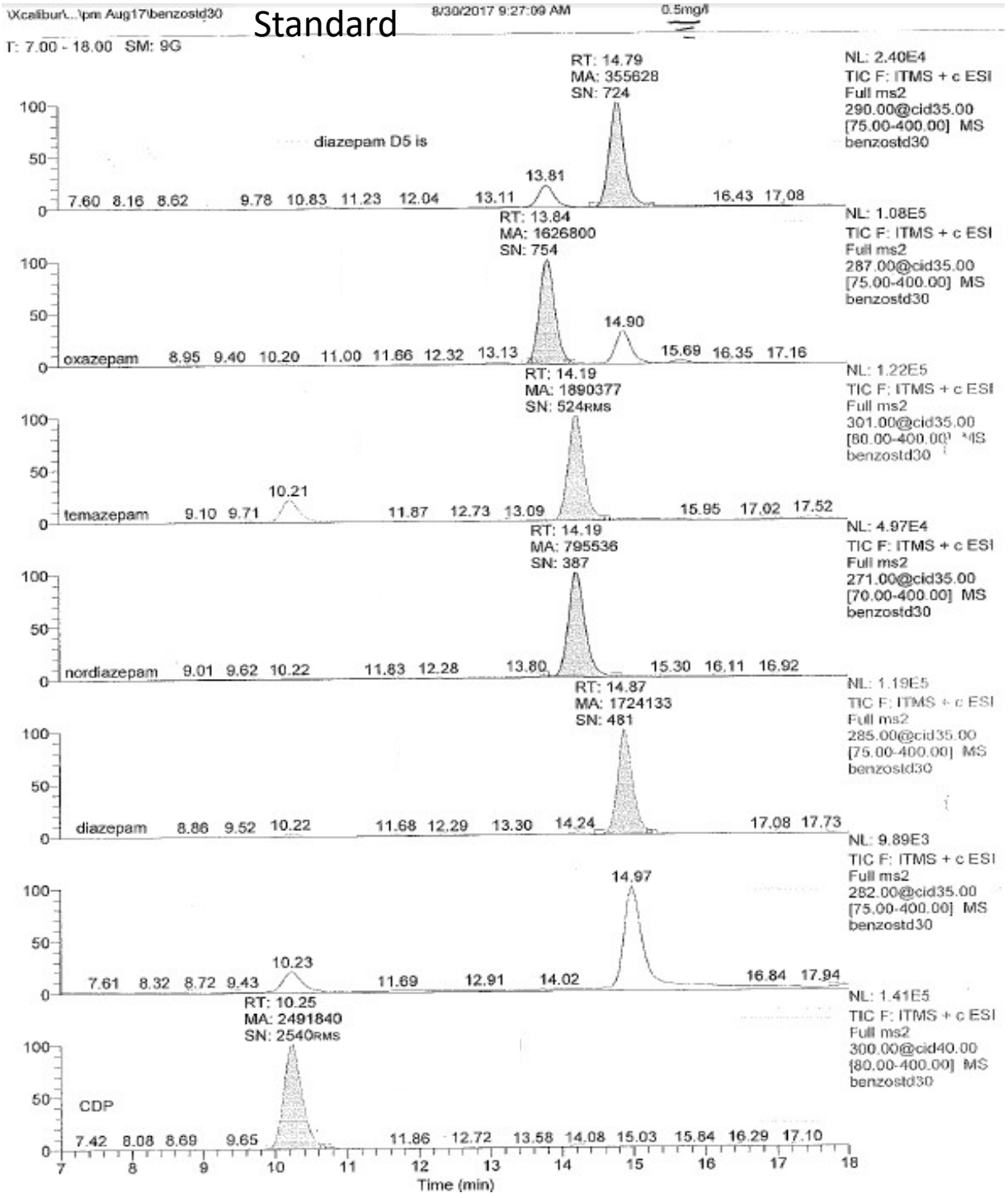
QUESTION 4

A 47 year old male was found deceased at home. A sample of his blood was analysed by Liquid Chromatography-Mass Spectrometry to look for benzodiazepines.

- D5-Diazepam was added as an Internal Standard.
- The following chromatograms are shown:
    - Sample
    - Standard containing 0.5 mg/L of each benzodiazepine
- The peak area is labelled “MA” in each case.

Calculate the concentration of temazepam in the sample, showing your working. [20 marks]





Internal standard peak area in sample = 364479

Internal standard peak area in standard mix = 355628

Temazepam peak area in sample = 196473

Temazepam peak area in standard mix = 1890377

(Identification of correct values from chromatograms: 8 marks)

Concentration of temazepam in standard mix = 0.5 mg/L

$$F = \frac{\text{Internal standard peak area in standard mix}}{\text{Internal standard peak area in sample}}$$

$$= \frac{355628}{364479}$$

$$= 0.97571602$$

(4 marks)

$$[\text{Temazepam}] = \frac{\text{Temazepam peak area in sample}}{\text{Temazepam peak area in std mix}} \times [\text{Temazepam in std}] \times F$$

$$= \frac{196473}{1890377} \times 0.5 \text{ mg/L} \times 0.97571602$$

$$= 0.051 \text{ mg/L}$$

(8 marks)

(Accept any correct variation on the above method, with full marks for correct answer.)

QUESTION 5

You have been provided with a CSF haemoglobin breakdown product trace.

(a) i. At what wavelengths should the tangent be drawn? [2 marks]

350-400 and 430-530

ii. At what wavelength is oxyhaemoglobin measured? [1 mark]

415 nm (410-420)

iii. At what wavelength is bilirubin measured? [1 mark]

476 nm (470-480)

(b) (i) Using the trace provided, calculate the oxyhaemoglobin and bilirubin absorbance.

[4 marks]

NBA~0.0834

NOA ~0.2203

(ii) Comment on the results. [4 marks]

Bilirubin and oxyhaemoglobin increased (2). Consistent with SAH (2).

(c) State four pre-analytical errors and how they might affect CSF haemoglobin breakdown product interpretation. [8 marks]

Any four (2 marks each, 1 for error and 1 for effect) from:

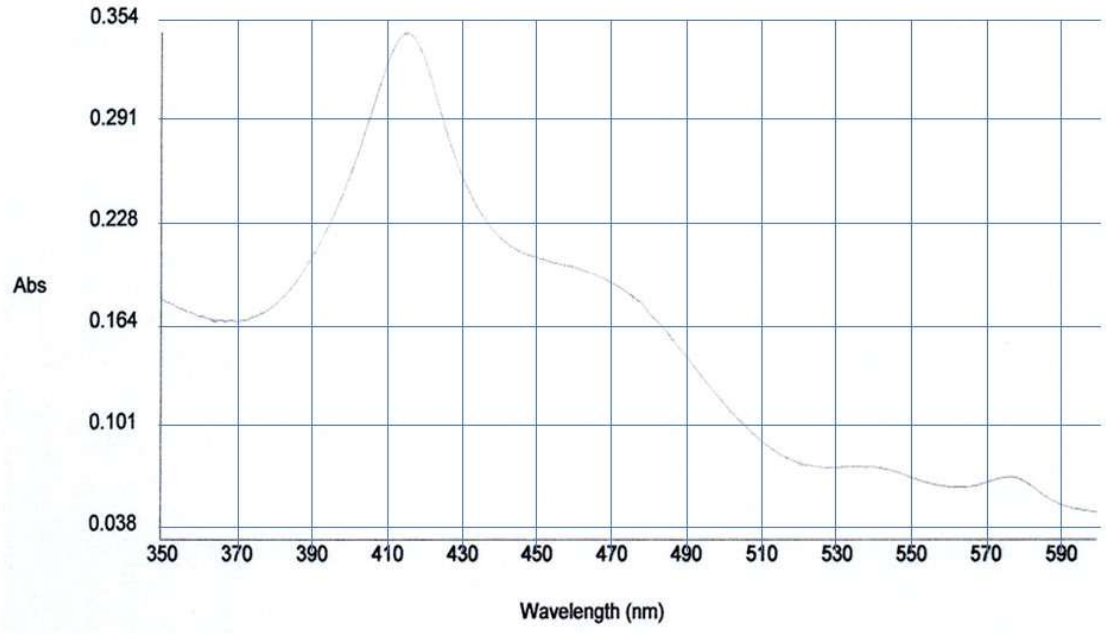
Not protected from light- degradation of bilirubin (false negative)

Traumatic tap- increase in oxyhaemoglobin (may mask bilirubin)

CSF collected before 12 hrs- bilirubin not formed (false negative)

CSF collected after 14 days- bilirubin metabolised (false negative)

Transported by tube system- haemolysis of cells (increase in oxyhaemoglobin)



QUESTION 6

In patient appropriate language, list the relevant information you would provide in a patient information leaflet for a generic 24 hour urine collection. [20 marks]

Mandatory marks (14 total):

Uses clear patient friendly language [2 marks]

Drink normally [2 marks]

When you start pass your urine and flush it down the toilet and note the exact time [2 marks]

Collect every drop for the next 24 hours and finish at the same time you started the day before [2 marks]

Note the start and finish times on the bottle; with name and DOB [2 marks]

Some bottles will contain preservatives, DO NOT discard, rinse or get into contact with the skin [2 marks]

Use a clean pot to collect your urine into, e.g. a jug, then pour into the collection bottle (do not pee directly into bottle) [2 marks]

Max 20 with any other relevant points including:

We routinely give jugs out to female patients [2 marks]

If going to pee more than 2.5 L ask for a second bottle [2 marks]

Some collections may require a special diet in the preceding days [2 marks]

Some collections may require you to stop specific medications [2 marks]

If going out, remember to take your bottle with you [2 marks]

Consider selecting a day when you are not working to do the collection [2 marks]

An incomplete collection will give false results [2 marks]

Directions to Lab team, or LTOL etc for more information/queries [2 marks]

Include form, labels, clinic info etc (i.e. more information about labelling) [2 marks]

Keep it cool and lid closed (and out of direct sunlight etc) [2 marks]

Leave it at GP, phlebotomy or main reception etc once complete [2 marks]

Version control, lab contact details, author name and date etc [2 marks]