Bioanalytical Challenges from a Clinical Perspective

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Bioanalytical challenges from a clinical perspective

Bioanalytical challenges from a clinical perspective

Bioanalytical samples from a clinical perspective:

Why so different from a clinical chemistry sample?

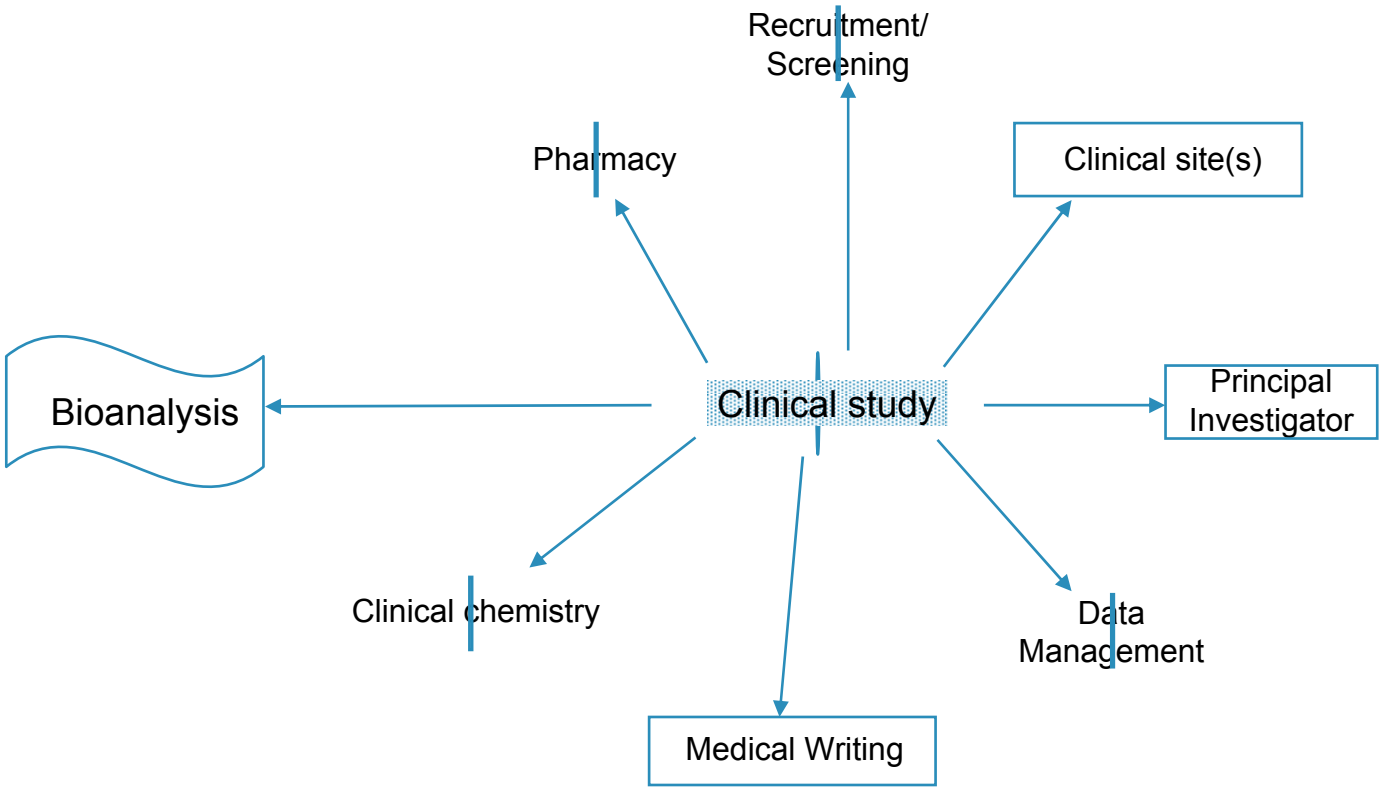
- Analysis takes much longer
- Collection specifications not always known at start study
- Special tubes/labels
- Back-up samples
- Co-medications
- Long-term storage of samples
- (Deep/ultra cold) freezers
- Dry ice shipments

Bioanalytical challenges from a clinical perspective

EMA Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples (28 February 2012)

- GCP training for all staff
- Clinical trial protocol and amendments
- Informed consent
- Interpretation of results in relation to safety of trial patients/subjects
- Establishment of lines of communication

Bioanalytical challenges from a clinical perspective



Bioanalytical challenges from a clinical perspective

Communication – Instructions on Sample Collection

Example:

- 4 mL of whole blood should be drawn in order to obtain approx. 2 mL of plasma.
- Centrifuge the samples and transfer the plasma into polypropylene tubes containing 20µL H_3PO_4 directly after centrifugation (within 15 min).
- Split the plasma phase of each sample into 2 tubes (1.0 mL for Aliquot A, rest for Aliquot B).

Bioanalytical challenges from a clinical perspective

Communication – Instructions on Sample Collection

Example:

- 4 mL of whole blood should be drawn in order to obtain approx. 2 mL of plasma.

Specification tubes?

Anticoagulant?

- 4 mL of whole blood should be collected in sampling tubes with Na-Heparin coagulation inhibitor (Na-Heparin PET-Vacutainers, 4 mL, BD, #354126) to obtain approx. 2 ml of plasma

Bioanalytical challenges from a clinical perspective

Communication – Instructions on Sample Collection

Example:

Speed/time/temp/when?

Ordered/pre-filled

- Centrifuge the samples and transfer the plasma into polypropylene tubes containing 20µL H3PO4 directly after centrifugation (within 15 min).

???

- Split the plasma phase of each sample into 2 tubes (1.0 mL for Aliquot A, rest for Aliquot B).

Minimum?

What if less plasma is available?

Bioanalytical challenges from a clinical perspective

Communication – Instructions on Sample Collection

Example:

- Centrifugation (pre-cooled centrifuge 4°C, approx. 10 min, 2000g) at latest within 15 min after collecting the samples.
- Transfer as much as available of the plasma into correspondingly labeled pre-cooled polypropylene tubes for Aliquot B containing 20µL H3PO4 (Baker, 6024, Phosphoric acid 85% or comparable) directly after centrifugation (within 15 min). Mix matrix and acid using a Vortex mixer for 1-2 seconds.
- In cases that the matrix volume of the sample is substantially less then 2 mL plasma: e.g. ~1 ml of plasma or even ~0.5 ml the amount of phosphoric acid has to be adapted. Therefore some vials have to be pre-prepared containing 10 µL phosphoric acid (for ~1 mL plasma) and 5 µL phosphoric acid (for ~0.5 mL plasma).

Bioanalytical challenges from a clinical perspective

Communication – Instructions on Sample Collection

Example cont.:

- Tubes can be prepared with Phosphoric acid within 48 hours before use.
- Transfer ~1 mL of the plasma of each sample into a second tube (no additional Phosphoric acid required) (1.0 mL for Aliquot A).
- Subsequent storage of plasma sample tubes at approx. –70°C ± 10°C until shipment to laboratory. Shipment to the laboratory on dry ice. Ship Aliquots A and B separately.

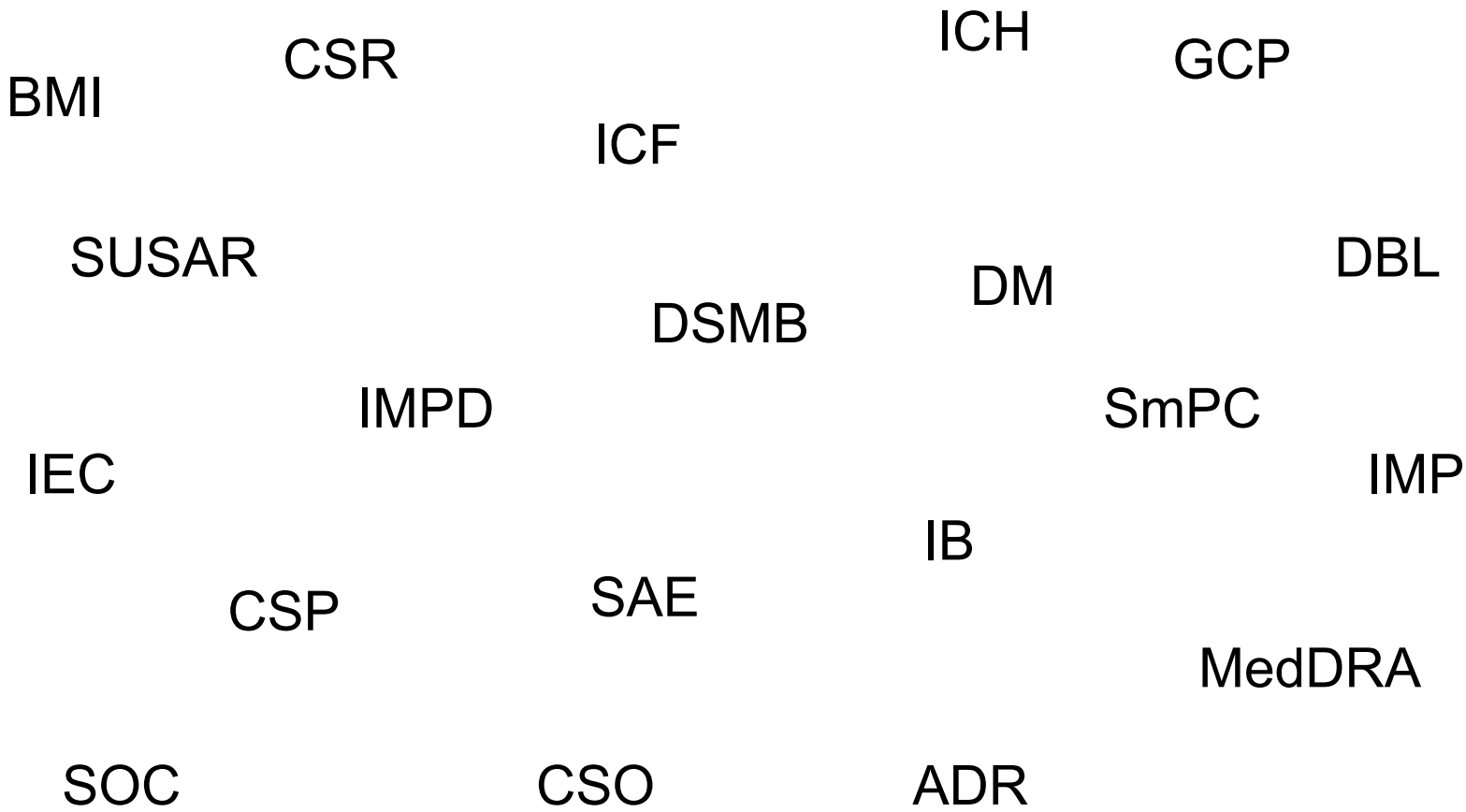
Bioanalytical challenges from a clinical perspective

Communication – Instructions on Sample Collection

- Provide separate document with sample collection details – including table with calculations in case of additives
  Avoid description of sample collection in clinical protocol
- At start of method development, think of practice
- Show interest in clinical team after first sample collection and check if all is well understood
- Avoid abbreviations

Bioanalytical challenges from a clinical perspective

Avoid abbreviations! Otherwise….



Bioanalytical challenges from a clinical perspective

Informed Consent Forms

EMA Reflection paper:

The laboratory should be informed by the sponsor in a timely manner if consent is withdrawn.

The laboratory should seek assurance from the sponsor that requests for additional work does not compromise the informed consent given by the trial subjects.

Bioanalytical challenges from a clinical perspective

Informed Consent Forms (ICF)

- Make contact person aware that you need this information
- Set-up agreements before start of clinical study.
- Persons who organize shipment of samples at clinical site should also check availability ICF. Are they aware?

  What if a batch of samples of withdrawn subject has already been sent to bioanalytical lab?
- Copies of ICFs may not always be helpful. ICFs are written in local language.

Bioanalytical challenges from a clinical perspective

Back-up samples

Why are back-up samples collected?

- To have a duplicate sample available when shipment or storage of first sample fails.
- When sample analysis fails
- Not enough sample available for duplicate analysis
- Exceeds number of validated freeze/thaw cycles

But how often does this happen?

Bioanalytical challenges from a clinical perspective

Back-up samples

- Is it always required to collect back-up samples?
- Is a back-up sample an exact duplicate of the primary sample?
- Storage capacity at clinical sites is limited
- Additional shipment and storage costs
- When not needed, back-up samples are often forgotten (when not stored at own lab facility…)
  - ➢ risk of violation with GCP

Bioanalytical challenges from a clinical perspective

Conclusion/recommendations

- Communicate clear and in detail on what you need (sample collection, ICF, protocol, back-up samples) and check if information is understood
- Keep clinical practice in mind
- Document agreements in writing
- Set-up communication lines before start of clinical study
- Define who to contact at bioanalytical lab outside office hours
- Show interest in clinical study and acknowledge their challenges

Bioanalytical challenges from a clinical perspective

Thank you for your attention