Clinical Analysers

Presenter: Christian Herling
on behalf of the EBF TT 50

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Agenda

- Definition of Clinical Analysers
- Use of Clinical Analysers
- Why is EBF interested in Clinical Analysers
- Recommendations regarding validation
- Future for Clinical Analysers in Bioanalysis (BA)

Definition of “Clinical Analysers”

- Highly automated: “Black box”
- Analytes
  - Endogenous (hormones, proteins etc.)
  - non-endogenous (biopharmaceuticals)
  - large and small molecular mass
- Detection types: chemical (spectrophotometry), cell counting, conductivity, immunoassay, coagulation, haematology, …

Why Clinical Analysers

- Why should EBF be interested in Clinical Analysers?
  - Clinical Analysers represent analytical platforms for biomarker measurement
  - Validation requirements may increase
  - Validation requirements may move toward adhering to BA validation
  - May get more authority focus
  - Moving into the regulated BA laboratories

Clinical Analysers used for

- Used for different applications:
  - Diagnostics
  - Safety assessment
  - Efficacy biomarkers
  - Bioanalysis of drugs (PK) in clinical and pre-clinical trials/studies

Clinical Pathology

- Mostly under the "**Clinical Pathology**" type of testing
- Safety biomarkers
- CAP/CLIA regulated

Sample

Sodium
Potassium
Creatinine
ASAT
ALAT
Bilirubin
Albumin
Etc.

Scope for this presentation

- Automated Immunoassays
  - used for PD endpoints (e.g. Insulin and C-peptide)
- Automated Immunoassays examples
  - Siemens Centaur
  - Siemens Immulite
  - Roche Elecsys

Advantages using Clinical analysers vs manual methods

Clinical Analyser	Manual kit format
Less manual interaction	Manual
Minimal human error	Risk of human error
Better precision	Poorer precision
Higher throughput	(S)Low throughput

Disadvantages using Clinical analysers vs manual methods

Clinical Analyser	Manual kit format
High cost	Low Cost
Inflexibility	Flexible
“in-built “ calibration with 1-2 “adjusters”	6 or more calibrators
Limited possibility for optimisation	Can be modified/optimised

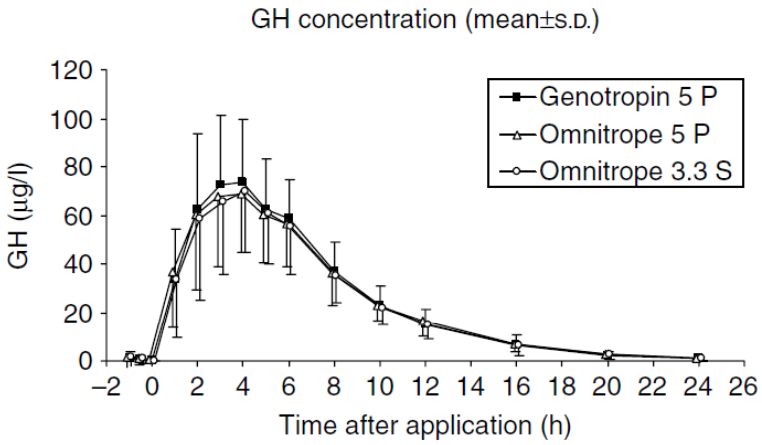
Clinical Analysers used for PK!

European Journal of Endocrinology (2010) **162** 1051–1058 ISSN 0804-4643

CLINICAL STUDY

Bioequivalence between novel ready-to-use liquid formulations of the recombinant human GH Omnitrope and the original lyophilized formulations for reconstitution of Omnitrope and Genotropin

Uwe Fuhr, Daniel Tuculanu[1], Alexander Berghout[2], Sigrid Balser[2], Arnd Schwebi
Clinical Pharmacology Unit, Department of Pharmacology, Hospital of the University of Cologne, D-50931 C
Timisoara University of Medicine and Pharmacy, RO-300173 Timisoara, Romania, [2]Sandoz Biopharmaceuti
D-83607 Holzkirchen, Germany and [3]Endocrinology, Albert Einstein College of Medicine, Bronx, NY-10467
(Correspondence should be addressed to A Berghout; Email: alexander.berghout@sandoz.com)



Analytical methods

Blood samples were allowed to clot at room temperature. Serum was obtained by centrifugation, and stored at ≤ -20 °C until analysis. The concentrations of hGH, IGF1, and IGFBP3 in serum were measured using the respective commercially available and fully validated chemiluminescent immunometric assay kits of the Immulite 2000 series with the Immulite 2000 Analyzer (DPC Biermann GmbH, Bad Nauheim, Germany). The lower limit of quantification (LLOQ) was 0.2 ng/ml for GH, 25 ng/ml for IGF1, and 500 ng/ml for IGFBP3. The concentration of NEFA in serum was measured using a commercially available and fully validated assay kit obtained from Wako Chemicals GmbH (Neuss, Germany). The LLOQ was 100 nmol/ml. The assays were additionally validated according to the requirements of the FDA guideline for bioanalytical method validation (24). Within the validation, the accuracy and

Method Validation

- Tiered approach
  - Follow EBF recommendations
  - Follow CC-VI recommendations

- Focus on late stage decision making BMs
  - Endogenous protein
  - Useful reference standard
  - QCs in matrix
    - Spiked, non-spiked (incurred samples)
    - Target value
    - Adjust number to account for lack of calibrators
- Re-calibration

Method validation - Biomarkers

- Precision
- Relative Accuracy (taking endogenous into account)
- Selectivity
- Linearity – calibration verification
- Stability
  - ISS

Equipment Validation

- A completely different story- not for this TT!

Documentation

- Compliance
- Data evaluation
  - Single Determination
- Interfacing with LIMS system
  - Clinical lab LIMS system
  - Watson interface?
- May be hard to obtain in-study validation data
  - No back calculated calibrators
  - QC relative accuracy and precision

Future Steps for TT 50

- Assess the use of Clinical Analysers in the BA community
- EBF Clinical Analyser method validation recommendation

Topic Team 50

- Marcel van der Linden, Eurofins Central Laboratory
- Janice Adcock, Envigo
- Eginhard Schick, Roche
- Malcolm York, GSK
- Petra Vinken, Janssen R&D
- Nathalie Mokrzycki, Merck & Co
- Christian Herling, Novo Nordisk