

The Siesta Group

Services for Preclinical and Clinical Trials

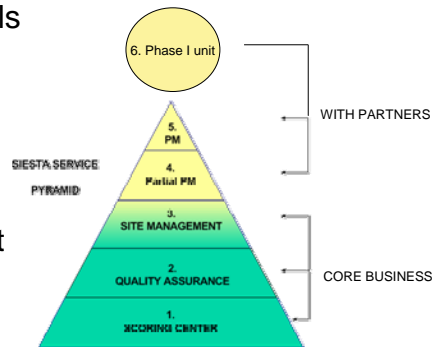
The company

- The competence center for sleep and EEG analysis – worldwide
- CRO specialised in sleep and/or EEG
- Tight network of partners and associates
- Headquarter :
Vienna, Austria ,Europe
- US Subsidiary :
Salisbury, MD
Cleveland, OH



The Siesta Group Clinical Trial Services

- Scoring and data analysis for single and multi-site trials
- Quality control and monitoring
- Site & Project management
- Investigator site(s) and global networks

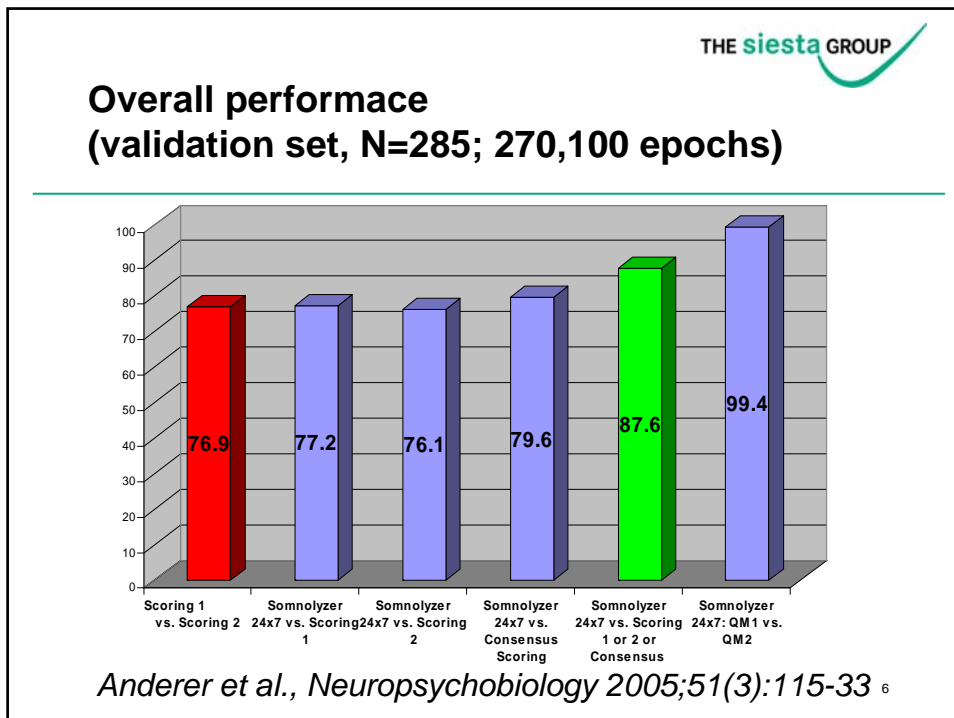
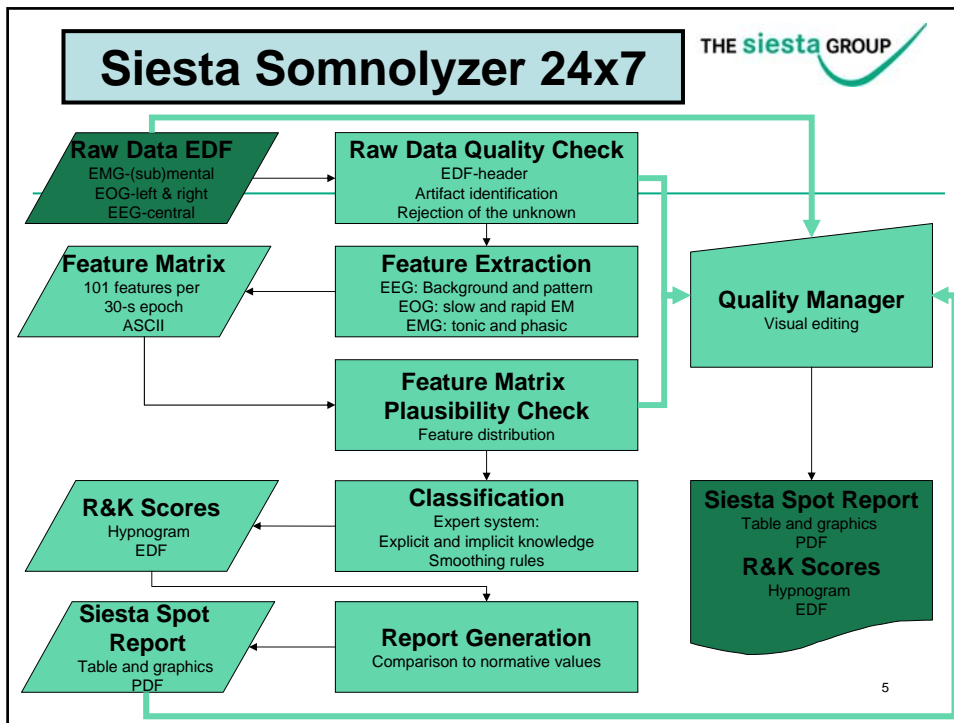


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Core technology sleep: Somnolyzer 24x7

- Computer supported analysis of polysomnography (PSG):
 - Sleep staging / sleep architecture
 - Respiratory analysis
 - PLM analysis
 - Arousal analysis
 - Spindle and K-complex analysis
 - Artefact detection
 - FFT analysis (incl. Pharmaco-EEG)
 - New ways of describing sleep (innovative biomarkers)
 - Norm data comparisons
- Reliable, validated, according to published standards (incl. latest AASM standards)

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Advantages of computer supported analysis

Issues in PSG

- Variance in PSG scoring
 - Interrater agreement around 75%
- Delay in scoring
 - Difficulty for screening and dosing decisions
- Deviations from standard (montage, filter settings, etc.)
 - Non-homogenous data in multi-center trials
- Difficult quality maintenance, artefacts
 - Loss of information, loss of data
 - EDF as pseudo-standard
- Costly



Computer supported analysis

- Very low variance in scoring
 - Over 98% reliability
 - Increases power of significance tests
- No delay in scoring
 - Same day decisions, for screening, dosing, etc.
 - Trial results immediately after LPLV
- Full abidance to standard
 - Ensuring homogenous data
 - AASM and R&K
- Quality monitoring
 - Minimum loss of information
 - Clean data sets
- Much more cost-efficient
 - From feasibility to study conduct

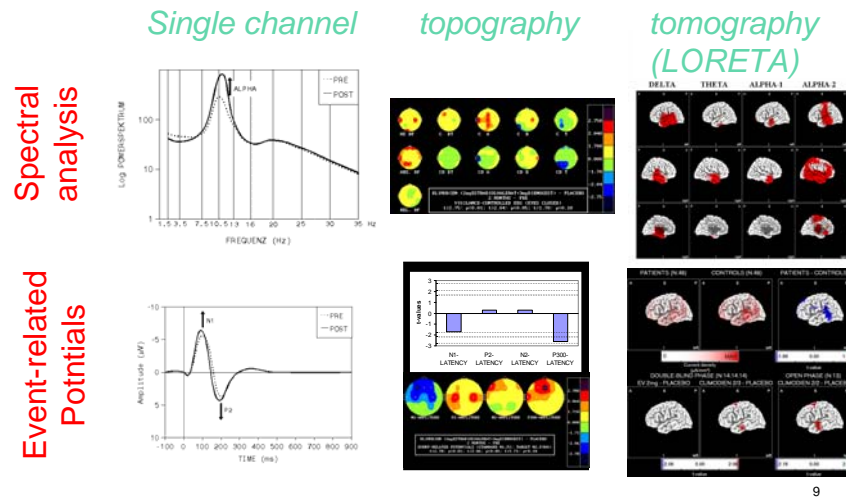
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References

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Validation on almost 300 PSGs
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- Penzel T, Hirshkowitz M, Harsh J, et al. Digital analysis and technical specifications, *Journal of Clinical Sleep Medicine* 2007;3(2)109-120.
Lists Somnolyzer 24x7 as the top "grade 1" autoscoring solution
- Svetnik V, Ma J, Soper K, et al.: Evaluation of automatic and semi-automatic scoring of polysomnographic recordings from a clinical trial using Zolpidem in the treatment of insomnia, *Sleep*, in print.
Independent validation on clinical trial data
- Dingemans J, Dorffner G, Hajak G, Benes H, Danker-Hopfe H, Polo O, Saletu B, Barbanj MJ, Pillar G, Penzel T, Chioffi E, Hoever P: Proof-of-concept study in primary insomnia patients with almorexant (ACT-078573), a dual orexin receptor antagonist, *Sleep and Biological Rhythms*, *Worldsleep07* supplement, 2007.
Somnolyzer in a successful PoC trial

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Core technologies: Pharmaco-EEG



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Pharmaco-EEG: main applications

- classification of psychotropic drugs
- demonstration of the time course of the cerebral bioavailability of a psychotropic drug at its target organ – the human brain
- demonstration of dose-efficacy relations
- exploration of bioequipotency
- exploration of pharmacokinetic/pharmacodynamic relationships
- exploration of the relationship between CNS effectiveness and therapeutic efficacy (pharmaco-EEG as a predictive model)
- therapeutic monitoring of patients or patient groups

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Pharmaco-EEG: Our strengths

- Covering full spectrum of pharmaco-EEG
- High level quality control
- Superior artefact treatment
- 30 years of experience
- State-of-the-art technology
- Top experts in psychiatry and neurology

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Selected References

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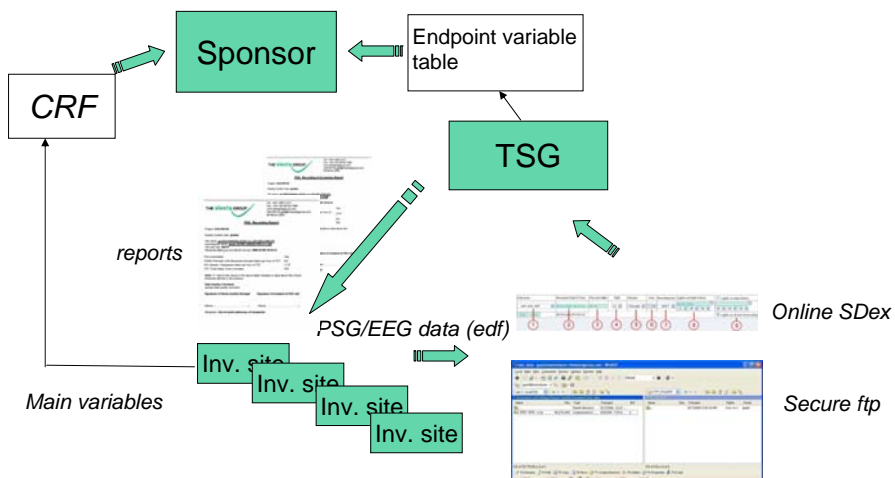
Service Level 1 & 2 : Scoring / reading center

- Sleep: PSG, actigraphy, psychometric tests, etc.
- Pharmaco-EEG: Spectral analysis, mapping, LORETA, ERP
- Scoring (reading) and endpoint calculation
- Process harmonization and data quality monitoring
- Remote or on-site training

- Advantages:
 - Reliable data analysis (low variance)
 - Fast responses (e.g. for screening decisions)
 - Immediate quality control
 - Expert visual scoring, where needed
 - Raw data handling by the EDF experts

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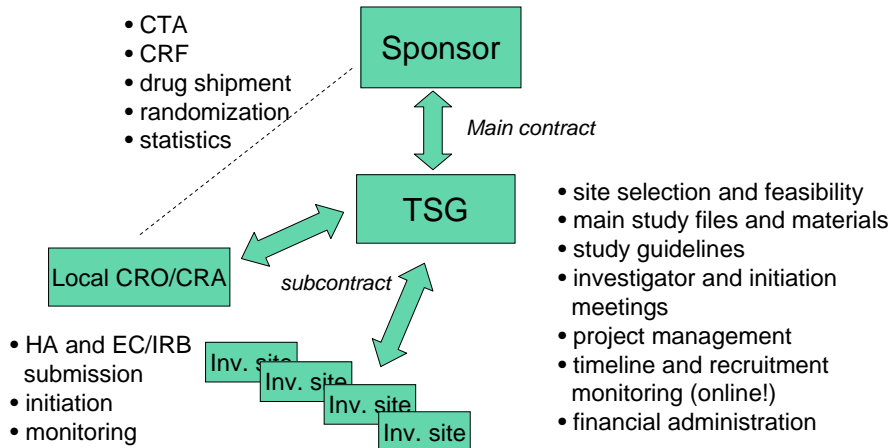
Scoring/Reading center – data flow



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Services Level 3 & 4: Site and Project Management



Siesta Investigator Network

- USA: 10+
- EU: 30+
(Austria, Germany, Switzerland, Netherlands, Scandinavia, France, Spain, UK)
- Rest of the world: 10+
(Israel, Australia, South Africa, South America)
- Continuously expanding



Preclinical Research

- Working with top experts and animal facilities, The Siesta Group can be your partner for
 - Consulting on protocols
 - Efficiently conducting single or multi-dose protocols in select animal groups
 - Scoring animal EEG and sleep
 - Exploratory analysis of data to identify differentiating drug effects

- Integrative/translational approach
 - From preclinical research, via phase I to late-phase clinical trials

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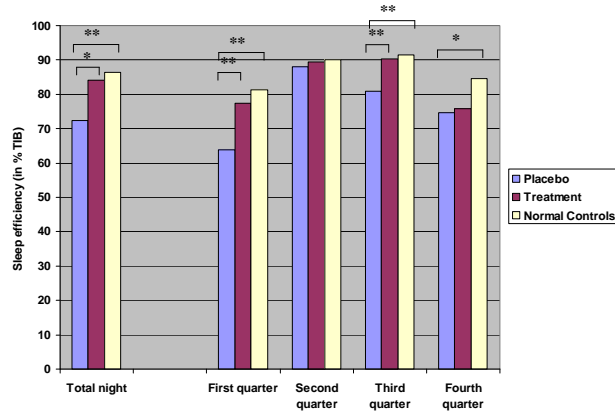
Additional services: Consulting and support

- Consulting on study protocol
- Rental or support with purchase of equipment
- Retrospective data analysis
- Biomarker research
- Scientific writing

- Advantages:
 - Access to experts with >20 years of experience in sleep trials
 - Network of sleep labs
 - Close contacts to equipment manufacturers
 - State-of-the-art signal processing
 - High reputation scientists

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Norm data comparison



- Key-lock-principle (Saletu)

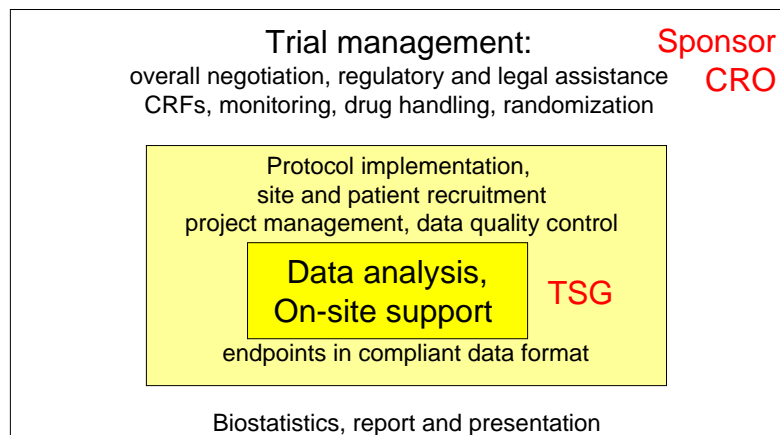
Core medical partners and references

- Michael Decker, PhD
Atlanta, GA
- Hartmut Schneider, Naresh Punjabi, Alan Schwartz, MD
Johns Hopkins University, Baltimore, MD
- Riccardo Stoohs, MD
Stanford University, CA
- Joseph Golish, MD
Cleveland, OH
- Bernd Saletu, MD; Josef Zeithofer, MD PhD
Medical University of Vienna, Austria
- Dieter Kunz, MD, Heidi Danker-Hopfe, PhD; Thomas Penzel, PhD;
Charité University Medicine, Berlin, Germany
- Manel Barbanoj, MD
University of Barcelona, Spain
- Bob Kemp, PhD
Holland Sleep Research, The Hague, Netherlands
- Irshaad Ebrahim, MD
London Sleep Center, UK

Experiences

- Scoring center
 - > 10 Phase I and II + device trials
 - Insomnia, narcolepsy, RLS, OSAS, others
 - Europe and USA
- Site and project management
 - 2 Phase I and II
 - Insomnia, narcolepsy
 - Europe
- Reference:
 - Insomnia phase Ib, Orexin receptor antagonist, Actelion, CH

Seamless cooperation with other CROs





Our motto

Measurement of EEG and sleep is a most complex matter



Make it simple by working with the experts



THE **siesta** GROUP

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