COST Domain Committee "BMBS"

COST Action B26
Start Date 31 May 2005
End Date 30 May 2010

Obstructive Sleep Apnea

FINAL EVALUATION REPORT

This Report stems from the relevant Domain Committee. It contains four parts:

I. Management Report prepared by the COST Office
II. Scientific Report prepared by the Chair of the Management Committee of the Action.
III. Evaluation Report prepared by the “ad hoc” Evaluation Panel, established by the Domain Committee, and edited by the COST Office.
IV. DC General Assessment prepared by the Domain Committee

Appendices:

Confidentiality: the documents will be made available to the public via the COST Action web page except for chapter II.D. Self evaluation and III. Evaluation Report.

Executive summary of the Scientific Report (max.250 words):

Action B26 had the objectives to (i) assess the role of OSAS as a cause of cardiovascular co-morbidity, and coordinate European studies on pathogenetic mechanisms including genetic aspects; (ii) promote exchanges between European research groups on OSAS diagnosis and management; and (iii) address medico-legal implications of OSAS and sleepiness. 21 countries joined the Action.

The principal achievements were:
The ESADA (European Sleep Apnea DAtabase)
I. Management Report

I.A. COST Action Fact Sheet

- **COST Action** B26  Obstructive Sleep Apnea
- **Domain** name BMBS

**Action details:**

CSO Approval: 15/03/2005  
End date: 30/05/2010  
Entry into force: 13/04/2005  
Extension: 30/05/2010

**Objectives** *(from DB as in About COST)*

The main objectives of the COST Action B26 are: (i) to assess the role of OSAS as a possible cause of increased cardiovascular risk. Collaboration among different countries will provide a critical mass of data in both untreated and treated patients, and result in the development of guidelines on preventive measures; (ii) to coordinate studies on pathogenetic mechanisms of increased cardiovascular risk of OSAS (i.e., inflammation, oxidative stress, endothelial dysfunction, metabolic derangements, altered autonomic control associated with exposure to intermittent hypoxia). These studies will highlight possible factors susceptible to correction by therapy. Secondary objectives are to promote exchanges between groups in the following fields: (i) diagnosis of OSAS and patient management: guidelines exists on diagnosis of OSAS, but evaluation of cardiovascular risk factors is not routinely performed in OSAS patients. The joint effort of several groups will be helpful in setting up a useful and cost-effective European protocol to longitudinally evaluate cardiovascular risk in OSAS patients; (ii) excessive daytime somnolence (EDS) and medico-legal implications of OSAS: problems still exist on the assessment of EDS in OSAS. OSAS increases the risk of car accidents, but legislation addresses the problem in different ways throughout Europe. A European Network will contribute in developing guidelines and promotion of their application in European countries. In this respect, the COST Action B26 will be complementary to the ongoing FP6 Integrated Project on sleepiness entitled: Advanced sensor development for attention, stress, vigilance and sleep/wakefulness monitoring (acronym: SENSATION, project number: 507231); (iii) establish a common protocol to be adopted by all participating Centres for data collection at baseline and during clinical follow-up of treated and untreated OSAS patients, in order to cross-sectionally and prospectively assess the association between OSAS and cardiovascular morbidity in a sufficiently large patient sample representative of the European population.

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Total: 24
# Management Committee

<table>
<thead>
<tr>
<th>Chair</th>
<th>Vice Chair</th>
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| Prof. Walter MCNICHOLAS  
St. Vincent's University Hospital Elm Park 4 Dublin Ireland  
N.A. | Prof. Patrick LEVY  
Grenoble University Hospital CHU Michallon, BP 217 38043  
GRENOBLE CEDEX 09 France  
N.A. |

## Domain Committee Rapporteur

<table>
<thead>
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| Prof. Jaroslav VESELY  
DC Rapporteur of B26 BMBS  
Pathological Physiology  
Medical Faculty  
Palacky University  
Hnevotinska 3 77515 Olomouc Czech Republic  
N.A. |

## Austria

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| Dr Wolfgang MALLIN  
MC Member  
LKH Hoergas - Enzenbach Department for Pulmonology Sleep Lab, Hoergas 30 8112 GRATWEIN Austria  
N.A. |

## Belgium

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| Dr Wilfried DE BACKER  
MC Member  
UNIVERSITY HOSPITAL ANTWERP WILRIJKSTRAAT 10 2650  
EDEGEM Belgium  
N.A. | Prof. Daniel RODENSTEIN  
MC Member  
Cliniques universitaires Saint-Luc  
Faculte de Medicine  
Universite catholique de Louvain  
avenue Hippocrate 10 1200 Bruxelles Belgium  
N.A. |
| Prof. Johan VERBRAECKEN  
MC Substitute Member  
Universitair Ziekenhuis Antwerpen N/A - Please update this record Antwerpen Belgium  
N.A. |

## Cyprus

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| Dr Eleftherios PAPATHANASIOU  
MC Member  
The Cyprus Institute of Neurology & Genetics  
6 International Airport Avenue, P.O.Box 23462, PO Box 23462 1683 Nicosia Cyprus  
N.A. |

## Czech Republic

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| Dr Martin PRETL  
MC Member  
Centre for Sleep Disorders First Faculty of Medicine  
Charles University  
Katerinska 30 12000 Prague 2 Czech Republic  
N.A. |

## Denmark

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| Dr Poul JENNUM  
MC Member  
Danish Center for Sleep Medicine  
Glostrup University Hospital N/A  
- Please update this record 2600 Glostrup Denmark  
N.A. | Dr Philip TONNESEN  
MC Member  
Philip TonnessenGentofte Hospital  
Copenhagen Opgang 3A, 2.sal,  
Niels Andersensvej 65 2900 Hellerup Denmark  
N.A. |
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<td>Finland</td>
<td>Dr Tarja SAARESRANTA</td>
<td>MC Member</td>
<td>University of Turku Sleep Research Unit, Medical Faculty University of Turku Dentalia, Lemminkaisenkatu 2 20520 Turku Finland</td>
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<td>Prof. Patrick LEVY</td>
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<td>Prof. Thomas PENZEL</td>
<td>MC Member</td>
<td>Center of Sleep Medicine, Charite - Universitätsmedizin Berlin</td>
<td>Luisenstrasse 13 10117 Berlin Germany</td>
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<td>Dr Konstanze DIEFENBACH</td>
<td>MC Member</td>
<td>Interdisciplinary Center of Sleep Medicine, Charite - Universitätsmedizin</td>
<td>Berlin Chariteplatz 1 10117 Berlin Germany</td>
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<td>Dr Paschalis STEIPOULOS</td>
<td>MC Member</td>
<td>University Hospital of Alexandroupolis Department of Pneumonology, Dragana,</td>
<td>Alexandroupolis 68100 Alexandroupolis Greece</td>
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<td>Prof. Thorarinn GISLASON</td>
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<td>Fossvogi 105 Reykjavik Iceland</td>
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<td>Prof. Peretz LAVIE</td>
<td>MC Member</td>
<td>Diagnostic Sleep Laboratory, Faculty of Medicine, Technion</td>
<td>N/A - Please update this record 32000 Technion-Haifa Israel</td>
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<td>Italy</td>
<td>Prof. Gianfranco PARATI</td>
<td>MC Member</td>
<td>Istituto Auxologico Italiano Cardiology Medicine, University of Milano-Bicocca S. Luca Hospital, via Spagnaletto, 3 20149 Milano</td>
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<td>Prof. Maria Rosaria BONSIGNORE</td>
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<td>Dip Biomedico Medicina Interna e Specialistica (DIBIMIS) Sezione di Pneumologia c/o Ospedale V Cervello, Via Trabucco 180 90146 Palermo Italy</td>
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<td>Prof. Andris VITOLS</td>
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<td>Institute of Cardiology, University of Latvia</td>
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<td>Prof. Giedrius VARONECKAS</td>
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<td>Bulevar Despota Stefana 142 11060 Belgrade</td>
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<td>Prof. Viliam DONIC</td>
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<td>Faculty Of MedicineSafarik University Kosice Tr SNP1 4000</td>
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<td>Prof. Zoltan TOMORI</td>
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<td>MedicineUniversity of P.J. Safarik SNP 1 040 66 KOSICE Slovak Republic</td>
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<td>Dr Ferran BARBE ILLA</td>
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<td>Prof. Jan HEDNER</td>
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## I.C. Overview activities and expenditure

### Budget 2005 - 2010: 250.547 €

#### Meetings

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**Honoraria**

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**Dissemination**

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**Action Total** 250547,6
II. **Scientific Report** prepared by the Chair of the Management Committee of the Action (same layout as in the Monitoring Progress Report)

II. **Scientific Report** prepared by the Chair of the Management Committee of the Action (same layout as in the Monitoring Progress Report)

II. RESULTS ACHIEVED DURING THE PERIOD APRIL 2005-MAY 2010

1. OBJECTIVES

The main objectives of the COST Action B26 are: (i) to assess the role of OSAS as a possible cause of increased cardiovascular risk. Collaboration among different countries will provide a critical mass of data in both untreated and treated patients, and result in the development of guidelines on preventive measures; (ii) to coordinate studies on pathogenetic mechanisms of increased cardiovascular risk of OSAS (i.e., inflammation, oxidative stress, endothelial dysfunction, metabolic derangements, altered autonomic control associated with exposure to intermittent hypoxia), in order to highlight possible factors susceptible to correction by therapy.

Secondary objectives are to promote exchanges between European research groups on the following topics: (i) diagnosis of OSAS and patient management; (ii) excessive daytime somnolence (EDS) and medico-legal implications of OSAS, in collaboration with the ongoing FP6 IP on sleepiness “Advanced sensor development for attention, stress, vigilance and sleep/wakefulness monitoring” (acronym: SENSATION, project number: 507231); (iii) a common protocol to be adopted by all participating Centres for data collection during clinical follow-up of treated and untreated OSAS patients representative of the European population (iv) genetic mechanisms of OSAS with particular reference to cardiovascular disease, obesity and the metabolic syndrome.

2. TECHNICAL DESCRIPTION AND IMPLEMENTATION

The work has been subdivided into the following three Working Groups:

- **WG 1**: Cardiovascular complications in OSAS: pathogenetic mechanisms and markers of increased cardiovascular risk.
- **WG 2**: Daytime somnolence and medico-legal implications of OSAS
- **WG 3**: Epidemiology and genetics of OSAS.

3. Participating Institutions
4. Meetings

4.1 Meetings of the Management Committee

- **Brussels, Belgium**
  - May 31, 2005
- **Milan, Italy**
  - December 6, 2005
- **Brussels**
  - July 3, 2006
- **Copenhagen**
  - November 18, 2006
4.2 Meetings of the Working Groups

Copenhagen, Denmark  WG1, September 19, 2005
Milan, Italy  WG1, WG2, WG3, December 5, 2005
Marburg, Germany  WG1, WG3 March 16, 2006.
Munich, Germany  WG1, September 4, 2006.
Copenhagen, Denmark  WG1, WG2, WG3, November 18, 2006
Dusseldorf, Germany  WG1, WG3 December 2, 2007
Brussels, Belgium  WG1, WG2, WG3 June 30, 2008
Antwerp  WG1, WG3, November 21, 2008
Brussels  WG1, WG2, WG3, April 27, 2009
Palermo  WG1, WG3, October 23-24, 2009
Brussels  WG1, WG3, Jan 25, 2010

5. Short-term Scientific Missions

A panel to examine proposals and take decisions for STSM was nominated on December 6, 2005. The members consist *ex officio* of the WG secretaries. Panel Chair, P Jennum, Secretary of WG3.

Participants in STSM and other Scientific Missions:

Christin Lundquist (Sweden) 2006: Visits to individual participating ESADA centres to coordinate recruitment procedures

Jeanette Norum (Sweden) 2006: Visits to individual participating ESADA centres to coordinate recruitment procedures

Dr Piotr Bielicki (Poland), 2007 – STSM/ERS Short-term Scientific Fellowship from Prof Zielinski's Institution (COSTB26 MC member) to Dr. Renata Riha for 3 months to investigate cytokine gene polymorphisms in sleep apnoea
Dr. Anna Zito – STSM from Palermo to Greece in May 2009 to analyse data on the Metabolic Syndrome in OSAS patients from Mediterranean Countries

Dr. Brian Kent – STSM approved from Dublin to Liverpool (P Trayhurn) in mid 2010 to investigate role of intermittent hypoxia in adipocyte dysfunction. STSM postponed because of logistical difficulties at the host centre.

Prof. Marisa Bonsignore: Sabbatical year in the Sleep Laboratory of Prof. Josep M Montserrat, University of Barcelona, Spain, 2009-2010

6. RESULTS AND STATUS

6.1 WG1: CARDIOVASCULAR RISK IN OBSTRUCTIVE SLEEP APNEA

WG1 Chair: Jan Hedner

WG1 Activities 2005

Since its institution in May 2005, this Working Group has held one formal meeting in Milan, Italy on December 5, 2005. An informal updating meeting was also held in September 2005 in conjunction with the Annual European Respiratory Society meeting in Copenhagen, Denmark.

- 31 May 2005, Brussels, Belgium.
First formal meeting of the MC core members. The themes of the different Working Groups of the action were defined. The WG1 was launched to specifically address the association between obstructive sleep apnea and cardiovascular disease. The WG1 Chair (Jan Hedner) and Vice-Chair (Peter Calverley) were elected.

- 19 September 2005, Copenhagen, Denmark.
This was an informal session held in conjunction with the annual ERS meeting in Copenhagen. The meeting was attended by 9 members of the MC and the intent was to give updated information on the possibilities and obligations associated with the COST action. WG1 is very complex since it involves basic and clinical science. Several European Scientists working in this field has a chance to compare their ideas and research projects during the “brainstorming” at the ERS meeting. It was also decided that a draft for a position paper on sleep apnea and cardiovascular risk should be completed by the Chair (Bonsignore) and Vice-Chair (McNicholas) of the MC.

- December 5, Milan 2005
This meeting reviewed the structure of the WG and identified its core members defined as;
Immediate tasks for this group were decided to include

(i) listing of resources for a joint European network within this specific area of expertise,
(ii) educational activities,
(iii) exchange of personnel and scientists,
(iv) generation of a joint scientific activity.

It was also decided that a specific research seminar on sleep apnea and CV disease would be arranged in association with the 2006 Madrid ESH meeting. Additional meetings were planned in conjunction with the 2006 Marburg Sleep Apnea meeting (informal WG meeting). Preliminary plans were made to provide a consensus paper on diagnosis and treatment of OSA in patients with CV disease. If possible this should be prepared in cooperation with the European Society of Hypertension (GP, LG, PL, WMN, JH and PS).

The Milan meeting specifically focussed on the possibility to generate a registry to identify potential exchange opportunities for young scientists between European laboratories. Such visits should be minimum 5 days and the cost is maximized to Euro 1400 per occasion. The total budget 2006 would allow for approximately three such study visits. Further details of this possibility have subsequently not been pursued by the WG during 2006.

A final and important decision of the meeting was to initiate a framework for a larger joint multi centre follow-up trial that should include routinely scheduled patients at the different sleep laboratories headed by the WG members. In brief, eligible patients for this study would be those given a diagnosis of OSA. The intent of this action would be manifold. First, a larger joint effort would enable a standardisation among European sleep diagnostic centres. It would also provide a possibility to reflect on differences in treatments and outcomes in different European countries. Second, the collaborative work would enable an improved exchange between European researchers in the field. Third, and importantly, the data base would in a scientific perspective potentially collect a database of 7-8000 patients with OSA yearly.

The study material would be available an immediate cross sectional analysis and would in a prospective manner enable a follow-up to determine the natural history of the disease as well as complications associated with OSA. The details of this trial were outlined during the
meeting and it was determined that a web based report format would be used to sample data on each patient with a minimum level defined by criteria that essentially conform to those applied in routine clinical medicine. Laboratories would also be requested to undertake a more extensive cardiovascular risk classification including metabolic status, clinical renal function and potentially measures of structural vascular and cardiac status (to be determined). This first step would be obtained by the individual input from each participating laboratory independent of any joint funding from the COST action. In a second step this data base would be expanded to a more elaborate protocol that includes e.g. collection of blood samples to generate a bio bank for feno- and genotyping of the cohort. Other objectives could be interventional studies or specific sub protocols of particular patient groups. All such extended studies could be generated based on the collaboration of any limited number of participants in the study and would be referred to as sub studies. Finally, it was anticipated that the patients in this study will be investigated at multiple occasions thereby generating a possibility to have study arms with treatment intervention. The final end-points of this study are still to be determined but are likely to focus on cardiovascular events.

The issue of financing of the work is yet to be determined. However, as a consequence of a steadily growing study cohort it is expected that financing opportunities will be identified on both national and international levels, e.g. the European framework program FP7, national funding programs, industry etc.

Upon closing of the meeting it was decided that a draft study protocol would be completed and presented at the Marburg Sleep Meeting in April 2006.

WG1 Activities 2006

WG1 meeting in Marburg, April 6, 2006
This meeting was held in conjunction with the international symposium “Sleep and the Cardiovascular System” in Marburg, Germany. The WG was presented with an update of a State of the Art paper on OSA and CV disease submitted to the ERJ by McNicholas and Bonsignore.

The remainder of this WG1 meeting dealt with further aspects of the planned multi centric study previously outlined at the Milan meeting. A draft study outline had been prepared and an inventory was made prior to the meeting on the current investigated patient volumes at each centre. Among the 10 centres there were approximately 8000 referrals yearly and in the order of 3000 new cases with obstructive sleep apnoea will be diagnosed. The centres jointly produce approximately 3000 PSG recordings and 3600 polygraphic recordings per year and
in the excess of 2100 pts/y will receive CPAP treatment. Approximately 450-500 patients are allocated to other treatment modalities including surgery.

It was agreed that the study starting phase alone (anticipated to be approximately 1 year) will require a financial input and commitment from each centre in order to cover the costs for local data management and potentially slightly modified and expanded clinical routines. Additional funding from an external industry source (ResMed Inc.) had been identified. This additional funding would enable joint organizational work including building of a web based report form, space and quality assurance of a joint data base and support a study monitor to initiate all participating centers. Additional funding of the study will be attempted once procedures have been initiated and a significant database has been generated. Further discussions dealt with the formation of the joint study committee which essentially will contain two representatives from each participating center. An initial discussion dealt with ethics review board requirements in the different countries. National regulations on data base information storage may differ between participating countries and these issues need to be reviewed.

It was decided that a draft protocol would be prepared by the Gothenburg group and that the outline would be presented during a meeting held in Brussels, July, 2006.

The European Society of Hypertension presentation, Madrid, June 13, 2006
A symposium at the annual ESH meeting was organised in collaboration with the Cost action B26 on OSA by G. Parati (Milan, I). The topics covered Cardiovascular variability and prognosis (P.van de Borne, Brussels, B), OSAS and circadian cardiovascular regulation (P. Levy, Grenoble, F), OSAS, metabolic alterations and cardiovascular complications (F. Barbè, Lleida, E), OSAS, stroke and ischemic heart disease (K. Narkiewiz, Gdansk, PL) and OSAS treatment and outcome (W.McNicholas, Dublin, IRL). This meeting was well attended and covered the major topics to be addressed in the WG 1.

WG1 meeting in Brussels, July 3, 2006
The meeting in Brussels dealt solely with protocol details. A draft protocol had been specifically prepared for this meeting. Detailed issues related to patient recruitment, diagnostic methods to be applied, the web based report form, issues of good clinical trial practice and end points of the study were reviewed. It was further decided that the proposed data base format would be applicable and that preparations to generate a data base under the hospice of the Gothenburg University should be initiated. It was also decided that a contract intended to regulate availability to data and the database by each and every participant of the steering committee should be generated. A first formatted draft of the web
based questionnaire was demonstrated. It was decided that a further informal discussion relating to these issues would take place in conjunction with the European Respiratory Society meeting in Munich in September 2006.

**WG1 meeting in Munich, September 4, 2006**

This meeting again dealt with issues related to the multi centre study. The focus was now put on the study organization, in particular issues on organization structure, formation of the scientific board, study centre contracts, clinical research monitor and details on data base construction as well as financial issues. In addition, the meeting attempted to reach an agreement on the study design including study block contents, settlement of content, overall primary end-points, potential future and secondary endpoints, statistical considerations and insurance issues. The study project was officially labeled as ESADA – European Sleep Apnea Data Base. It was decided that the final steps to formalize the protocol should be completed prior to the planned brief meeting to be held in conjunction with the B26, MC meeting planned in Copenhagen, November 18, 2006. Finally, providing this time schedule could be met there is a plan to enter the first patients in the data base by January 2007.

It is concluded that a substantial part of the activities in WG 1 during 2006 have focused on the generation of the ESADA cohort. The planning has proceeded to the stage when initiation of the practical work is imminent. It is recognized that this process was enabled by the support provided by the COST action.

**WG1 Activities 2007**

This Working group 1 has held one separate meeting during the year. In addition there have been meetings and activities organized by the Management Committee that in part have covered aspects that fall within the scope of the Working group1. A considerable effort has also been put into the finalization of the ESADA study program – a collaborative initiative between European Sleep Centres aiming to generate data from a large joint cohort of patients referred to sleep laboratories (see also below).

1. **21-22 March, Milan, Italy**

An informal working meeting that gathered Marisa Bonsignore, Jan Hedner, Ludger Grote, Carolina Lombardi and Gianfranco Parati. This meeting aimed to formalize and approve a format for presentation of COST guidelines during an ESH Workshop scheduled for the June 2007 ESH Congress in Milan (June 16, 2007). This workshop was subsequently held with a good attendance. The Milan meeting also generated the framework and timetable for a Guidelines manuscript intended for double submission to the Journal of Hypertension and the European Respiratory Journal. The Writing Committee was appointed and the work on
this manuscript has continued throughout the year.

2. 30 November-1 December, Düsseldorf, Germany
A second and more specific meeting of the WG was held in association with the joint ERS/COST Research Seminar on "Metabolic Aspects of the Obstructive Sleep Apnea Syndrome (OSAS)" in Düsseldorf in November. This meeting specifically dealt with practical aspects of construction and maintenance of the ESADA cohort. The meeting was attended by 12 WG members.

The ESADA (European Sleep Apnea DAtabase) programme.
The ESADA web based report format was launched in April but the first patients outside Gothenburg were not included until September. Two study nurses from the Gothenburg team have visited all sites during the autumn in order to provide maximum alignment of reporting strategies. Altogether 20 sites are currently listed and contribute to the data base. By November the database included 219 patients and this number was more than doubled to reach approximately 240 by the end of the year. The current recruitment speed suggests that the target of 1000 patients during the first year will be reached. Recruitment is still skewed between centres but the somewhat low numbers at some centres could mainly be explained by the extended start-up processes. The last few months of work has also been devoted to the initiation of two sub studies which were originally identified during the early start up process. These sub studies will be linked to the main data base and will include paediatric patients and a blood bank for future genetic analyses.

The initial start-up phase of this cohort has mainly been funded by seeding money from the industry. There are plans to generate an application for the EU frame programs providing the first year recruitment goal is reached.

WG1 Activities 2008

This Working group 1 (Chair, Jan Hedner) held one formal meeting during 2008. The continued focus of the working group has been devoted to further development and refinement of the ongoing collaborative multi centric European Sleep Apnea Database (ESADA, see also below). A separate phone conference dealing with procedures in the ESADA study program was held in October. The ESADA work has generated a number of sustained networks between centers participating in the program and thereby a high number of direct informal contact between centers.

The previously initiated work to produce a Guidelines manuscript on hypertension in sleep apnea intended for double submission to the Journal of Hypertension and the European
Respiratory Journal has continued and the project has entered into the final publishing phase.

**WG1 meeting, Brussels, June 30 2008**

Formation of ESADA study committee and introduction of new WG members. Issues on expansion of recruitment outside the B26 group and expansion of cohort by entering retrospective data were discussed. The ESADA cohort has grown considerably during the year from approximately 430 patients to reach almost 3000 patients by the end of 2008. The monthly recruitment rate is currently between 200 and 300 cases. There are 25 European sleep centers that continuously feed patients into the data base. There is an ongoing quality audit of materials entered into the data base in Gothenburg and it has been decided that a first interim analysis should be performed during the spring 2009. The study committee will decide on the practical aspects of this procedure. The ESADA sub study that involves sampling of materials for genetic analysis will be expanded during 2009.

Financing of the study is still incomplete. The study committee is searching for continued industry seed financing and continued support from the COST action would enable this process. A proposal for the FP7 program has repeatedly been discussed and suitable topics are actively searched for.

**Consensus document on hypertension in obstructive sleep apnea patients**

The Writing Committee for this document was formed in 2007 and the work has continued throughout 2008. The document will be published in two versions: a long one, for which the publication of a book is planned, and a short one, which will be a journal article. The former is ready, and offers from different publishers are currently evaluated by the COST Office. The short article version could be published by the official journals of the European Society of Hypertension (ESH) and the European Respiratory Society (ERS).

**WG1 Activities 2009**

The principal activities of WG1 during 2009 was the continuing recruitment to the ESADA cohort study. The recruitment rate stabilised in the region of 500 new enrolments per quarter and close to 5,000 patients were enrolled by end 2009.

At the WG meeting in Palermo held in October 2009, planning was initiated to write several cross-sectional reports concerning various aspects of the ESADA cohort, particularly the relationship of OSA with hypertension, demographics of OSA in Europe, and the relationship of professional driver licencing to OSA.

The writing of the Consensus document on hypertension in obstructive sleep apnea patients
was completed during 2009 and a publisher for the long version to be published as a book was selected. Publication will be in Spring 2010. The writing committee next plans to produce a shortened version suitable for publication in a journal. Agreement has been reached to publish in the official journals of the European Society of Hypertension (ESH) and the European Respiratory Society (ERS), namely the Journal of Hypertension and the European Respiratory Journal.

6.2 WG2: Medico-Legal Implications of Obstructive Sleep Apnea

WG2 Chair: Daniel Rodenstein

WG2 2005 activities report

After the initial meeting of the Action on 31 May 2005, WG2 participants met in December 2005. An informal updating meeting was also held in conjunction with the 2006 Annual European Respiratory Society meeting in Copenhagen, Denmark.

- 31 May 2005, Brussels, Belgium.
  First formal meeting of the MC core members. The WG2 was launched to specifically address the medico-legal implications of obstructive sleep apnea, with a special regard to driving accidents. The WG2 Chair (Daniel Rodenstein) and Vice-Chair (Emilia Sforza) were elected.

- 19 September 2005, Copenhagen, Denmark
  Informal discussion about initiatives to be undertaken by WG2 participants. It was agreed to:
  a) revise the Task Force paper on “Traffic regulation throughout Europe” published in 2002;
  b) invite Dr. CF George, Canada, who is an expert in the field, to join the Action as a participant of a non-COST Country;
  c) establish a reliable protocol and instrument to evaluate daytime sleepiness either in the laboratory or while driving/working;
  d) set a minimum set of criteria for accreditation of Sleep Laboratories in EU Countries.

- 5 December 2005, Milan, Italy
  The European Respiratory Society Special Task Force document: “Public health and medico-legal implications of the obstructive sleep apnea syndrome (OSAS)”, prepared by Jean Krieger and Walter McNicholas and published in the Eur Respir J in 2002, needs to be updated about driving license regulations in Europe since the issue of traffic accidents is a major topic in OSAS. WG2 members unanimously proposed to invite J. Krieger to join the
group as the second French representative. A draft standard questionnaire was prepared for each country delegate to fill-in concerning driving license regulations, especially centred on the issue of sleepiness and specifically on OSAS. The group agreed to aim, on the basis of this questionnaire, at completing a full report by end of June 2006 yielding updated information on all 25 EU Countries.

**WG2 2006 activities report**

During 2006, Working Group 2 prepared a position paper on driving license medical regulations in the European Union. The main activities concentrated in obtaining the national medical regulations for driving license obtention, withdrawal and relicensing. Of the whole European countries, we obtained data for 23 countries plus Norway and Switzerland. Only Latvia and Cyprus are missing.

The main conclusions are that there is a great heterogeneity in medical requirements, and that obstructive sleep apnoea, probably the disease carrying the greater risk for traffic accidents, is taken into account in only a minority of countries. Moreover, the attitudes in case of diagnosis in a licensed driver are very variable from country to country with respect to the driving capacity, the physician responsibility and duties, and the intervening authorities. Working Group 2 considers that a European Directive is urgently needed to unify the criteria on the effects of obstructive sleep apnoea on driving abilities, and to put sleep apnoea at the forefront of the diseases to be considered within the framework of driving license regulations.

The preliminary results were presented at the 2006 annual Congress of the European Respiratory Society in September 2006 in Munich. The European Respiratory Society selected this abstract as important for the lay press, and several press accounts were published/aired in several European countries (among them Belgium and France).

Working Group 2 prepared a full manuscript which is now ready for final reading and approval by the group and then the Management Committee before being sent for publication.

Working Group 2 was happy to receive collaboration and support from Pr. Jean Krieger, and Drs. A. Sanna and F. Fanfulla.
WG2 2007 activities report

As agreed in previous meetings, the manuscript on ‘Medico-legal implications of sleep apnoea syndrome: Driving license regulations in Europe’ was completed with the comments and remarks of all authors, and was accepted for publication in Sleep Medicine. The citation follows:


Following the last meeting in Copenhagen, the Working Group 2 had agreed to organize a working meeting during 2007 to try to improve the situation of the European legislation concerning sleep apnoea and driving. I invited a number of international experts, as well as all members of the Management Committee of COST Action B-26. Fortunately, most people answered enthusiastically, as if the right time to treat this subject had come. We had the great chance to be joined by a representative from the Belgian Ministry of Transport, as well as from M. Joël Valmain, from the Transport Directorate of the European Union. The list of attendees and their countries is joined in the appendix.

The meeting was held on October 12th – 13th 2007 at the Cliniques universitaires Saint-Luc (Université catholique de Louvain) in Brussels and was organized by the Center for Sleep Medicine of the Cliniques, supported financially by COST. The format was one of open sessions, with short introductions made both by some members of COST Action B-26 and by the external Invited Experts, followed by lengthy and vivid discussions. Several matters were agreed upon as, for instance, to tackle first sleep apnea but to join to it all sleep disorders inducing pathological sleepiness; to include sleep apnea in the curriculum of the continuous education for professional drivers to be implemented in the next years; to propose that sleepiness be included in the Police Forms to be completed after serious traffic accidents.

The meeting can be considered as successful on several grounds: Prof. Peretz Lavie, new Chief Editor of the Journal of Sleep Medicine, invited us to submit a manuscript on the meeting to be considered for publication in the Journal; Prof. Daniel Rodenstein was invited to a plenary session of the Transport Committee of the European Union in early November to present a short introduction on the subject of sleepiness, sleep apnea and road safety. This seems to have attracted quite a level of interest, as many representatives of Member States
made comments and remarks following the presentation. It is hoped that during 2008 the Directorate of Transport of the European Union will take action to include sleep apnea in the Annex III of the Directive 91/439/EEC on Driving License Regulations.

At the same time, the European Society for Sleep Research decided to devote one session during its next annual Congress in Glasgow to the issue of Driving License Regulations. Finally, Prof. Daniel Rodenstein has been invited to participate in a meeting on the same subject to be held during next Annual Congress of the American Thoracic Society in Toronto in May 2008.

**WG2 2008 activities report**

The focus of WG2 activities during 2008 was on the subject of sleep apnea and driving risk and the related topic of driver licensing regulations.

The WG2 chair, Daniel Rodenstein, made invited presentations to a number of international conferences on this topic:

- **Sleep, Sleep Apnea and Driving Risk.** American Thoracic Society workshop held in Toronto, on May 16th, 2008, chaired by K. Strohl.


- **Presentation on Sleep Apnea and Driving in Europe.** Spanish Sleep Society Annual Meeting, Palma de Mallorca, June 21-24, 2008.

- **Driving and Sleep.** Scientific Meeting organized by Comisiones Obreras, Spanish Workers Union. D. Rodenstein, President. Burgos, Spain, November 13th, 2008.

**WG2 2009 activities report**

During 2009, continued efforts were made to promote the issue of Sleep, Sleep Apnea and driving risk.

Some difficulties were encountered in engaging with EU officials because of changing personnel but efforts are ongoing.
During 2010, contact has been re-established with the EC, Directorate 4, and that something may finally be considered in the next future in relation to sleep apnea and driving license regulations.

WG2 has maintained an input to the ESADA cohort study and anticipates producing a report during 2010 on driving practices in Europe, particularly among professional drivers.

Several publications on this topic were published by B26 members during 2009:


2. Assessment of sleepiness. Gimbada BM, Rodenstein D. Arch Bronconeumol. 2009 Jul;45(7):349-

6.3 WG3: GENETICS AND EPIDEMIOLOGY OF OBSTRUCTIVE SLEEP APNEA

WG3 Chair: RL Riha

WG3 2005 activities report

WG3 participants met in May and December 2005.

1. 31 May 2005, Brussels, Belgium.
First formal meeting of the MC core members. The WG3 was launched to specifically address genetics and epidemiology of obstructive sleep apnea in Europe. The WG3 Chair (Renata Riha) and Vice-Chair (Poul Jennum) were elected.

2. 5 December 2005, Milan, Italy
WG3 discussed research priorities for both genetic and epidemiology of OSAS.

**Genetics:**
The following points were discussed: a) Establishment of a directory of National Centers able to participate in genetic research in OSAHS with their capabilities and their interests; b) Establishment of an international (COST) directory of participants, lab facilities and research interests and expertise; 3) Reassessment of the failed STREP submission (GENOSA) and reworking to be submitted for FP7; 4) Genetics in children, given the increasing prevalence
of obesity also at very young age.

Future plans
- Organize a one-day workshop in collaboration with the European Society of Human Genetics, including speakers expert in the field of molecular biology, genetics and statistics;
- Prepare a Task Force paper outlining the current state of the art in genetics and issues to be addressed at a research level;
- Organize a COST workshop/training school for young scientist in 2006;
- Contact groups or Scientific Societies interested in research on children.

Epidemiology
Several relevant topics were identified: a) pathogenesis of symptoms (and of absence of symptoms) in subjects with sleep apnea: revision of current definition of sleep apnea and sleep apnea syndrome; b) relationship between respiratory and other measures (e.g. AHI) associated with morbidity; c) Identification of individuals susceptible to sleepiness; d) Markers of severity; e) Patient evaluation and follow-up studies vs population studies; f) Consequences of sleep apnea at different ages; g) Adequacy of current sleep apnea diagnosis and organizational aspects.

WG 3 2006 Activities report

This was a difficult year due to illness.
However, the group did accomplish some goals in promoting genetic research in sleep apnoea:
1. Organisation of a one-day symposium in Copenhagen (17.22.2006) looking at the Genetics of Cardiovascular disease in the context of Obstructive Sleep Apnoea. (see appendix with programme).
2. Collaborative work between Scotland and Poland in terms of grant applications for future work in this area.
3. Scholarship application to the ERS for Poland from Scotland
4. Support of WG1 group in terms of the proposed database and expansion in the future of a genetic component.
5. Publications in the area of genetics (see attached list and individual contributions from WG and MC members).
6. A position paper on Cardiovascular Genetics in the Sleep Apnoea Syndrome has been commissioned to be delivered for 2007 on behalf of WG3 and COST B26.
Future plans

a) Prepare a paper on new or still unsolved research topics in epidemiology to be submitted to a Sleep or a Respiratory Journal;

b) Questionnaire study to obtain information on diagnostic procedures, treatment, organizational aspects including socio-economical ones adopted for OSA patients in different European countries. Focus on consequences of sleep apnea versus the current capacity and organization; accreditation of sleep apnea centers (in collaboration with WG2).

WG 3 2007 Activities report

Working group 3 has been relatively quiet this year. After the successful symposium held in Copenhagen in November last year, we have focussed on commissioning papers from the excellent presentations given at that meeting.

To this end, we have been successful in obtaining a commitment from the European Respiratory Society for running a series entitled:

*The Genetic and Cardiovascular Aspects of the Obstructive Sleep Apnoea/Hypopnoea Syndrome: State-of-the-Art*

(Series editors: RL Riha and WT McNicholas)

Proposed topics and authors to be serialised over 6 months in 2008 are as follows:


2. *Epidemiology of OSAHS in relation to the design of genetic studies* – Poul Jennum et al.

3. *Phenotype and Genotype in OSAHS* – Renata Riha, Konstanze Diefenbach, Thorarinn Gislason

4. *Cardiovascular disease in OSAHS: the role of hypoxia and inflammation* – Walter McNicholas, Cormac Taylor

5. *Molecular mechanisms of cardiovascular disease in OSAHS* – Lena Lavie

6. *Candidate genes for hypertension in OSAHS* – Javier Navarro – Antolin and Patricia Munroe

7. *Metabolic syndrome and OSAHS* – Marisa Bonsignore and Patrick Levy

The Working Group has also focussed on developing a protocol for genetic sub-studies from the ESADA project. This will be circulated to members for adapting to their own place of work.

Furthermore, the group has had a review paper re: the genetics of hypertension and
metabolic syndrome in OSAHS accepted for publication by Sleep Medicine Reviews.
In anticipation of next year’s scientific activities, we have had a proposal accepted for hosting a symposium on Paediatric Sleep Apnoea next year in Antwerpen (November 2008).
There were no short term scientific missions sponsored by COST per se, but a short-term training fellowship from the ERS allowed an exchange visit for a Polish Fellow from Warsaw to the Department of Sleep Medicine in Edinburgh, Scotland.
We look forward to completing and extending some of our activities next year and embarking on making concrete the genetic sub-studies on the European cohort of sleep apnoea patients.

WG 3 2008 Activities report

The European Respiratory Journal series on The Genetic and Cardiovascular Aspects of the Obstructive Sleep Apnoea Hypopnoea Syndrome was finalised, which includes 6 papers based on the symposium held in Copenhagen in November 2006. This series will begin publication in the ERJ in February 2009.
Additionally, a protocol was developed for blood storage for genetic samples as part of ESADA database and this will be sent to all members in January 2009.
WG3 was approached by Thorarinn Gislasson and Alan Pack to form an International Genetics Consortium and this was discussed at the MC in November 2008 in Antwerp. All contributors of genetic material to the ESADA database will be included in this.

WG3 was invited to put in a grant application to the Wellcome Trust for genome-wide scans in OSAHS together with Allan Pack, Lyle Palmer and Martin Tobin in which the ESADA database would play a crucial role. The WG3 chair, Renata Riha, is listed as co-applicant representing WG3 and COSTB26 and this represents an opportunity for all contributors to ESADA to eventually have their names in the project. No decisions will be made without full consultation with all members contributing material to the database. If funded, the project will allow all samples to be accepted in Edinburgh, with funds for storage and to have DNA extracted in a timely manner. This will take the burden of extraction costs from participating centres.

WG 3 2009 Activities report

The European Respiratory Journal series on The Genetic and Cardiovascular Aspects of the Obstructive Sleep Apnoea Hypopnoea Syndrome was published as a sequential series of 6 review articles during 2009 and is now complete. The series has proved very
successful and several articles are already being frequently cited in other papers as authoratative state of the art reviews on the topic.

The genetic component of the ESADA project progressed during 2009 and several hundred samples were placed in storage by end 2009. It is anticipated that recuitment will continue and it is hoped that several thousand samples will ultimately be available for genetic studies.

7. LIST OF PUBLICATIONS (in Annex I)

8 CONFERENCES AND WORKSHOPS

Conferences and Workshop in 2005-2006

The MC took the following initiatives, with the aim to promote exchanges among Scientists in the field and increase the visibility of the Action at different levels:

- The COST Action B26 endorsed the Satellite International Workshop on “Cardiorespiratory effects of hypoxia: from high altitude to bedside”, held in Milan, on June 16, 2005, in conjunction with the 15th Meeting of the European Society of Hypertension, organized by the European Society of Hypertension Working Group on Blood Pressure and Heart Rate Variability (EURO-BAVAR). The rationale for such support is that OSAS causes nocturnal intermittent hypoxemia, due to the cyclic occurrence of apneas during sleep. A similar situation also occurs at high altitude in healthy subjects due to periodic breathing in response to exposure to hypobaric hypoxia;

- The COST Action B26 was presented by Maria R. Bonsignore in a Symposium of the Meeting of the German Society of Sleep Medicine (DSGM), which was held in Berlin on October 14, 2005, in conjunction with the First Congress of the World Association of Sleep Medicine (WASM), Berlin, October 15-18, 2005. Initiatives similar to the COST Action B26 have been planned by the European Society of Sleep Research to increase the awareness of OSAS in EU policy makers and general public;

- The COST Action endorsed the Meeting on: “Sleep and the Cardiovascular System” organized by Prof. Thomas Penzel in Marburg, Germany, on April 6-8, 2006. On that occasion, WG1 and WG3 met to discuss current and future activities (see individual WG reports).

- The COST Action actively participated in the Meeting “X Hot Topics in sleep apnea
syndrome” organized in Lleida, Spain by Ferran Barbé and SEPAR (Sociedad Española de Neumología y Cirugía Torácica) on May 5-6, 2006. All sessions were accessible on line through the web and were interactive, allowing the possibility to ask questions to the speakers from any place in the world.

- COST WG2 actively participated in the International Conference: “Monitoring sleep and sleepiness – from physiology to new sensors”, jointly organized by the FP6 Integrated Project SENSATION*, the European Sleep Research Society, held in Basel, Switzerland, on May 29-30, 2006. COST B26 WG2 presented preliminary results on current legislation regarding sleepiness and driving license in EU Countries.

- Active collaboration was established between the COST Action WG1 and the European Society of Hypertension (ESH). In particular, a Teaching Session was held at the 2006 ESH Meeting in Madrid, Spain, 12-16 June 2006. In addition, a Research Seminar could be organized in Marburg in 2007 in collaboration with the European Society of Cardiology (ESC) to increase awareness about sleep apnea and cardiovascular risk among ESC members.

- A one day symposium on Genetics of Cardiovascular disease in OSAS was held in Copenhagen, Nov 17 2006, in conjunction with management committee and working group meetings (see appendix). This symposium provided the basis for a comprehensive review and discussion of this rapidly developing area between COST B26 members, outside invited experts, and other scientists with an interest in this topic. A review paper based on this symposium will be published in a leading international journal by special invitation from the Chief Editor.

Conferences and Workshops in 2007

- A Joint Symposium between COST B26 and European Society of Hypertension was held in June 2007 during the annual meeting of that society in Milan.

- A Symposium on sleepiness and driving was organised in October 2007 by Working Group 2. This symposium was a development from the position paper on Medicolegal aspects of driving risk in patients with OSAS that was approved by the Management Committee in November 2006 and is now published by the journal Sleep Medicine.

- A Research Seminar was held on Nov 30 – Dec 1 in Dusseldorf on Metabolic aspects of Sleep Apnea Syndrome. This seminar was jointly organised with the new COST Action on Adipose Tissue Metabolism and also with the European Respiratory Society.

Other Activities in 2007.

- The European Sleep Apnoea Database (ESADA) was fully established in mid 2007 and is now actively recruiting. To date, over 500 patients have been entered and the rate of entry
is rapidly growing. Recruitment to the database will continue through 2008.

- COST B26 is currently preparing a consensus document on hypertension and sleep apnoea syndrome and the project has been officially endorsed by the European Respiratory Society and the European Society of Hypertension. This consensus is expected to be finalised by end 2008.

**Planned Activities for 2008:**

- The ESADA project will continue through 2008 and into 2009. It is expected that the bulk of recruitment (minimum 5,000 patients) will be completed by end 2008.
- There will be at least one meeting of the steering group responsible for the consensus document on hypertension and sleep apnoea in the first half of 2008.
- A full Management committee meeting of Action B26 is planned for June 30 in Brussels that will be preceded by meetings of the individual working groups.
- A Research seminar on Paediatric Aspects of sleep apnoea is planned for November 2008 to be jointly organised between Action B26 and the ERS.
- Action B26 has endorsed the meeting “Hot Topics in sleep apnea syndrome” organized in Lleida, Spain by Ferran Barbé and SEPAR (Sociedad Española de Neumología y Cirugía Toracica) on April 25-26, 2008.

**Conferences and Workshops in 2008**
A Research Seminar was held on Nov 20 – 22 in Antwerp, Belgium on Paediatric aspects of Sleep Apnea Syndrome, and organised by Prof. Wilfried de Backer. This seminar was attended by over 100 participants and included invited speakers from Europe and USA.

**Planned Activities for 2009:**

- The ESADA project will continue through 2009 and into 2010. The recruitment of the target number of 5,000 subjects is expected to be completed by mid/late 2009.
- An international consortium involving Europe and North America on the genetics of sleep apnoea is currently under development, with WG3 taking a leading role.
- There will be at least one meeting of the steering group responsible for the consensus document on hypertension and sleep apnoea in the first half of 2009.
- A full Management committee meeting of Action B26 is planned for April 27 in Brussels that will be preceded by meetings of the individual working groups.
- A Research seminar on “Intermittent hypoxia and adipose tissue: insight into the pathophysiology of the Obstructive Sleep Apnea Syndrome (OSAS) and treatment options”
is planned for Autumn 2009 to be jointly organised between Action B26 and the ERS.

Conferences and Workshops in 2009

A Research Seminar was held on October 16-17 in Palermo, Italy on the interactions between intermittent hypoxia and obesity. This seminar was jointly organised with the COST Action on Adipose Tissue Metabolism and also with the European Respiratory Society.

MR Bonsignore participated in the Greek national sleep conference in Athens from 30. Oct. 2009 to 1. Nov. 2009 where she presented the COST Action B26 and the Sleep lab accreditation.

Conferences and Workshops in 2010

- End of Action Meeting, Prague, June 2010.

PRAGUE FINAL COST B26 SYMPOSIUM (25 – 27 JUNE 2010)

PROGRAM

FRIDAY 25TH JUNE
Chairpersons: Martin Pretl and Renata Riha
14:00 INTRODUCTORY REMARKS AND WELCOME – Marisa Bonsignore
14:15 LET’S START WITH CHILDREN
SCOPE OF THE PROBLEM OF OSAHS IN CHILDHOOD – Athanasios Kaditis
14:45 PHENOTYPING OSAHS IN CHILDREN – Wilfried de Backer

15:15 Afternoon tea

16:00 OSAHS AND HEART FAILURE – AN UPDATE – Ruzena Tkacova
16:30 HOW DO WE MEASURE OSAHS ACROSS EUROPE? – Ingo Fietze
IS THERE AN ARGUMENT FOR STANDARDISATION OF PRACTISE ACROSS COUNTRIES?
17.00 DRIVING REGULATIONS RE: OSAHS ACROSS EUROPE – Thomas Penzel

17:45 END

19:00 ”PARTY ON THE VLTAVA RIVER”

SATURDAY 26TH JUNE
Morning Session
Chairpersons: Patrick Levy and Jan Hedner
09:00 CVS DISEASE AND OSAHS – THE EVIDENCE CONTINUES – Walter McNicholas
09:30 SUMMARY OF THE EUROPEAN HYPERTENSION GUIDELINES IN OSAHS – Gianfranco Parati and Carolina Lombardi

10.15 Morning tea

10:30 CARDIOVASCULAR AND METABOLIC PROBLEMS IN CHILDREN WITH OSAHS – Stijn Verhulst
11:00 THE ROLE OF OBESITY IN OSAHS - AN UPDATE – Marisa Bonsignore
11:45 EVIDENCE LINKING THE METABOLIC SYNDROME WITH OSAHS – Patrick Levy

12:30 Buffet lunch

Afternoon session
Chairpersons: Josep Montserrat and Marisa Bonsignore
13:30 LESSONS ABOUT METABOLIC SYNDROME FROM OTHER SLEEP DISORDERS – Francesca Poli
14:15 INFLAMMATION AND OXIDATIVE STRESS IN OSAHS – AN UPDATE – Lena Laviel
15:00 GENETIC STUDIES IN OSAHS – STATE OF PLAY - Thorarinn Gisslasson

15:30 Afternoon tea

15:45 OSAHS AND THE ELDERLY – Mary Morrell
WHAT DO WE KNOW?
WHAT ARE THE IMPORTANT QUESTIONS?
16:30 ESADA – Jan Hedner
HOW DID WE GET HERE?
WHAT ARE THE RESULTS SO FAR?
WHERE TO NEXT?
17:30 CONCLUDING REMARKS ON B26 AND FUTURE DIRECTIONS – Walter McNicholas
18:00 END

19:00 BEER PARTY "U MEDVÍDKŮ"

SUNDAY 27TH JUNE
09:00 – 12:00 FINAL MEETING OF THE MC COST ACTION B26

9. Action Website
The Action website has been established and is currently maintained and updated with the latest news from COSTB26.

Maria R Bonsignore is in charge of setting and supervising it.

The website will facilitate interaction among Action members and will also assist in the dissemination of reports and other Action outcomes.

The website has got two main sections (see the left column menu of the website):
1) Generic information about the Action such as Background, Objectives and Benefits, Scientific Programme, Timetable and Organization, Added value of the action, Economic
Dimension, Dissemination

2) Details about the Action such as Memorandum of Understanding, Members of the Management Committee, Scheduled MC Meetings, Minutes of the MC Meeting, Working Groups, Scheduled WG Meetings, Annual Reports, Short Term Scientific Missions (STSMs), Relevant Links, Patient Organizations, COST Related Events. Every item of the second section is regularly updated by using a back office web application thus providing the most updated news regarding the action and its developments.

10. Scientific and Technical Cooperation

All these indicate new ongoing collaborations which have arisen due to the Action.

Collaborations have been established with several major European Societies as detailed in individual Working Group reports above. These include the European Respiratory Society and European Society of Hypertension resulting in several joint stand-alone meetings (Dusseldorf 2007 and Palermo 2009). Furthermore, several joint symposia were held in conjunction with both Societies during their annual conferences including ESH in 2006 and 2010, and ERS in 2010. Finally, the Consensus Document on hypertension and OSAS represents a joint project between COST Action B26 and both ERS and ESH.

Furthermore, the planned European multi-centre cohort study will provide a solid framework for active scientific co-operation between a large number of European sleep centres. The details of this co-operation are provided in the report of WG1 above. **Developments during 2008 included moves towards inter-continental co-operation in the study of genetic aspects of OSAS with the European component of this co-operation predominantly driven by WG3 of COST Action B26.**

Collaborations between Action B26 members: **Collaborative project on genetics of metabolic comorbidities in patients with OSA.**

**Partners:** Tkacova R, Department of Respiratory Medicine, Faculty of Medicine, P.J. Safarik University and L. Pasteur Teaching Hospital, Rastislavova 43, Kosice, Slovakia; Riha R, Department of Sleep Medicine, Royal Infirmary Edinburgh 51, Little France Crescent EH 164 SA, Scotland.

**Aim of the project:** To analyse CETP, PPARG, and LPL gene polymorphisms with respect to cholesterol (total and HDL) and glycaemia/HOMA index in patients with/without OSA.

**Progress:** The aim is to collect and genotype 500 samples of subjects examined in the Sleep research laboratory at the Department of Respiratory Medicine, Faculty of Medicine, P.J.
Safarik University in Kosice. Samples from 270 patients were already analysed. Recruitment is expected to end in July 2011.

**Vision:** This project represents a pilot study that might contribute to further genetic analyses in the entire ESADA cohort.

**2009-2012 MRC-HTA Multicentre Trial (£ 1.5 million)**

**PREDICT: Positive airways pREssure in older people: a ranDomised Controlled Trial**

*Principal applicants: RL Riha, MJ Morrell with* Prof. RJO Davies, Prof. AJ Nunn, Prof. M Sculpher, Ms S Griffin, Dr JM Starr

Prof Walter McNicholas (COST B26 MC) is Chair of the Trial Monitoring Committee.

**Collaboration with members of other COST Activities at the national level.** Slovakian members of COSTB26 Action collaborate with members of the COST FA0602 Action Bioactive food components, mitochondrial function and health (MITOFOOD) at the national level

11. **Transfer of results**

- A detailed position paper on scientific topics on OSAS and cardiovascular risk has been published by the European Respiratory Journal in Jan 2007. This paper has become the second most highly cited paper published by the journal since 2007.
- A similar paper, specifically addressed to EU Policy Makers has been submitted during 2008 to the EU Commission in order to underline Public Health issues related to sleep apneas.
- A detailed update on traffic regulations in Europe has been published by the journal Sleep Medicine (see WG2 report).
- A further paper, based on the seminar held in Brussels, October 2007, has been published in the Journal of Sleep Reserarch during 2008
- A series of review papers based on the Action’s participation in the European Society of Hypertension meeting in Madrid (see above) has been published by the American Journal of Physiology in 2007
- WG3 has published a position paper on current status of OSAS genetics and epidemiology research in Europe in the journal Sleep Medicine Reviews in 2008, to identify topics for future initiatives at the EU level.
- WG3 has also produced a series of papers, based on the 2007 Genetics in OSAS symposium held in Copenhagen, that was published during 2009 in the European Respiratory Journal.
- A series of papers is planned for the Journal of Sleep Research based on the symposium on Paediatric OSAS, held in Antwerp in November 2008.
- An original paper based on sleep medicien practices throughout Europe is currently under revision for the journal Sleep Medicine.
- A series of original papers based on the first 5,000 patients in the ESADA cohort are currently either submitted or in an advanced stage of preparation.
- A book containing the Consensus document on the management of patients with obstructive sleep apnea and hypertension has been published with the support of COST.
- A monograph on Sleep Apnoea will be published by the European Respiratory Monograph in Dec 2010.

12 SELF EVALUATION

Successes
- The Action B26 is the first large initiative at the European level dedicated to the Obstructive Sleep Apnea Syndrome.
- The Action has facilitated the establishment of a large Network of Sleep Centres throughout Europe which has encouraged the implementation of common standards and procedures for clinical practice and research.
- Scientists from several COST Countries worked together to establish common protocols for clinical and basic research projects and to provide European guidelines for diagnosis and treatment of OSAS.
- A large-scale European study of OSAS (ESADA) was established which contained uniform and standardised details on a large cohort of patients suspected of OSAS. Over 7,000 patients were in the database by the end of Action B26 but the study will continue for the foreseeable future with an ongoing recruitment rate of c. 500 patients per calendar quarter.
- Major Guidelines on the management of patients with OSAS and Hypertension were published by the Action, in collaboration with the European Respiratory Society and the European Society of Hypertension.
- Several major publications have been produced by the Action, or are underway.

Drawbacks
No particular drawbacks were identified.

Key difficulties
No difficulties have arisen.

III. Evaluation Report prepared by the “ad hoc” Evaluation Panel established by the Domain Committee and edited by the COST Office (approximately 2 pages)
1. Evaluation panel and evaluation procedures

Dr Jaroslav Vesely: Pathological Physiology Medical Faculty Palacky University, Olomouc, Czech Republic, Tel. +420 (0)585 632 501-2, vesely@lf.upol.cz

Dr Jozef Molnar: Institute of Medical Microbiology and Immunobiology, University of Szeged, Hungary, Tel: 36 62 545 114, Fax: 36 62 545 113, molnarj@comser.u-szeged.hu

Documents used: final report, publications, website

2. Results versus objectives

The objectives of the COST Action B26 were (i) to assess the role of the obstructive sleep apnea syndrome (OSAS) in increased cardiovascular risk; (ii) to coordinate studies on pathogenic mechanisms of OSAS (i.e., inflammation, oxidative stress, endothelial dysfunction, metabolic derangements, altered autonomic control associated with exposure to intermittent hypoxia) and its genetic aspects. Secondary objectives were (i) to promote exchanges between national groups in diagnosis and treatment of OSAS and (ii) to address medico-legal implications of OSAS as well as excessive daytime somnolence (EDS) aiming at prevention of car accidents associated with OSAS and EDS.

The following principal outcomes demonstrate this action as matching the above objectives successfully:

1. Extensive number of publications, involving over 40 joint publications, in particular. Notably, the publications include a series of extensive reviews in high-ranked journals, book chapters and a monograph with high impact in the field.

2. Extensive interdisciplinary activities represented by several research and teaching symposia including Genetics of OSAS (2006), Metabolic Aspects of OSAS (2007, together with Action BM0602), Paediatric OSAS (2008), and Intermittent hypoxia and adipose tissue (2009, together with BM0602). Importantly, these interdisciplinary activities fertilized research projects as well as a number of publications generated in the course of the Action.

3. A Consensus Document on Hypertension and OSAS (to be published in ERJ and J Hypertension).

4. A principal support this Action has provided to The ESADA (European Sleep Apnea Database) Network.

5. Furthermore, B26 facilitated a momentum for EU officials so that sleepiness and OSAS could be formally recognized in future Driving License Medical Regulations in the EU. Although this has not been followed through yet, interactions with Transport Directorate officials continue.

The major dissemination routes were (i) scientific publications including two books, as specified above; (ii) workshops, satellite workshops, joint stand-alone meetings, and/or joint symposia organized in conjunction with international meetings, also specified above; (iii) the Action B26 web pages. Of these, the publications and books represent the major dissemination route and demonstrate the success of the COST B26 Action.

The impact of the Action is impressive in several aspects:

1. An impressive feature of the Action to be highlighted is in how they evolved fruitful and branched multidisciplinary links when approaching the theme of OSAS. This found its expression in a number of high level scientific papers, books, meetings, joint symposia, and numerous contacts with professional medical societies.

2. Outcomes involve a list of over 40 joint publications, 2 books (monographs) published collectively by the group, over 700 journal publications, and almost 20 individual book chapters.

3. Important interdisciplinary research and teaching symposia were organized in the course of the Action including Genetics of OSAS (2006), Metabolic Aspects of OSAS (2007,
together with Action BM0602), Paediatric aspects of OSAS (2008), and Intermitent hypoxia and adipose tissue (2009, together with BM0602). The impulses elevated by these meetings have created appreciable motivation and extended the scope of this Action. This found its expression in a number of publications and in the monographs.

4. In addition, by means of organizing joint stand-alone meetings, satellite workshops, and/or joint symposia in conjunction with international meetings, the Action has been presented to and established efficient synergetic links with several major professional societies, including:
   a. World Association of Sleep Medicine
   b. European Respiratory Society
   c. European Society of Hypertension
   d. European Sleep Research Society
   e. European Society of Cardiology
   f. German Society of Sleep Medicine
   g. Spanish Sleep Society
   h. Spanish Society of Pneumology and Thoracic Surgery
   i. Spanish Thoracic Society
   j. Greek national sleep conference
   k. American Thoracic Society

5. The Action has provided a principal support to The ESADA (European Sleep Apnea DAtabase) Network. ESASA represents continuing collaboration between European Sleep Centers generating a cohort of over 7,000 patients to date. The project allows prospective follow-up of treatment outcomes. It is the largest European study and one of the largest global studies on OSAS.

6. B26 organized several symposia and facilitated a momentum for EU officials so that sleepiness and OSAS could be formally recognized in future Driving License Medical Regulations in the EU. Although this has not been followed through yet, interactions with Transport Directorate officials continue.

7. Six scientific missions, two of them being STSMs, were realised within the group in the period from 2006 to 2010.

4. Innovative networking and inter-disciplinary networking

1. The Action allowed continuous collaboration between 24 institutions from 20 EU countries plus Israel.
2. B26 Action synergies have been established with several major European Societies as detailed above.
3. COST Action B26 collaborative projects on genetics of several aspects of OSAS using a European multi-centre cohort study has provided a solid framework for active co-operation between a large number of European sleep centres as well as moves towards inter-continental co-operation in the study of genetic aspects of OSAS with the European component of this co-operation predominantly driven by Action B26.
4. The Action has provided a principal support to The ESADA (European Sleep Apnea DAtabase) Network. ESASA represents continuing collaboration between European Sleep Centers generating a cohort of over 7,000 patients to date. The project allows prospective follow-up of treatment outcomes. It is the largest European study and one of the largest global studies on OSAS.
5. COST Action B26 has recognized that a European Directive is urgently needed to unify the criteria on the effects of obstructive sleep apnoea on driving abilities, and to put sleep apnoea at the forefront of the diseases to be considered within the framework of driving license regulations. Although this task has not been followed through yet, interactions with Transport Directorate officials have been established and continue.

All these activities are well documented by an extensive list of publications. Those with the highest impact a exemplified, in the Final Report, as follows:

- A detailed position paper on scientific topics on OSAS and cardiovascular risk has been published by the European Respiratory Journal in Jan 2007. This paper has become the
second most highly cited paper published by the journal since 2007.
- A similar paper, specifically addressed to EU Policy Makers, has been submitted during 2008 to the EU Commission in order to underline Public Health issues related to sleep apneas.
- A detailed update on traffic regulations in Europe has been published in 2008. This has been followed by a series of papers in journals and meeting abstracts.
- A series of review papers based on the Action’s cooperation with the European Society of Hypertension has been published by the American Journal of Physiology. These reviews have been followed by a series of other papers.
- A position paper on current status of OSAS genetics and epidemiology research in Europe has been published in the journal Sleep Medicine Reviews, to identify topics for future initiatives at the EU level. This report has been followed by a series of other papers.
- An original paper based on sleep medicine practices throughout Europe is currently under revision for the journal Sleep Medicine.
- A series of original papers based on the first 5,000 patients in the ESADA cohort are currently either submitted or in an advanced stage of preparation.
- A book containing the Consensus document on the management of patients with obstructive sleep apnea and hypertension has been published with the support of COST.
- A monograph on Sleep Apnoea will be published by the European Respiratory Monograph in Dec 2010.

5. Coordination and management
Twenty one countries including Israel and 24 institutions were represented by 36 MC delegates.
MC meetings were organized regularly, twice a year, in the mean, mostly together with joint WG meetings.
The work has been organised in three Working Groups:
- WG 1: Cardiovascular complications in OSAS – Pathogenetic mechanisms and markers of increased cardiovascular risk.
- WG 2: Daytime somnolence and medico-legal implications of OSAS
- WG 3: Epidemiology and genetics of OSAS.
WG meetings were organized regularly, twice a year, in the mean, most frequently together with MC meetings. Of the three WGs, WG1 was the most active one.

6. Strengths and weaknesses
The following achievements can be highlighted, based on the Final Report, to document the quality of the management, level of the synergy, and general success of the B26 Action:
- The Action B26 was the first large initiative at the European level dedicated to the Obstructive Sleep Apnea Syndrome.
- The Action has facilitated the establishment of a large Network of Sleep Centres throughout Europe which has encouraged the implementation of common standards and procedures for clinical practice and research.
- Scientists from several COST Countries worked together to establish common protocols for clinical and basic research projects and to provide European guidelines for diagnosis and treatment of OSAS.
- A large-scale European study of OSAS (ESADA) was established which contained uniform
and standardised details on a large cohort of patients suspected of OSAS. Over 7,000 patients were in the database by the end of Action B26 but the study will continue for the foreseeable future with an ongoing recruitment rate of c. 500 patients per calendar quarter.

- Major Guidelines on the management of patients with OSAS and Hypertension were published by the Action, in collaboration with the European Respiratory Society and the European Society of Hypertension.

- Several major publications have been produced by the Action, or are underway.

**IV. DC General Assessment prepared by the Domain Committee**

DC comments on the quality of the Action in no more than one page. It should illustrate the "success story" (if applicable) of the Action, with concrete examples and names of persons who can be contacted for further details.