STATEMENT OF THE PROGRAMME RETIC COORDINATOR

RETIC CODE:
RD12/0026/0001

RETIC NAME: **RED DE SALUD MATERNO-INFANTIL Y DEL DESARROLLO**

RETIC PROGRAMME COORDINATOR: **ADOLF VALLS SOLER**

SCIENTIFIC AND TECHNOLOGICAL BACKGROUND OF THE PARTICIPATING GROUPS

Describe the major contributions focused on the area of the programme (publications, funding, technology transfer) of the different groups.

For 6 groups max. 3 pages, up to 10 groups max. 6 pages, up to 15 groups max. 9 pages

The major research contributions of the 12 Research Groups included in this proposal are briefly outlined, mainly in relation to the research program proposed. The profiles of their scientific activities in the last 5 years have been summarised by each group and thus, although heterogeneous, represent their views on their main achievements in the areas covered by the proposed research programme.

If more information is needed to evaluate the scientific background of all or any of the Research Groups, this is available at the "Instituto de Salud Carlos iii" (ISCiii), as part of the yearly and final evaluations of our network (Red SAMID) for the last four years.

Research Group 1. Neonatology Division at the Cruces University Hospital (Vizcaya)
Agency: Basque Foundation for Health Innovation and Research

SCIENTIFIC ACTIVITY: This Group acts as Coordinating Group of the RETIC as well as both, The Scientific and the Training and Educational programmes. The group in mainly centered on the two topics, all related to the proposed Research Programme:
1. Prematurity: Its causes, prevention and consequences, from 1) a epidemiological studies (Assisted Reproduction, Intrauterine Growth Restriction; 2) RCT: low molecular weight heparin in Eclampsia, effects of measuring cerebral oxygenation on outcomes; 3) animal models: nebulised surfactant, neuroprotection, and drug modeling (fentanyl and dobutamine).
2. Infection: 1) Epidemiological studies: Early diagnosis of candidiasis; 2) RCT: Prevention of nosocomial infection with a behavioral intervention.

Our Group maintains three platforms:
1) ***Animal models.*** The following models are available for all Research Groups: 1) Neonatal respiratory failure: RDS (foetal lambs), meconium aspiration (piglets); 2) Neuroprotection in asphyxia (piglets), hypovolemic shock (piglets), acute RDS 3). Several projects are ongoing (nebulised surfactant, neuroprotection with hypothermia and canabinol, drug modeling).
2) **Epidemiology:** The Group has a multidisciplinary team (neonatologists, epidemiologist, microbiologist, pharmacists, biostatistician and administrative staff are financed from multiple local, regional, national and European sources. It is specialist in paediatric RCT and coordinates the DG SANCO project (EuroNeoNet) and participates in to EC¨7thRP: GRIP (Global Research in Paediatrics) and NeoCirculation.
3) **Website:** It maintains the website: www.redsamid.net

FINANCIAL SUPPORT: The Group has received financing support from public and privet funding agencies for nine national and four international projects. The most important project with Spanish financing agency (ISCiii) has been the funds received as coordinators of the RETICS in Maternal and Child Health and Development, from 2009 to 2012 (total funds for the Network €2.5 million (nº Exp. RD08/0072).
At international level the projects are: two from DGSANCO: EuroNeoStat I and II (A/101106 and 2008131, 2006-12; two from the 7thRP; *GRIP (*UE09/GRIP261060), 2010-15 and Neo-Circ (health 2011.4.2-1 grant agreement nº 282533), 2011-15; and one from TEMPUS IV Programme: *Egyptian Neonatal Network for Training Paediatrician* (UE/2009/ TEMPUS), 2009-11.
The group, in the last four years, has achieved in funding research projects at European and national totaling slightly

more than 2,600,000 Euros

PUBLICATIONS: Regarding scientific publication, the members of the Group are authors of 26 papers in international and three in national journals, and also for two book´s chapters. Two papers where place in the first 10th and in the first quartile.

Research Group 2. Zaragoza University
Agency Organismo: Zaragoza University

SCIENTIFIC ACTIVITY: This group at the University of Zaragoza has a multidisciplinary background, implementing a multidisciplinary-based intervention combining nutritional-physical activity-psychological support approach. The main research activity of the group concerns the study of nutritional status and body composition in children and adolescents, including children obesity: epidemiology, prevention, complications and treatment and a nutritional program.
FINANCIAL SUPPORT: At the international level in the last 5 years the group participates in five research projects funded by the European Commission whose amount is close to three million euros:Identification and prevention of dietary- and lifestyle-induced health effects in children and infants (IDEFICS-FP6-2004-Food y FOOD-CT-2006-016181-2), European Recommendations Aligned (EURRECA-FP6-2005-Food y FOOD-CT-2007-036196-2), European energy balance research to prevent excessive weight gain among youth (ENERGY-HEALTH-2007-3.3-1), Multifactorial evidence based approach using behavioral models in understanding and promoting fun, healthy food, play and policy for the prevention of obesity in early childhood (TOYBOX), Prévenons l´Obésité des Enfants (EPODE-I/2008).

PUBLICATIONS: In recent years the group has published 9 articles in international journals located in the upper quartile of impact with a cumulative impact factor of over 40: Arch Pediatr Adolesc Med. 2007 Feb;161(2):166-71, Obesity 2007; 15: 1918-1924, Obesity 2007; 15: 1589-1599, Int J Obes 2007 Dec;31(12):1798-805, Int J Obes 2008 33: 758-767, Diabetes Care 2009; 32: 2120-2122, J Clin Endocrinol Metab 2009; 94: 5070-5077, Int J Obes 2009; 33: 1126-1135, Crit Rev Food Sci Nutr 2010; 50: 106-112. In addition to publishing over 15 articles in international journals located in Q2 within their area of research whose cumulative impact factor exceeds 35.

Research Group 3. SANT JOAN DE DÉU HOSPITAL (Barcelona)
Agency Organismo : Sant Joan de Deu Foundation

SCIENTIFIC ACTIVITY: Researches of the Obstetrics Services of the Sant Joan de Déu Hospital (HUSJD) of Barcelona develop their scientific activity mainly in two fields:
1- Intrauterine growth restriction (IUGR) conducting studies in pregnant women and fetuses to get standardise protocols between centers and facilitate multicenter outcomes, and study the prenatal pathology based on growth and biomarkers in this group of chronic hypoxia. In this line, has been studied the amniotic fluid levels of IGF-I, IGFBP-I, lectin in the first 18 weeks as precocious markers, the influence of genetic polymorphisms and fetal growth, maternal nutrition influence, the diagnostic value of VEGF and PLGF in maternal serum, along the pulsatility index of uterine arteries and hypertensive status of pregnancy, the diagnostic value of fetal corticosteroids and adrenal flow Doppler, the diagnostic value of vascular indices with tridimensional echography and the influence of feeding in early stages of life on future cardiovascular risk and psychoneurological development, diagnostic and prognostic value of the study of cardiac function and its association with markers of myocardial cell damage and cardiac dysfunction in cord blood in fetuses with IGR.
2- Perinatal hypoxic-ischemic injury, the group also has focused on the acute study, effects on metabolism and postnatal growth of this deficit. In the neonatal period have shown for the first time the utility of the ENE and IL-6 as markers of brain damage in hypoxic-ischemic encephalopathy, as well as the B2-microglobulin in CNS infections. Currently evaluates the usefulness of S100, ENE, B2-microglobulin and myelin basic protein as markers of neurological damage, and characterized the gene expression profile in peripheral blood lymphocytes.

FINANCIAL SUPPORT: The close collaboration with other members of the network has resulted in four multicenter studies been launched: EC10/147: Low molecular weight heparin; P11/02613: Prognostic factors of brain damage in foetuses with early IUGF; PI11/02590: Prenatal exposure assessment to antidepressants and anxiolytics by determination in biological alternatives matrices; EC11-375: MgSO4 in continuous versus discontinuous pattern in the expectant management of severe preeclampsia. In addition to receiving continued funding from the ISCIII through several projects in recent years.

PUBLICATIONS: The group has over 20 publications in the last 4 years in national and international journals several of them in quartiles 1 and 2 of its area (J Pediatr, Ultrasound Obstet Gynecol, Neonatology, Acta Obstet Gynecol Scand, J Clin Endocr Metab…). One result of integration in the Network is the publication of an article in collaboration with other members of the network: Gómez Roig MD, García-Algar O. An Pediatr 2011.

Research Group 4. Vall d´Hebron Hospital (Barcelona)
Agency: Foundation Research Institute Hospital Vall d'Hebron

SCIENTIFIC ACTIVITY: The Research Group in Research in Maternal-Fetal Medicine and Neonatology has 3 lines of research, all related to the Proposed Research Programme, which have led to a significant scientific contribution:
1- Preterm bith prevention: The prediction of patients at risk of preterm delivery by measuring the cervical length at 20 weeks and placement of cervical pessary. The application of this screening is reflected in 4 studies: - Cervical pessary to prevent prematurity: PECEP. - PECEP-retard. - PECEP-Twins. - PECEP uterine surgery. This strategy has proved its usefulness through a multicenter randomized clinical trial.
2- Placental diseases: Preeclampsia and fetal growth retardation. Pathophysiological studies on the mechanisms of placental disease and its complications, particularly on the involvement of oxidative stress and placental angiogenic factors in the development of preeclampsia and prenatal detection in pre-clinical phase.
3- Fetal heart function and cardiovascular diseases: The funding from FIS allows the study of the pathophysiological mechanisms leading to increased cardiovascular risk in mothers and children suffering from preeclampsia and / or growth restriction.

FINANCIAL SUPPORT: Research line on placental disease has received funding from ISCIII to perform a multicentric study (Prognostic factors for brain injury in fetuses with IUGF) and funding for a non-commercial Clinical Trials by the CAIBER (low molecular weight Heparin) and HOPPE trial. While a line on the fetal heart function, has a collaboration agreement with the company GENETADI BIOTECH S.L to perform the PRE_CARDIO study and funding from the program INNPACTO.

PUBLICATIONS: The results obtained in line 1 have been recently published: The Lancet, 2012 (PMID: 22475493) and Guidelines for the management of spontaneous preterm labour: identification of spontaneous preterm labor, diagnosis of preterm premature rupture of membranes, and preventive tools for preterm birth (J Matern Fetal Neonatal Med 2011). Also worth noting that in recent months have generated 4 other scientific publications in international journals with impact factor (Lupus. 2012 Mar;21:257-63, Hum Reprod. 2012 Feb;27:358-65; Am J Reprod Immunol. 2012 Feb;67:140-51; Ultrasound Obstet Gynecol. 2011), as well as several prior publications (Obstet Gynecol Int. 2009;:275613, Ultrasound Obstet Gynecol 2008; Am J Reprod Immunol. 2008, Obstetrics and Gynecol International, 2009).

Research Group 5: Hospital del Mar (Barcelona)
Agency: Municipal Institute of Health Care

SCIENTIFIC ACTIVITY: 1. Research line on foetal and paediatric tobacco exposure**;** 2. Research line on effects of maternal consumption of drugs of abuse and alcohol during pregnancy and effects of postnatal exposure to drugs of abuse on children**;** 3. Research line on prevalence of foetal exposure to drugs of abuse and alcohol biomarkers analysis in meconium and other alternative matrices**;** 4. Non commercial clinical investigation with drugs of prescription in children (therapeutic drug monitoring and effectiveness assays)

FINANCIAL SUPPORT: In the last 5 years the group has achieved both regional and state funding in excess of € 750,000 in more than 10 research projects related to scientific lines developed by the group. highlights include: 2009SGR1388, FIS 06/1221, SAF2007-64535, 2008-I-085, IM-Parc de Salut Mar, Programa de Salut Materno-Infantil Programme of Maternal and Child Health, Departament de Salut Department of Health, Generalitat de Catalunya, FIS 09/0040, FIS PI10/02593 and CAIBER 1526-KI-123.

PUBLICATIONS: The group has performed more than 65 publications in the last 5 years in international and national journals with impact factor. These include:Ther Drug Monit. 2008;30:725-732; J Pharmaceut Biomed. 2009;49:434-439; Ther Drug Monit. 2009;31:391-395; Ther Drug Monit. 2009;31:283-318; Anal Bioanal Chem. 2010;396:379-399; Forensic Sci Int 2010;196:38-42; Forensic Sci Int 2010;196:97-100; Forensic Sci Int 2010;196:74-7; Forensic Sci Int 2010;196:22-6; Forensic Sci Int 2010;196:59-63; Clin Chem. 2010;56:585-92; Anal Bioanal Chem. 2010 Jun;397

(3):1157-79; Ther Drug Monit. 2010 Aug;32(4):508-11; J Pharm Biomed Anal. 2011 Jan 28; Forensic Sci Int. 2011 Oct 27; J Pharm Biomed Anal. 2012 Feb 23;60:26-31; J Pharm Biomed Anal. 2012 Jan 16.

TRANSFER RESULTS: (1) Publication and utilization of nicotine and cotinine values in deciduous teeth as a reliable quantitative biomarker of prenatal and postnatal exposure to environmental tobacco smoke and as a biomarker to study directly its effects on asthma appearance in childhood. (2) Alarming published results about children exposure to cocaine (24%) detected in emergency room and prenatal alcohol exposure (43%) detected in a prenatal cohort of mother-newborn dyads. (3) Recruitment of the biggest newborns cohort in Europe with meconium samples and results of prenatal exposure to drugs of abuse, tobacco and alcohol to be followed. (4) Collection for the first time of ovular remains from abortions as a biological matrix. (5) Publication of methodologies of analysis of methylphenidate and atomoxetine in hair (children treated because of an ADHD diagnosis) and validation of its correlation with clinical effects and compliance of prescription.

Research Group 6: General University Hospital Gregorio Marañón (Madrid)
Agency: Biomedical Research Foundation Gregorio Maranon hospital.

SCIENTIFIC ACTIVITY: The Pediatric Intensive Care Research Group University Hospital Gregorio Marañón includes clinical and experimental translational research coordinated activities on child health problems in critical condition. Its main lines are focused on the study of cardiac arrest and its neurological sequelae and the nutritional disorders.

FINANCIAL SUPPORT: In the last five years has coordinated 11 research projects most of them funded by ISCIII. In addition, the principal investigator of the group has obtained in three occasions funds for research.
In the field of clinical research has coordinated national and international multicentric studies on cardiac arrest in children and participates in the development of clinical practice guidelines both nationally and internationally on this topic.
Also has developed several multicentric studies on child nutrition, some in collaboration with other “SAMID Network” groups. In the field of experimental research has developed a line of ongoing research in experimental models of neurological damage by asphyxial cardiac arrest and shock that has led to numerous scientific studies.
Participation in research networks: Their incorporation in 2009 to the SAMID Network has allowed them to consolidate research in their Pediatric Intensive Care unit and coordinate lines of research with other pediatric groups. The principal investigator of the group also coordinates an international research network, the “Ibero-American Study of cardiac arrest in Childhood, (RIBEPCI)” within the program CYTED.

PUBLICATIONS: The group has a high scientific output over 110 scientific publications in the last five years between articles published in indexed journals and books with an impact factor greater than 300 over the past five years.
The group participates in the development of national and international guidelines for clinical practice as a member of ILCOR (International Liaison Committee on Resuscitation).

TRAINING: The group develops an important role in training researchers and trainers in various fields of pediatric intensive care and paediatrics. Develop innovative education programs and implementation of advanced simulation methods in teaching both undergraduate and postgraduate clinical and research programs

Research Group 7. Marques de Valdecilla Hospital (Cantabria)
Agency: Marques de Valdecilla Foundation

SCIENTIFIC ACTIVITY: The research group has a multidisciplinary background, clinical-traslational. The current main research activity of the group concerns the prevention and the treatment of the cardiovascular risk. It is composed by the Research Institute Marques de Valdecilla (IFIMAV) & University of Cantabria The research activities of the group are focused in metabolism, genetics and nutrition, disposing a complete technical support and infrastructures.
1. Line in Nutrition: the group participated in the multicenter AVENA STUDY and EVASYON Study on nutritional status, prevention and treatment of Spanish adolescents. The multidisciplinary group has a translational projection based on clinical activity, oriented to the search for new therapeutic strategies for prevention and treatment of child and adolescent obesity, establishing new approaches, such as e-health, through address www.pontesano.com.
2. **Line of Metabolism**: The clinical activity of the group focuses the study of patients with developmental disorders in

which metabolic alterations are determinant. Many of these patients have complex diseases. The facilities of the Laboratory, allows studies of molecular genetics and metabolic with direct clinical application. In this regard, we have been conducting studies of alterations in the glycosylation of proteins as an index of cellular metabolic dysfunction, and also of oxidative metabolism in different clinical situations, including monitoring of the intervention on generalized alterations of development. In the field of environmental factors in the pathology of development, we have conducted several collaborative studies on the influence of certain factors in the expression of genes related to cell death and sensitivity to chemotherapy. Recently the group initiated a collaborative project with a company of child nutrition on the influence of dietary factors on cognitive development of experimental animals.

FINANCIAL SUPPORT: In the last years the group has collaborated in more than 20 research projects (funding by ISCIII). Moreover, the group collaborates with several companies focused on pediatric nutrition and dietary and pharmaceutical management of patients. Currently the group participates in the 7th EU Framework Program as a group of NUTRIMETHE research consortium that examines the influence of certain environmental factors in child development. Apart from that the realization of projects aimed to the prevention of childhood obesity (Project HEALTH (A) WARE: An Experienced-based learning and teaching approach for physical and health education 128737-CP-1-DE-Comenius-C21) and EVASYON Project (Development, implementation and evaluation of the efficacy of a therapeutic program for adolescents with overweight and obesity, PI050855).
PUBLICATIONS: During the last three years, the average is 9 publications per year, what are focused on pediatrics, cardiovascular risk, and nutrition (average impact factor of 21 per year). Some of the journals with impact where we have published are: BMC Med Genet, Molec Gen Metab, Arch Pediatr Adolesc Med, Pediatr Res, Acta Paediatr, Pediatr Nephrol, Eur J Public Health, J Pediatr, Obesity, Pediatr Cardiol, Ann Nutr Metab, etc.

Research Group 8. La Paz University Hospital (Madrid) -neonatal group
Agency: Biomedical Research Foundation La Paz

SCIENTIFIC ACTIVITY: The group has focused in recent years in investigating the pathogenesis of neonatal brain injury both born premature and the term, as well as risk factors affecting neurodevelopment, with special attention to nutrition and endocrine-metabolic aspects. The different areas are:
1. Perinatal neurological disorder: From the standpoint of clinical, biochemical and neuroimaging, aiming at the prevention of brain injury, both in the preterm infant as in the term. The group has worked on developing and implementing noninvasive technology for monitoring of cerebral hemodynamics and oxygenation in the newborn, including studies of Doppler color flow image (CDFI), or Power Doppler (PD) and near-infrared spectroscopy (NIRS-SRS). These techniques have been different study protocols (routine interventions for the care of ventilated patients, pharmacodynamic monitoring of different therapeutic interventions, systematic evaluation of hemodynamic changes that occur in different pathophysiological situations).

In addition, echocardiography has been incorporated functional overall hemodynamic evaluation of the newborn, for simultaneous assessment of hemodynamic changes in organ-specific level by NIRS and PD in different pathophysiological situations. Also, it has developed software for the calculation of hemodynamic variables, being patent pending the integration program of biological signals developed by a member of the research team under contract through the SAMID Network.

2. Nutrition and development: whose line priority is to improve the neurodevelopment of preterm infants. Several funded studies are underway, including: a longitudinal study in children of very low birth weight to determine body composition, hormonal and neurological impact and genetic factors that influence prenatal and postnatal malnutrition; a sequential prospective study to improve enteral tolerance and growth of infants with gestational age equal to or less than 28 weeks; study the effect of hyperproteic diet on protein metabolism and caloric intake in critically ill children.

3. Infection and Inflammation: Is a priority line of the group. This group has participated in many international clinical trials in relation to vaccines and infection with high impact recent publications.

FINANCIAL SUPPORT: In the last three years the group has participated in 27 research projects and / or in funded clinical trials. Notably collaboration in NEOCIRCULATION multicentric study funded by the 7th EU FP (FP/-HEALTH-2010-single-stageHealth) dedicated to the study of early circulatory failure in preterm infants before 32 weeks gestation, and dobutamine treatment; the project SafeBoosC trial, funded by the Danish Technological Development Agency, aims to test the impact of cerebral oximetry in the management of extreme prematurity, and the multicenter

study funded by the EU in relation to PK, safety and efficacy of Meropenem in neonatal sepsis (NEOMERO, HEALTH-F5-2009-242146). Currently coordinated a national multicenter study through the Samid Network on the impact of assisted reproduction techniques in health of the newborn.

PUBLICATIONS: Considering only the articles in the first decile and first or second quartile, the group published in the last three years 14 manuscripts with a cumulative FI of 119.67.

Research Group 9. La Paz University Hospital (Madrid) - experimental and surgical group
Agency: Fundación Investigación Biomedica La Paz

SCIENTIFIC ACTIVITY: Our group works in one of the largest pediatric surgical centres in Europe and has had a leading role in the progress of the specialty in our country. We developed many years ago the first pediatric surgical neonatal ICU in Spain and are currently the referral center for prenatally diagnosed malformations in our region and in a large share of the country. In parallel, our group started transplantation programs (kidney, liver and heart) more than 20 years ago and developed the first and only small bowel transplantation program in the 15 years.
Our research activity in the last 5 years is focused on topics, like malformations and transplantation. Our laboratory, has conducted investigation on different aspects of pediatric surgery. This work has been permanent along the last 20 years both in the field of malformations and in that of gastroesophageal reflux (GER).
In the last 15 years we centred our research on the pathogenesis of lung hypoplasia in the frequently lethal malformation known as congenital diaphragmatic hernia (CDH) and in the mechanisms of another important malformation, esophageal atresia (EA). We unraveled some of the cellular and molecular mechanisms of both defects in the rat and mouse experimental models. We determined the influence of the teratogen on some of the genes and transcription factors involved in the morphogenic cascades and attempted at modifying their action by using anti-oxidant vitamins and retinoic acid.
More recently, we concentrated our research on the participation of the neural crest in morphogenesis and on its abnormal activity in malformations. Studies on visceral innervation (in charge of neural crest cells) led us to unravel tracheobronchial dysmotility as one of the mechanisms of lung hypoplasia in CDH and esophageal dysmotility as one of the mechanisms of gastrointestinal disease in both CDH and EA.
Simultaneously, we studied some aspects of translocation in a rat model of small bowel transplantation using different forms of venous outflow and the influence of inclusion of colonic segments in the graft. These studies were carried out in syngenic and allogenic sets of animals to identify the participation of rejection in this phenomenon. These studies were recently extended to the mechanisms of graft-versus-host disease after small bowel transplantation in rats. We recently developed minimally invasive foetal surgery in a lamb model of neural tube defects and the nature of the central nervous system lesions in this particular malformation and studied the possibilities of the neural plate coverage with different constructs in this model and in another rat model of neural tube defect.
PUBLICATIONS AND FINANCIAL SUPPORT: With 18 articles in Q1 and Q2 international journals with an accumulative impact factor higher than 40 in the last 4 years and a continuous funding through ISCIII.

Research Group 10. 12 de Octubre University Hospital (Madrid)
Organismo: Biomedical Research Foundation Hospital 12 de Octubre

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SCIENTIFIC ACTIVITY: This The 12 de Octubre Hospital Research Group began its activity in research 15 years ago. In recent years, participating in the *SAMID Network,* has been key to initiating collaborative efforts with other national groups thereby significantly strengthening various lines of research. The main areas of the group's research, related to the program being presented, have been concentrated on the areas appearing below:
1. Follow up/Cerebral Palsy: The first Cerebral Palsy (CP) register based on a Spanish population was created by various members of the group and it has been accepted as Official Register number 18 of Europe. The hospital is currently the coordinating center for the project, Surveillance of CP in Europe. It has also participated in the preparation of the “Research and Training Manual for Surveillance on its in Europe-SCPE”.
2. Donated Human Milk: In 2007, the first Donated Human Milk Bank began operating in the Neonatal Unit. From the outset, one of the objectives of the Human Milk Bank was to incorporate research on the processing of donated human milk. In 2010, the Human Milk Bank (*BLH)* was certified by the Quality Management System. The information on the processing of mother's milk, acquired to date, will be included in the guidelines on clinical practices in the processing of mother's milk which are being prepared by the Spanish Association of Milk Banks.
3. Care Centered on Development: Research in care centered on development is very complex due to the difficulty in creating standardization for care and in the comparison of the different types of care given. A study which was initially

performed on the situation of care in Spain, "Care Centered on Development: the Situation in Spanish Neonatology Units", later led to the group's participation in a larger European project which evaluated the implementation of Care Centered on Development in different countries. Moreover, the Neonatology Service is now one of 9 centers certified as a NIDCAP (Newborn Individualized Developmental Care and Assessment Program) training center.

FINANCIAL SUPPORT: The group has obtained fundings in the last years through the ISCIII, apart form collaborate in several clinical trials and European projects like Euroneostat (Proposal Nº101106, UE-2PS-EAHC) and Surveillance of Cerebral Palsy in Europe (Proposal Nº101219. Financing Agency: UE-2PS-EAHC) that is coordinated by the group. In 2009, in collaboration with the Hospital del Mar, the research team got financing to develop the project, "Safety and Quality in Human Milk in an Assisted Clinical Environment: a Comparative Study of the International Recommendations for Milk Processing in a Neonatology Service", ISCIII (PI 09/00040) and is currently participating in research studies in conjunction with the Hospital Valle Hebron: ("*Staff Perceptions on NIDCAP During Its Implementation in Two Spanish Neonatal Units," EHD-D-12-00068*).

PUBLICATIONS: the group has more than 40 articles in these areas in the last 5 years in Q1 and Q2 international journals (J Pediatr Gastroenterol Nutr, J Pharm Biomed Anal, Anal Bioanal Chem, Acta Paediatr, Neonatology, Arch Dis Child Fetal Neonatal or Pediatr Crit Care Med…).

Research Group 11. La Fe University and Polytechnic Hospital (Valencia)
Organismo: La Fe Health Research Institute

SCIENTIFIC ACTIVITY: The main line of research in our group has focused on the study of the physiology and pathophysiology of fetal-neonatal transition especially with regard to oxygenation. Adaptive postnatal changes in physiological and pathological situations as well as knowledge of the oxidative stress process and redox regulation made □□in experimental and clinical studies have allowed us to contribute to change in the international protocols of resuscitation of the newborn asphyxia at term. They have also developed methodology for noninvasive monitoring of biomarkers of oxidative stress, redox signaling and oxidative damage that allows the clinical evaluation of interventions in any circumstance in which the use of oxygen is needed. As some of the most important contributions:

1. Resuscitation of asphyxiated newborn: the group has contributed to changes in international standards of resuscitation of asphyxiated term newborn starting today with room air.

2. Promoting the use of pulse oximetry in the Delivery Room: the group has contributed to the development of a "nomogram" of pre-ductal arterial oxygen saturation in term and preterm born at international reference for the management of oxygen in the delivery room.

3. Recommendations on the use of DRICU method in the Delivery Room: The group has contributed to the use of available technology to optimize the resuscitation of the newborn in the delivery room using the concept "Delivery Room Intensive Care Unit".

4. Noninvasive management of the premature infant in the Delivery Room: collaborative studies have been made □□to encourage the use of noninvasive ventilation in the delivery room to reduce iatrogenic especially in high-risk preterm infants.

5. Development of laboratory method for noninvasive monitoring of oxidative stress in newborn: We have developed methodology for HPLC-MS / MS for the determination of markers of stress and oxidative injury in neonatal patients.

6. Resuscitation Protocol and early moderate hypothermia in neonatal hypoxic-ischemic encephalopathy of the Spanish Society of Neonatology: Our group has been active in the development of protocols and clinical guidelines in these areas.

FINANCIAL SUPPORT: With regard to research projects include continued funding by the ISCIII and the coordination and participation of several clinical trials funded through the Ministry of Health and Social Services. At the international level is important to emphasize group participation in two projects: NIH Research Grant R34, 2010. (PRESOX TRIAL) about the resuscitation of preterm infants with different oxygen concentrations in the delivery room and Byosynexus Incorporated (USA). MAB-NOO7, 2009-2011. Safety and Efficacy of Pagibaximab Injection in Very Low Birth Weight (VLBW) Neonates for the Prevention of Staphylococcal Sepsis.

PUBLICATIONS: Over the past 5 years the average is 7 publications per year, in international journals with impact factor as,: Acta Paediatr; Nat Común; Clin Perinatol; J Matern Fetal Neonatal Med; Early Hum Dev.; Free Radic Biol Med; Pediatr Res; Neonatology; Biochem Pharmacol; J Pediatr; Pediatrics; Am J Clin Nutr; Antioxid Redox Signal; Arch Dis Child Fetal Neonatal; Am J Med Genet; Semin Perinatol.

Research Group 12. Granada University.
Agency: Granada University.

The University of Granada (UGR) is among the top three Spanish universities, particularly in the field of Health Sciences. More than 400 research groups are working in all different areas of knowledge, in collaboration with national as well as foreign research groups. In addition, the UGR´s Research-Transfer Office promotes and manages university relations with the corporate world. The research group leads by **Prof. Angel Gil** has a multidisciplinary background. It is composed by the department of Biochemistry and Molecular Biology II and the Department of Paediatric Endocrinology from Reina Sofia University Hospital.

SCIENTIFIC ACTIVITY: The group has a dilated experience recruiting obese children from primary attention care centers and hospital. The principal research activity of the group concerns the study of metabolic and cardiovascular risk factors in prepubertal children with obesity. This includes plasma metabolic risk factors analysis and molecular biology analysis on adipose tissue. In a current project, (FIS PI11/02042 GENOBOX) personnel of the partner are measuring markers associated with oxidative stress, inflammation and cardiovascular diseases using Luminex 200 System built on xMAP technology. This technique may determine up to 100 analytes in a single microplate well, using very small sample volumes, which is a very important condition working with children.
Our group is researching the importance of genetic factors on early obesity. Polymorphisms of altered genes involved in the development of insulin resistance and other observed in our studies are demonstrated to have an important role in the etiology of pediatric obesity.
After the study of gene expression by arrays in adipose tissue from prepubertal children which results are in writing process, we are working on the functional study of those altered genes using a model of adipose tissue derived stem cells and siRNA to knock down the studied genes.

FINANCIAL SUPPORT: the group has been receiving along the years nacional and international funding and has participated in several clinical trials. The group has participated in the development of different patents in the nutritional area.

PUBLICATIONS: 6 articles in the last 2 years in internacional journals (*Int J Obesity; Antioxid Redox Sign; Am J Clin Nutr; Nutr, Metab Cardiovas; Ann Nutr Metab; Int J Pediatr Obes)* with an accumulative impact factor of 28.205.

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RETIC CODE:
RD12/0026/0001

TABLE 1.- PUBLICATIONS

FIVE PUBLICATIONS RELATED WITH THE PROGRAMME (YEARS 2009-2010-2011-2012)

AUTHORS:	Goya M, Pratcorona L, Merced C, Rodó C, Valle L, Romero A, Juan M, Rodríguez A, Muñoz B, Santacruz B, Bello-Muñoz JC, Llurba E, Higueras T, **Cabero L**, Carreras E; on behalf of the Pesario Cervical para Evitar Prematuridad (PECEP) Trial Group.		
TITLE:	Cervical pessary in pregnant women with a short cervix (PECEP): an open-label randomised controlled trial.	**PMID:**	**22475493**
JOURNAL:	Lancet	**TYPE OF PAPER:** ARTICLE	**PUBLICATION YEAR:** 2012

AUTHORS:	Mercier JC, Hummler H, Sanchez-Luna M, Carnielli V, Field D, Greenough A, Senn S, Van Overmeire B, Jonsson B, Hallman M, Baldassarre J, Halliday HL, Hey E, Ford I, Cuttini M, Debauche C, Lecart C, Maton P, Van Overmeire B, Field D, Greenough A, Soe A, Hallman M, Aikio O, Danan C, Dassieu G, Decobert F, Durrmeyer X, Baud O, Rozé JC, Arand J, Beedgen B, Hummler H, Maier RF, Zemlin M, Schaible T, Schulze A, Flemmer AW, Wauer RR, Hammer H, Carnielli V, Chiandetti L, Trevisanuto D, Doglioni N, Colombo A, Dani C, Rubaltelli FF, Pratesi S, Romagnoli C, Vento G, Van Goudoever JB, Roofthooft D, van Vliet I, Damhuis G, Bos AF, Doménech Martínez E, Hernández Borges A, Concepción García A, Murray Hurtado M, Losada A, Núñez Solís JM, Morcillo F, Gutierrez Laso A, Saenz González P, Gimeno Navarro A, Escrig R, Quero J, Elorza MD, Pérez J, **Cabañas F**, Salcedo S, Hernández Pérez S, Ortiz Morell M, Ribes Bautista C, Ruiz Campillo C, Sánchez-Luna M, Franco ML, Bernardo B, Zamora E, Casanova A, Ruiz Y, **Valls-i-Soler A,** Ansó Oliván S, Loureiro González B, Sjörs UE, Jonsson B, Bartocci M, Edner A.		
TITLE:	Inhaled nitric oxide for prevention of bronchopulmonary dysplasia in premature babies (EUNO): a randomised controlled trial.	**PMID:**	**20655106**
JOURNAL:	LANCET	**TYPE OF PAPER:** ARTICLE	**PUBLICATION YEAR:** 2010

AUTHORS:	Verier C, Meirhaeghe A, Bokor S, Breidenassel C, Manios Y, Molnár D, Artero EG, Nova E, De Henauw S, **Moreno LA**, Amouyel P, Labayen I, Bevilacqua N, Turck D, Béghin L, Dallongeville J, Gottrand F; Healthy Lifestyle in Europe by Nutrition in Adolescence (HELENA) Study Group.		
TITLE:	Breast-feeding modulates the influence of the peroxisome proliferator-activated receptor-gamma (PPARG2) Pro12Ala polymorphism on adiposity in adolescents: The Healthy Lifestyle in Europe by Nutrition in Adolescence (HELENA) cross-sectional study.	**PMID:**	**19846795**
JOURNAL:	Diabetes Care	**TYPE OF PAPER:** ARTICLE	**PUBLICATION YEAR:** 2010

	Vento M, Aguar M, Escobar J, Arduini A, Escrig R, Brugada M, Izquierdo I, Asensi MA, Sastre J,

AUTHORS:	Saenz P, Gimeno A.		
TITLE:	Antenatal steroids and antioxidant enzyme activity in preterm infants: influence of gender and timing.	**PMID:**	**19645572**
JOURNAL:	Antioxid Redox Signal	**TYPE OF PAPER:** ARTICLE	**PUBLICATION YEAR:** 2009

AUTHORS:	Pellicer A, Bravo MC, Madero R, Salas S, Quero J, **Cabañas F**.		
TITLE:	Early systemic hypotension and vasopressor support in low birth weight infants: impact on neurodevelopment.	**PMID:**	**19403504**
JOURNAL:	Pediatrics	**TYPE OF PAPER:** ARTICLE	**PUBLICATION YEAR:** 2009

STATEMENT OF THE PROGRAMME RETIC COORDINATOR

RETIC CODE:
RD12/0026/0001

TABLE 2.- PROJECTS

FIVE PROJECTS RELATED WITH THE PROGRAMME (YEARS 2009-2010-2011-2012)

PI NAME:	ADOLF VALLS SOLER
PI INSTITUTION:	BIOEF
TITLE:	GRIP. Global Research in Paediatrics
FUNDING AGENCY:	FP7-Health-2010 (2ª llamada). European Comission. (ref.: propuesta: 261060)
REFERENCE NUMBER: UE09/GRIP261060 GRIP	**START-END YEARS:** 2011-2015

PI NAME:	F Cabañas PI HU La Paz; A Pellicer: Responsible of the european trial. WP leaders.
PI INSTITUTION:	HU LA PAZ
TITLE:	Dobutamine for NEOnatal CIRCulatory falure defined by novel biomarkers
FUNDING AGENCY:	Sevent Framework Programme (Health-2011.4.2-1 Investigator-driven clinical trials on off-patent medicines for children
REFERENCE NUMBER: NEO-CIRC HEALTH-2011.4.2-1-GRANT AGREE	**START-END YEARS:** 2012-2017

PI NAME:	ADOLF VALLS i SOLER
PI INSTITUTION:	BIOEF
TITLE:	Euroneostat II. Expanded European Information System to monitor short and long-term outcomes and improve quality of care and safety for very low birth
FUNDING AGENCY:	DG-SANCO
REFERENCE NUMBER: SANCO 2009/101106	**START-END YEARS:** 2009-2012

PI NAME:	Dr. J. De La Cruz
PI INSTITUTION:	H 12 DE OCTUBRE
TITLE:	SCPE-NET
FUNDING AGENCY:	Unión Europea-2º Programa en Salud-Executive Agency for Health and Consumers
REFERENCE NUMBER: SCPE-NET	**START-END YEARS:** 2008-2013

STATEMENT OF THE PROGRAMME RETIC COORDINATOR

RETIC CODE:
RD12/0026/0001

PI NAME:	Luis A. Moreno Aznar
PI INSTITUTION:	UNIVERSIDAD DE ZARAGOZA
TITLE:	IDEFICS - Identification and Prevention of Dietary and Lifestyle induced Health Effects ind Children and Infants
FUNDING AGENCY:	UE
REFERENCE NUMBER: I-21676	**START-END YEARS:** 2007-2011

STATEMENT OF THE PROGRAMME RETIC COORDINATOR

RETIC CODE:
RD12/0026/0001

TABLE 3- CLINICAL TRIALS

FIVE CLINICAL TRIALS RELATED WITH THE PROGRAMME (YEARS 2009-2010-2011-2012)

PARTICIPANTS OF THE PROGRAMME:	RD08/0072/0018; RD08/0072/0039; RD08/0072/0022; RD08/0072/0031; RD08/0072/0034;RD08/0072/0000
TITLE:	CAIBER 1677-EKI-096, EDUCATIONAL INTERVENTION TO PREVENT HOSPITAL ACQUIRED INFECTIONS IN VERY LOW BIRTH WEIGHT INFANTS: INTERNATIONAL CLUSTER RANDOMIZED CONTROLLED TRIAL (EuroNeoKiss); No pharmacological trial, NO-EPA study.
EUDRACT:	**PROMOTOR:** BIOEF **PHASE:** Phase 3

MULTICENTER TRIALS NATIONAL	MULTICENTER TRIALS INTERNATIONAL	STARTING DATE	ACTIVE	ENDING DATE
x	x	ene-2013	YES	dic-2015

PARTICIPANTS OF THE PROGRAMME:	RD08/0072/0018; RD08/0072/0000
TITLE:	CIP n: SafeBoosC-DP-202; CTU n:SB010512 y CAIBER 1392-CI399; Safeguarding the brains of our smallest children-a feasibility randomised trial on nearinfrared pectroscopy combined with treatmentguidelines in premature infants
EUDRACT:	**PROMOTOR:** G Greisen (DK) and A Pellicer (PI in Spain) **PHASE:** Phase 3

MULTICENTER TRIALS NATIONAL	MULTICENTER TRIALS INTERNATIONAL	STARTING DATE	ACTIVE	ENDING DATE
	x	ene-2012	YES	dic-2014

PARTICIPANTS OF THE PROGRAMME:	RD08/0072/0018; RD08/0072/0000 in a european consortium
TITLE:	Dobutamine for NEOnatal CIRCulatory falure defined by novel biomarkers
EUDRACT:	**PROMOTOR:** F Cabañas PI HU La Paz; A Pellicer: Trial Chief Investig **PHASE:** Phase 3

MULTICENTER TRIALS NATIONAL	MULTICENTER TRIALS INTERNATIONAL	STARTING DATE	ACTIVE	ENDING DATE
	x	ene-2012	YES	dic-2014

STATEMENT OF THE PROGRAMME RETIC COORDINATOR

RETIC CODE:
RD12/0026/0001

PARTICIPANTS OF THE PROGRAMME:	rd08/0072/0031; rd08/0072/0034; rd08/0072/0000 de la actual RED SAMID.
TITLE:	2010-023597-39. " Low molecular weight heparin (LMWH) for the prevention of complications of placental insufficiency in patients without thrombophilia risk: ramdomized multicentric trial" HOPPE trial: Low weight Heparin prOphylaxis for Placental-mediated complications of PrEgnancy (Protocol identifying number: 1557-H-125)
EUDRACT:	**PROMOTOR:** Luis Cabero Roura **PHASE:** Phase 3

MULTICENTER TRIALS NATIONAL	MULTICENTER TRIALS INTERNATIONAL	STARTING DATE	ACTIVE	ENDING DATE
x			YES	

PARTICIPANTS OF THE PROGRAMME:	rd08/0072/0025; rd08/0072/0030; RD08/0072/0031 de la actual Red SAMID.
TITLE:	2010-023061-21 . "Clinical trial on the effects of metformin in pediatric obesity: effects on body weight, profile of inflammatory biomarkers and cardiovascular risk, and impact on factors related to metabolic syndrome".
EUDRACT:	**PROMOTOR:** Ramón Cañete Estrada. Funding agency: Dirección Gene **PHASE:** Phase 3

MULTICENTER TRIALS NATIONAL	MULTICENTER TRIALS INTERNATIONAL	STARTING DATE	ACTIVE	ENDING DATE
x		nov-2011	YES	

STATEMENT OF THE PROGRAMME RETIC COORDINATOR

RETIC CODE:
RD12/0026/0001

TABLE 4.- EPIDEMIOLOGICAL STUDIES

FIVE EPIDEMIOLOGICAL STUDIES RELATED WITH THE PROGRAMME (YEARS 2009-2010-2011-2012)

RESEARCHER:	Adolf Valls Soler (H de Cruces), Carmen Rosa Pallás Alonso (H 12 de Octubre), Manuel Cuenca-Estrella (Director del Centro Nacional de Microbiología, ISCIII)
TITLE:	Epidemiological study of early diagnosis of invasive candidiasis in preterm neonates with very low weight
INSTITUTION/S:	17 national hospitals that have neonatal intensitive care units..
REFERENCE:	**AST-MYC-2010-01**
FUNDING AGENCY:	**ASTELLAS PHARMA, S.A.**

UNICENTER / MULTICENTER	NATIONAL / INTERNATIONAL	STARTING DATE	ACTIVE	ENDING DATE
MULTICENTER	NATIONAL	01/2010	YES	12/2014

RESEARCHER:	groups: RD08/0072/0031, RD08/0072/0034, RD08/0072/0000, RD08/0072/0039
TITLE:	Pronostics factors of brain damage in fetuses with early growth restricion.
INSTITUTION/S:	Hospital Sant Joan de Deu, Hospital Vall de Hebron, Hospital de Cruces, Hospital 12 de Octubre
REFERENCE:	**PI11/02613**
FUNDING AGENCY:	**ISCIII**

UNICENTER / MULTICENTER	NATIONAL / INTERNATIONAL	STARTING DATE	ACTIVE	ENDING DATE
MULTICENTER	NATIONAL	01/01/2012	YES	31/12/2014

RESEARCHER:	Groups: RD08/0072/0039 (Pallás CR) y RD08/0072/0027 (Vall O.)
TITLE:	Safety and quality of donated human milk in clinical care setting. Comparative study of international recommendations on processing in a neonatology service.
INSTITUTION/S:	Hospital 12 de Octubre y Hospital del Mar
REFERENCE:	**PI09/0040**
FUNDING AGENCY:	**ISCIII**

UNICENTER / MULTICENTER	NATIONAL / INTERNATIONAL	STARTING DATE	ACTIVE	ENDING DATE
MULTICENTER	NATIONAL	01/12/2010	YES	31/12/2012

STATEMENT OF THE PROGRAMME RETIC COORDINATOR

RETIC CODE:
RD12/0026/0001

RESEARCHER:	groups: RD08/0072/0025, RD08/0072/0028			
TITLE:	Association between genetic variants, oxidative stress biomarkers, inflammation and cardiovascular risk in obese children (GENOBOX)			
INSTITUTION/S:	Universidad de Zaragoza, Universidad de Granada			
REFERENCE:	**PI11/01425, PI11/02042**	**FUNDING AGENCY:**	**ISCIII**	
UNICENTER / MULTICENTER	**NATIONAL / INTERNATIONAL**	**STARTING DATE**	**ACTIVE**	**ENDING DATE**
MULTICENTER	NATIONAL	01/01/2012	YES	31/12/2014

RESEARCHER:	Fernando Cabañas (PI), Adelina Pellicer, Eva Valverde, C Bravo, Pablo Lapunzina, Rosario Madero. J Diez del Hospital La Paz y resto de grupos de la Red.			
TITLE:	**Impacto de las técnicas de reproducción asistida en la salud del recién nacido**			
INSTITUTION/S:	Hospital La Paz as coordinator, and all SAMID NETWORK groups			
REFERENCE:	**PI 09/90332**	**FUNDING AGENCY:**	**ISCIII**	
UNICENTER / MULTICENTER	**NATIONAL / INTERNATIONAL**	**STARTING DATE**	**ACTIVE**	**ENDING DATE**
MULTICENTER	NATIONAL	01/01/2010	YES	31/12/2012

STATEMENT OF THE PROGRAMME RETIC COORDINATOR

RETIC CODE:
RD12/0026/0001

TABLE 5.- PATENTS

FIVE PATENTS RELATED WITH THE PROGRAMME (YEARS 2009-2010-2011)

APPLICANT:	Research foundation La Paz University Hospital.
TITLE:	Software tool for visualization, synchronization, recording and processing of biomedical signals from commercial medical devices.
INVENTORS:	Joan Riera, Adelina Pellicer, F Cabañas

PATENT OFFICE (ONLY OEPM-SPAIN)	DATE OF APPLICATION	APPLICATION NUMBER	DATE OF GRANT
en tramite	abril 2012		
PATENT OFFICE (OTHERS EPO, USPTO ...)	**DATE OF APPLICATION**	**APPLICATION NUMBER**	**DATE OF GRANT**

EXPLOTATION	EXPLOTATION INSTITUTION	STARTING DATE	ACTIVE	ENDING DATE
	Research Foundation La Paz University Hospital.		NO	

APPLICANT:	
TITLE:	Isolation, identification and characterisation of strains with probiotic activity, from faeces of infants fed exclusively with breast milk
INVENTORS:	Vieites Fernández, Jose María; Muñoz Quezada, Sergio; Llamas Company, Inmaculada; Maldonado Lozana, José; Romero Braquehais, Fernando; Suárez García, Antonio Francisco; Gil Hernández, Angel; Gómez Llorente, Carolina;; Bremúdez Brito, Miriam.

PATENT OFFICE (ONLY OEPM-SPAIN)	DATE OF APPLICATION	APPLICATION NUMBER	DATE OF GRANT
PATENT OFFICE (OTHERS EPO, USPTO ...)	**DATE OF APPLICATION**	**APPLICATION NUMBER**	**DATE OF GRANT**
European patent applicatio		PCT/ES2010/000097	18/01/2012

EXPLOTATION	EXPLOTATION INSTITUTION	STARTING DATE	ACTIVE	ENDING DATE
NO	HERO S.A 100%			

STATEMENT OF THE PROGRAMME RETIC COORDINATOR

RETIC CODE:
RD12/0026/0001

APPLICANT:	
TITLE:	Isolation, identification and characterisation of strains with probiotic activity, from faeces of infants fed exclusively with breast milk
INVENTORS:	Vieites JM, Muñoz-Quezada S, Llamas I, Maldonado J, Romero-Braquehais F, Suárez A, Gil A,

PATENT OFFICE (ONLY OEPM-SPAIN)	DATE OF APPLICATION	APPLICATION NUMBER	DATE OF GRANT
PCT/ES 2009/000130	10/03/2009		
PATENT OFFICE (OTHERS EPO, USPTO ...)	**DATE OF APPLICATION**	**APPLICATION NUMBER**	**DATE OF GRANT**

EXPLOTATION	EXPLOTATION INSTITUTION	STARTING DATE	ACTIVE	ENDING DATE
NO	HERO S.A 100%		YES	

APPLICANT:	
TITLE:	Enteral or oral food product designed especially for nutrition, prevention and improvement of neurological disorders, neurodegenerative or cognitive disorders
INVENTORS:	Gil Hernández A, San Román Pais P, Pérez Rodriguez M

PATENT OFFICE (ONLY OEPM-SPAIN)	DATE OF APPLICATION	APPLICATION NUMBER	DATE OF GRANT
PCT/ES 2010/070207	31/03/2010		
PATENT OFFICE (OTHERS EPO, USPTO ...)	**DATE OF APPLICATION**	**APPLICATION NUMBER**	**DATE OF GRANT**

EXPLOTATION	EXPLOTATION INSTITUTION	STARTING DATE	ACTIVE	ENDING DATE
NO	VEGENAT SA100%		NO	

STATEMENT OF THE PROGRAMME RETIC COORDINATOR

RETIC CODE:
RD12/0026/0001

APPLICANT:	
TITLE:	Functional food supplement specially designed for nutrition, prevention and improvement in cases of neurological disorders, neurodegenerative or cognitive disorders
INVENTORS:	Gil Hernández A, San Román Pais P, Pérez Rodriguez M

PATENT OFFICE (ONLY OEPM-SPAIN)	DATE OF APPLICATION	APPLICATION NUMBER	DATE OF GRANT
PCT/ES 2010/070208	31/03/2010		
PATENT OFFICE (OTHERS EPO, USPTO ...)	**DATE OF APPLICATION**	**APPLICATION NUMBER**	**DATE OF GRANT**

EXPLOTATION	EXPLOTATION INSTITUTION	STARTING DATE	ACTIVE	ENDING DATE
NO	VEGENAT SA100%		NO	

RETIC CODE:
RD12/0026/0001

DESCRIPTION OF THE RESEARCH ACTIVITY PROGRAMME

Background - Objectives - Workplan - Innovation - Technology transfer

It is very important to include in this section the importance and dimension of the programme at national and international level, background of weight on mortality, morbidity and disease weight, state of the art in Spain and in the international context as well as the objectives that are going to be accomplished.

Maximum 4 pages

In the last four years, our network (Red SAMID), and previously most of its research groups, have been studying different aspects on two key areas on paediatric growth and development: 1) **the factors causing brain injury in Childhood and thus affecting neurodevelopment, and 2) the early nutritional factors related to the latter development of the metabolic syndrome in preadolescent children**.

Although these two topics might not seem to be related at first though, indeed there is a close links between them since both affect the growth and development processes from the foetus to the adolescence, areas of expertise of the research groups that are included in our research network.

1) F**actors causing brain injury and thus affecting neurodevelopment (ND).** The developing brain is especially vulnerable to many different insults that can induce impairment of its growth and development, and cause later in life neurodevelopment (ND) delays (cerebral palsy, mental retardation, language or learning and behavioural disorders...). Those insults to the brain occurred during the foetal, neonatal or early post-neonatal periods, and although the specific mechanisms are complex and vary, all are related to cerebral hypoxia and ischemia, and reperfusion (Hilario E. Current Pediatr Review 2006;2:131).

The aetiology of the ND disability is multiple, and the most frequent causes are different in the foetus -intrauterine growth restriction (IUGR), exposure to drugs and environmental toxic substances, malformations...)-, in the neonate -hypoxic-ischemic encephalopathy (HIE), infections, and cerebral lesions related to prematurity like severe Intraventricular haemorrhage (IVH), periventricular leukomalacia (PVL)-, or in the early infancy -infections, injuries, toxics, nutrition…- (Mwaniki MK et al. Lancet 2012;379:445).

Although advances in obstetrics and intensive care management have improved the survival of those target populations, impairment of ND has not decrease in the same magnitude. Thus, research on scientific aspects related to its causes and its health consequences, specially related to its prevention are much needed.

The different ND disorders produce great stress to parents, families and communities; consume large resources in the health and educational systems for follow-up, diagnosis, management and rehabilitation. Moreover, affected children might not be able to achieve and ability to self support and care for themselves and thus a full integration in society.

Although the incidence of some of these disorders has been specifically measured, the overall burden and long-term sequelae have not been capture in estimates of the total burden of disease measured by disability-free years, either in Spain or at an international level (Olusanya BO. PloS 2007;4:e84).

2) **Early nutritional factors related to the latter development of the metabolic syndrome in preadolescent children**. Childhood obesity is one of the main problems affecting children in developed countries and some developing ones, having a real epidemic proportion. In Spain, its prevalence has been increasing steadily, and is been estimated that affects to a 27% of children, one of the highest rates of all European countries (Lobstein T et al. Obes Rev 2003;4:195). The causes of obesity are multiple, been influenced by genetic and environmental factors, although over-feeding is the single most important one.

Obesity plays a key role on insulin resistance and the metabolic syndrome (MS) with severe cardiovascular -hypertension- and metabolic risk factors (abdominal obesity, hyperglycemia due to type-2 diabetes, dyslipidemia) (Simmons R. Pediatr Clin N Amer 2009;56:449). However, only some obese susceptible individuals develop the MS, generally attributed to the interaction of genetic and environmental factors.

Many human and experimental studies have shown the relationship between low-birth-weight and obesity, insulin-

resistance and the MS. Recently studies showed that fetal IUGR is an independent risk factor for insulin-resistance that it is amplified by obesity in childhood. In fact, those observations following the initial Barker-hypothesis (Baker DJ et al Lancet 1986;1; 1077) introduced the concept of early programming induced by altered intrauterine environment related to the maternal or fetal protein restrictions, and induces epigenetic gene regulation, in the context of the developmental origins (foetal) of health and cardiovascular disease (Gluckman PD et al 2004;15;183). The concept of "developmental plasticity" is now used to describe the phenomena of generation of alternative genotypes forming a single genotype by the action of environmental factors during development (Gluckman PD et al. J Intern Med 2007;261;46).

On the other hand, produced much efforts to develop effective preventive strategies, but unfortunately little has been achieved so far.

Our research network, by its multidisciplinary approach, is formed by researchers and clinicians in obstetrics, neonatal and childhood health specialists as well as some basic scientists, so it seems especially well equipped to undertake this program and fulfil the objectives of the proposed scientific program. For this reasons, as well as for the experience on working together toward a common goal in these fields for the last four years, we believe on the importance and dimension of our research program both, at a national and international levels, since we have human and equipment resources and expertise to study the topics proposed from the bench -animal models- to the bed side -epidemiological and clinical trials-.

The state of the art in both Spain and in the international context is similar, as far as the clinical management of both cerebral damage and neurodevelopmental delays, and obesity and the MS. However, on the research aspects, in Spain there are no previous multidisciplinary research efforts in this topic, not only in Spain but there are some excellent studies on single aspects of the problems. The horizontal research approach -from the foetus to the adolescence- and the broad multidisciplinary groups involved, makes this research program almost unique even at an international level.

Hypothesis. There are perinatal and postnatal factors that lead to neurologic, nutritional and metabolic disorders from prenatal period to adolescence, that subsequently condition adult life health. The study of some of this factor might contribute to its prevention.

The Scientific Programme has its main strategic objective on the prevention and treatment of the perinatal and post-neonatal risk factors involved in the development of neurologic, nutritional and metabolic problems, from the foetal age to the adolescence.

More precisely, the operative scientific objectives are related to, 1) the factors causing brain injury and thus affecting neurodevelopment and 2) the early nutritional factors related to the latter development of the metabolic syndrome in preadolescent children.

To ensure the accomplishment of these two operative specific objectives, the research programme will be approached in several Work Packages (WP) appropriately linked and coordinated. Each WP will approach a specific objective that will be analysed by a few specific tasks. For each task, an outcome will be produced, that could be measurable to assure the correct progression of the program. Moreover, a timetable and a list of key milestones will be established for similar proposes.

Each of the two main areas of the programme will be studied in a horizontal timeline, from the foetal stage to the adolescence as appropriate. So, prenatal, neonatal and post-neonatal WP will be set for each of the two main study lines, as indicated in the next paragraphs.

WP-1. PRENATAL RISK FACTORS FOR ABNORMAL NEURODEVELOPMENT AND NUTRITIONAL AND METABOLIC OUTCOME.

General objective. To study on IUGR biomarkers able to predict the postnatal development of disorders of ND and MS.

Specific objectives.

1.1 To establish a protocol for the diagnosis and obstetrical management of IUGR agreed by all network centres.

1.2 To study the interrelation between epidemiological, toxic environmental, socio-economic variables and maternal

risk factors with the alteration/change in ND and MS

1.3 To study the relationship between Doppler hemodynamic compromise of umbilical blood flow and alteration of the ND and MS.

1.4 To study the interrelation between immediate perinatal complications with of ND and MS

1.5 To develop a foetal model of IUGR, to study factor affective fetal growth and test possible preventive and therapeutic strategies.

WP-2 NEONATAL RISK FACTORS FOR IMPAIRED NEURODEVELOPMENT OUTCOME.

General objective. To study early biochemical, biophysical and brain image biomarkers able to predict the postnatal development of disorders of ND.

Specific objectives.

1. To analyse the changes in the Redox status in foetal to neonatal transition, and the oxidative damage to membrane lipids, neuronal cell membranes, nitrosative damage caused to circulating proteins and inflammation caused to DNA.

2. Metabolic changes due to fetal to neonatal transition, oxygen supplementation, hypoxia, hyperoxia, etc. or factors changing Redox status (inflammation, infection, ventilation, etc.),

3. To study neonatal risk factor for brain injury and adverse ND in relation to: cerebral oxygenation, transient cardiovascular instability and hypoxic-ischemic encephalopathy.

4. To developed and integrated data acquisition e-system to validate the development of algorithms to be use of early biomarkers of brain and cardiovascular dysfunction.

5. Stalish animal models of neonatal hypoxic-isquemic brain injury.

WP-3 NEONATAL RISK FACTORS FOR ADVERSE NUTRITIONAL AND METABOLIC OUTCOME.

General objective. To study neonatal risk factors for adverse nutritional and metabolic outcomes and possible preventive nutritional strategies.

Specific outcomes.

3.1. Improve the ND of premature infants by changing the diet with the intake of DHA of the breast milk

3.2 To study the changes experienced by the fresh and pasteurized human milk throughout the administration process

3.3 To study the effect of nutritional status at discharge on body composition and glucose intolerance, and on later ND

3.4 To Know which probiotic allows better colonization of the gastrointestinal tract and better intestinal development, growth and neurodevelopment.

3.5.To learn the effect of a high protein diet on protein synthesis and overall synthesis of certain proteins such as albumin in critical pediatric patient.

WP-4. POST-NEONATAL RISK FACTORS FOR IMPAIR NEURODEVELOPMENT OUTCOME.

General objective. To identify risk factors of postnatal neurological development of children and evaluate the effectiveness of diagnostic methods on prevention and treatment.

Specific objectives:

4.1 To identify populations and postnatal risk factors for major ND impairment and neurological disorders in childhood: cardiac arrest , heart surgery, traumatic brain injury, stroke and poisoning.

4.2. To study the usefulness of methods for early detection of risk factors and neurological disorders: Neuroimaging methods: ultrasound, CT, MRI, PET, Monitoring of cerebral blood flow, Saturation brain using near-infrared spectroscopy (NIRS) ECG, Biochemical biomarkers.

4,3. To study the efficacy of prevention and treatment methods to reduce neurological disorders,/.Oxygenation: to analyze the influence of the fraction of inspired oxygen during cardiopulmonary resuscitation and treatment of hypoxic-ischemic alterations in the development and prevention of acute neurological injury.

4.4 To develop animal models of diagnosis, prevention and treatment of neurological diseases that occur in pediatric animal models of hypoxic neurological injury, ischemic neurologic injury and cardiac arrest.

WP-5. POST-NEONATAL: RISK FACTORS FOR NUTRITIONAL AND METABOLIC ADVERSE OUTCOME.

General objective. To study risk factors for adverse nutritional and metabolic outcomes in early childhood and possible preventive interventional strategies.

Specific objectives**:**
5.1 To investigate subclinical cardiovascular disease in children 8-10 years old, with perinatal developmental factors (IUGR or extreme low birth weight) that potentially influences the future risk of this disease.
5.2. To define non-invasive approaches to identify children with early changes in cardiovascular physiology that potentially affect future cardiovascular outcome, emphasizing their potential applications in childhood.
5.3 To evaluate the biological effects of early and realistic interventions in the selected population, analyzing potential changes in the defined biomarkers.
5.4 To investigate the influence of genetic variants on the development of obesity and yo evaluate the association between those genetic variants and food habits, physical activity and biomarkers of inflammation, cardiovascular diseases risk and oxidative stress.

WP-6: EPIGENETIC, TOXIC AND ENVIRONMENTAL RISK FACTORS FOR ABNORMAL NEURODEVELOPMENTAL, NUTRITIONAL AND METABOLIC OUTCOME.

General objective**.** Research on prenatal and postnatal environmental factors related to neurological, nutritional and metabolic disorders from prenatal period to adolescence.
Specific objectives.
6.1. Development of analytical methodology to describe and validate biomarkers of prenatal and postnatal exposure to substances and drugs of abuse, drugs of prescription, persistent organic toxics and heavy metals in different alternative matrix.
6.2 To study the prevalence of prenatal and postnatal exposure these several substances on prospective and retrospective cohorts of newborn infants born in different regions of Spain, and to perform follow-up of the cohorts of prenatally exposed newborns.
6.3 To develop animal models of prenatal exposure to xenobiotics, mainly alcohol to define biomarkers of different substances (parent substances and metabolites) to which foetus, newborn, child and adolescent can be exposed

To assure the accomplished of all specific objectives included in the six wp, a complete and detailed **Work plan** has been developed. It includes: 1) details about the human resources available (personnel provided by the institutions of the network partners and those specifically hired with the project's funds) as well as equipment (mainly provided by the partners from other sources), 2) details about the tasks planned to achieve the specific objectives just outlined, 3) a time schedule for all tasks and deliverables, 4) a detailed budget, and 5) a set of indicators to measure the research have been developed. Details on all of these different components of the Work plan are described on the appropriate sections of this proposal.

The innovative aspects of this proposed research project are not only related to the horizontal and multidisciplinary approach to be implemented, but also in regard to the real possibilities for several technological advances to be transfer to industry and eventually to clinical use. Some groups have or are developing several devices or systems. In this regard, among others, a device to be used to prevent preterm birth has been developed and proven effective (Goya M et al. Lancet 2012, April 3, 2012 DOI:10.1016/S0140-6736(12)60030-0), prototypes of devices to deliver nebulised exogenous surfactant without need for intubation in preterm and term neonates with severe respiratory failure, and a multichannel integrated system to capture and analyse multiple electronic signals from brain, cardiovascular and pulmonary function, will be eventually used for monitoring and treatment decisions..

Furthermore, several of the research groups have register patents to support liquid ventilation (Alvarez et al. No pat 2006/03096, Alvarez et al. No 1999/01420), that proves their ability to transfer rapidly research findings into technological innovations, assuring that it will also happen in this project.

RETIC CODE:
RD12/0026/0001

FUNCTIONAL STRUCTURE OF THE PROGRAMME

Describe the extension of the synergies and the added value to be obtained from the cooperative structure.

Maximum 3 pages

Both human and equipment resources have been summarised in the previous section “Scientific and technological background of the participating groups”.
Below are the tasks to be developed in relation to the specific objetives of each WP are brieftly descrived below. Moreover outpots for each tasks are also summarised.

WP1. PRENATAL RISK FACTORS FOR ABNORMAL NEURODEVELOPMENT AND NUTRITIONAL AND METABOLIC OUTCOME
In order to achieve the aims of this WP, the network will perfom the following tasks: 1) Establish a protocol for diagnosis and obstetric management of IUGR. 2) Design of an electronic notebook for data collection. 3) Study the correlation between epidemiological, toxic environment, socio-economic variables and maternal risk factors with altered and postnatal metabolic syndrome (MS). 4) Study on the correlation between Doppler hemodynamic compromise with impaired ND and postnatal MS. 5) Study on the correlation between immediate perinatal complications with impaired ND and postnatal MS. 6) Design of a bank from blood samples of: mothers, umbilical cord, neonates and children diagnosed with IUGR. 7) Development of animal IUGR model.
After reaching these tasks, the following outputs will be obtained: 1) Protocol for diagnosis and obstetric management of IUGR. 2) Provide 80% of the epidemiological, toxic environmental, socio-economic variables and maternal risk factors of patients enrolled in the study. 3) Have Doppler hemodynamic variables within a given period of less than 10 days after delivery in 100% of cases and controls. 4) Record of perinatal data in 80% of study population. 5) Disposal of blood samples from mothers in 50% of cases and controls, umbilical cord in 30% of infants and children.6) Using the animal model for testing different treatments with clinical potential.
In WP1, we will implement a clinical guideline for managing risk pregnancies with IUGR and fetal hypoxia.

WP2. NEONATAL RISK FACTORS FOR IMPAIRED NEURODEVELOPMENT OUTCOME
In order to achieve the aims of this WP, the network will develop the following tasks: 1) Study of cerebral hemodynamic imaging, macro- microcirculation and oxygen delivery (Cerebral Monitoring Techniques for the prevention of brain injury of prematurity). 2) Analysis of biomarkers involved in brain injury. 3) Development of strategies to prevent brain injury in neonatal hypoxic-ischemic encephalopathy. 4) Animal model of hypoxic-ischemic brain damage. 5) Design of electronic systems used as early markers of brain and cardiovascular damage.
After reaching these tasks, the following outputs will be obtained: 1) Clinical guidelines for the management of cerebral oxygenation in the extremely preterm during the transitional stage of movement. 2) Score of biomarkers in the premature circulatory failure, used to direct therapeutic interventions. 3) Score adverse prognostic risk based on analysis of parameters of different integrated monitoring systems 4) Pharmacokinetics, tolerability and toxicity of different experimental treatments in asphyxic neonates undergoing moderate hypothermia. 5) Testing of different treatments with clinical potential in animal models, and 6) Patent of electronic systems designed.
In summary, this WP2 will implement a clinical guideline for management of cardiovascular instability and the hypoxic-ischemic encephalopathy.

WP3 NEONATAL RISK FACTORS FOR ADVERSE NUTRITIONAL AND METABOLIC OUTCOME
In order to achieve the related aims of this WP, the network will develop the following tasks:
1) Design of a randomised controlled study to evaluate the effect of dietary advice on the concentration of DHA in breast milk. 2) Description of the relationship between nutritional status at discharge and sensitivity to insulin. 3) Description of the influence of probiotics administered in intestinal colonization in very preterm infants 4) Study of the effect of diet on overall protein metabolism and on specific individual protein synthesis. 5) Establishment of nutritional losses, immunological, antioxidants factors and vitamins that suffer mother's milk after HTS pasteurization and compare it to Holder pasteurization. 6) Evaluation of the effect of speed and infusion time for power management systems, and different homogenization treatments (routine, manual, ultrasonic), change in lipid content, caloric and immunoglobulins and cytokines in thawed milk.
After reaching these tasks, the following outputs will be obtained: 1) Dietary survey. Relation between intake of DHA

estimated by survey and longitudinal concentration of DHA. A clinical trial will be flamed. 2) Relationship between insulin sensitivity and nutritional status at discharge. Study sample size estimation to evaluate the effect of nutritional status on neurodevelopment. 3) Effect of administered probiotics on intestinal colonization during the initial admission. Changes in intestinal colonization of very preterm children during the following months of discharge. 4) Effect of diet on overall protein synthesis on the splanchnic sequestration of amino acids and the synthesis of specific proteins. 5) Comparative table of nutritional losses, immune factors, antioxidants and vitamins of Holder pasteurization and HTST. Clinical guideline on the HTST pasteurization process for use of donated human milk banks. 6) Clinical guideline on the management of mother's milk. 7)Design of an infusion system that incorporates a method of homogenization.

In summary, develop a dossier of recommendations on the implementation of human milk banks following Good Laboratory Practice.

WP4. POST-NEONATAL RISK FACTORS FOR IMPAIR NEURODEVELOPMENT OUTCOME
In order to achieve the related aims of this WP, the network will develop the following tasks: 1) Design and development of a multicenter prospective observational studies of risk factors for neurologic impairment secondary to cardiac arrest, congenital heart disease, cardiac surgery, or secondary injury in children with long-term observation and to encourage the participation in the international multicenter study on pediatric stroke and to perform the control of long-term Spanish cohort. 2) Correlation and predictive capacity of alterations in computerized tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), cerebral blood flow, cerebral saturation measured by near-infrared spectroscopy (NIRS), electroencephalographic (EEG) abnormalities and biomarkers of neurodevelopment damage with acute neurological and long-term neurological deficits. 3) Correlation between FiO2, respiratory rate and/ or PaCO2 used in cardiopulmonary resuscitation and mechanical ventilation with acute neurological and long-term neurological deficits in children. Multicenter prospective study to analyze the effect of hypothermia in the prevention of acute neurological and long term after cardiac arrest in children beyond the neonatal period. 4) Animal model of pediatric neurological injury induced by: ischemia, hypoxia and cardiac arrest. 5) Comparison of different respiratory rates and FiO2 on cerebral blood flow, cerebral saturation measured by NIRS and biomarkers of neuronal hypoxic-hyperoxic damage on randomized experimental studies of cardiac arrest, hypoxia and ischemia.
After reaching these tasks, the following outputs will be obtained: 1) Multicenter study protocol of neurological disorders in children with: cardiac arrest, congenital heart disease and cardiac surgery. Report of participation in the multicenter study of stroke in children. 2) Clinical guidelines recommending neuroimaging studies in children at risk of acute neurological disorders. Clinical Guide recommendation for the use and interpretation of measurements of cerebral blood flow, cerebral saturation measured by NIRS, EEG and brain damage biomarkers in children with risk of neurological disorders. 3) Clinical guidelines on the FiO2 during cardiopulmonary resuscitation in children. Clinical guidelines on respiratory rate during cardiopulmonary resuscitation in children. Multicenter study protocol of hypothermia after cardiac arrest in children. Report of potentially neuroprotective drugs during hypoxia-ischemia and biomarkers of neurodevelopment damage in childhood to raise future clinical studies. 4) Pediatric animal model for ischemic neurological damage, for hypoxic neurological damage, for cardiac arrest. Report of the alterations of cerebral blood flow and cerebral saturation by NIRS in experimental models of acute neurological injury. Report of hypoxic-hiperoxic biomarkers alterations in experimental models of acute neurological injury. Experimental study protocol of the influence of FiO2 in pediatric cardiac arrest. Experimental study protocol of the influence of respiratory arrest in pediatric cardiac arrest.
In summary, a clinical guideline will be proposed for the early management of the various disorders that can cause brain damage.

WP5. POST-NEONATAL RISK FACTORS FOR NUTRITIONAL AND METABOLIC ADVERSE OUTCOME
In order to achieve the related aims of this WP, the network will develop the following tasks: 1) Subjects recruitment for different risk situations. 2) Assessment of personal and family history of the metabolic syndrome components. 3) Clinical examination, including clinical signs of insulin resistance and maturation status, blood pressure, and anthropometry. 4) Assessment of nutrient intakes and food habits using a standardized interview computer assisted 24h recall and Food Frequency Questionnaire. 5) Measurements of traditional biomarkers associated with insulin resistance and metabolic syndrome. 6) Measurements of biomarkers associated with insulin resistance, inflammation and cardiovascular diseases risk. 7) Measurements of parameters associated with oxidative stress. 8) Analysis of genetic variants. 9) Detection of cardiovascular subclinical alterations (echocardiography), potentially related with future cardiovascular diseases risk.10) Effect of classic intervention (nutrition and physical activity) on plasma and vascular parameters. 11) Statistical analysis.
After reaching these tasks, the following outputs will be obtained: 1) Report on the influence of genetic variants on the development of obesity. Results from the case-control study. 2) Report on the relationship between genetic variants and

food habits, physical activity and biomarkers of inflammation, cardiovascular diseases risk and oxidative stress. 3) Report on the noninvasive (echocardiography) cardiovascular measurements and its correlation within the cardiovascular diseases risk factors. 5) Report on the efficacy of the intervention in terms of cardiovascular diseases risk factors reduction.
Protocol to define and to prevent metabolic syndrome in children by the use of early biomarkers. This protocol will be defined by consensus and based in our results.

WP6. EPIGENETIC, TOXIC AND ENVIRONMENTAL RISK FACTORS FOR ABNORMAL NERURODEVELOPMENTAL, NUTRITIONAL AND METABOLIC OUTCOME
In order to achieve the related aims of this WP, the network will develop the following tasks: 1) To define paediatric alternative matrices useful for the determination of biomarkers of damage, or exposure. Furthermore, to create a biobank of clinical samples. 2) To define biomarkers of different substances (parent substances and metabolites) to which foetus, newborn, child and adolescent can be exposed (alcohol, tobacco, drugs, toxics, heavy metals). These biomarkers can be used in studies of prevalence of prenatal or postnatal exposure or in studies of tissue damage due to exposure. 3) To describe and validate the analytical methodology for each biomarker in every alternative matrix. 4) To determine the prevalence of prenatal and postnatal exposure to several substances. 5) Clinical follow up of the cohorts of prenatally exposed newborns and children to several substances. 6) Research on pharmacokinetics of drugs of prescription in children (clinical trials with drugs of prescription). 7) Development of animal models of prenatal exposure to several substances.
After reaching these tasks, the following outputs will be obtained: 1) List, detection time window, analytical methodology, significance and importance, and applicability of the alternative matrices. 2) List and table of biomarkers (parent substance, metabolites) of exposure of different substances. 3) Description of the analytical methodologies and its applicability. 4) Prevalence figures of prenatal and postnatal exposure to several substances. 5) Clinical and analytical results derived from the follow up of several substances prenatal and postnatal exposure. 6) Pharmacokinetic results and prescription recommendations and indications of medicines in children. 7) Description of animal models of prenatal exposure to several substances.
Presentation of clinical guidelines, for example, human milk banks, and environmental toxic (legal and non legal drugs).

In summary, our network propose to study two hot topics in Paediatrics: 1) the factors causing brain injury, affecting neurodevelopment; and 2) the early nutritional factors related to the latter development of the metabolic syndrome in children. Our multidisciplinary research network has been formed by basic researchers and clinicians in obstetrics, neonatal and childhood health specialists to undertake the program and to fulfil the aims, with adequate human and equipment resources. The horizontal research approach (from foetus to adolescence) and the multidisciplinary groups (from bench to bed side), makes this research program almost unique even at international level. These topics will be approached by our research network in six work packages, which are our expertise area. Finally, we propose that the main outcomes obtained from the Work Plan will be freely presented to all Spanish health stakeholders, international scientist and the Spanish society as a whole for its dissemination and spreading.

RETIC CODE:
RD12/0026/0001

SCIENTIFIC RELATIONSHIP BETWEEN THE DIFFERENT RESEARCH GROUPS IN THE PROPOSED RESEARCH TOPICS

Describe the ongoing scientific collaboration between different groups of the program on the proposed objectives.

Maximum 1 page

Scheam of scientific relationships between groups to perfomce the tasks proposed for each WP.

Work Package	Leader WP´s	Collaborative Groups
WP1	Groups (3) (4)	Groups (1) (5) (8) (9) (10) (11)
WP2	Groups (8) (11)	Groups (1) (3) (4) (7) (10) (12)
WP3	Group (10)	Groups (1) (2) (3) (4) (5) (7) (8) (11) (12)
WP4	Group (6)	Groups (1) (7) (9) (10) (12)
WP5	Groups (2) (12)	Groups (3) (4) (5) (6) (7) (9) (10)
WP6	Group (5)	Groups (1) (3) (4) (8) (10)

Abbreviations used:
Groups: (1) HUC (A. Valls),(2) UZ (L.Moreno),(3) HUSJD (JM. Lailla),(4) HUVH (LL. Cabero),(5) HUM (O. Vall),(6) HUGM (J. Lopez-Herce),(7) HUMV (M. Garcia Fuentes),(8) HULP-neo. (F. Cabañas),(9) HULP-Surg. (J. Tovar),(10) HU12O (CR. Pallas),(11) HULF (M. Vento) and (12) UG (A. Gil)

The research groups included in our network have been collaborating in scientific projects and publications for many years. More specifically, this cooperation increased since January 2009, when the ISCiii funded our research network (Spanish Research Network on Maternal-Child Health and Development- Red SAMID).
Before the funding of our network, scientific relationships occurred mainly among groups from the same disciplines (two obstetric, four neonatal and seven paediatric sub-specialised on nutrition and metabolism, intensive care and surgery). Collaboration is proven by the participation of groups in collaborative projects funded at national and European levels. Moreover, since it´s funding the Network, the scientific collaboration was much enhanced taking a key interdisciplinary approach; so studies funded, published and ongoing acquired a horizontal approach from the foetus to the neonate and beyond. Thus, the basis were set to proceed more ambitious interdisciplinary research projects on the early origins of diseases originated in the foetus, newborn and young child, expressed latter in life.
The incorporation of junior scientists made possible by the ISCiii´s funding 2008-12, enhance research projects and publications in those years, since involved not only clinicians -obstetricians and paediatric subspecialists- but also clinical biomedical specialists –nutritionist and psychologists- and basic biologic researchers -biologists, biochemists, microbiologists...-. Thus, the basis to perform high impact translational research were set, and how we plan to archieve those goals.
The funded projects, publications, patents and other scientific achievements of our network, are detailed in other sections of this proposal (scientific and technological background of the participating groups, CV of the project coordinator, details on the five more important publications, funded projects, clinical trials, epidemiologic studies and patents on the last four years). Those achievements set the basis for further collaboration on this research project, and appear to guaranty that the specific objectives proposed might be achieved within the timeframe. Nevertheless, as examples of these collaborative scientific achievements, a few outcomes of these collaborations are given in the next paragraphs.
We like to stress that several National and European projects with external financing support have an active participation on several of our research groups. At a national level, seven clinical trials (CAIBER protocol indentifying numbers: 1645-CI-057, 1645-CI-058, 2156-B-028, 1677-EKI-096, 1557-H-125, 1392-GI-397, 1392-CI-399), and several projects are developed in close collaboration of some groups from our network.
It is noteworthy that two research groups lead European DGSANCO projects (EuroNeoStat I and II –collecting data from 200 neonatal units from 27 countries on causes and consequences of very premature infants- and the SCPE Registry –collecting data and performing epidemiological studies on children with Cerebral Palsy also at European-level).
Moreover, some groups participate in the consortium of several research projects funded by the EC´ 7th RFP (Global Research on Paediatrics –GRIP- aiming to overcome block on the development of appropriate medicines for foetuses, neonates and children and in a proyect funded in the Netherland, the NeoCirculation project, seeking development and study the effects of a pharmacological preparation of dobutamine for neonates, and the Safebooth Trial, to study if non-invasive monitoring of cerebral oxygenation improves the neurodevelopmental outcome of very premature infants).

RETIC CODE:
RD12/0026/0001

DETAILED BUDGET FOR THE PROPOSED RESEARCH PROGRAMME (one for each research group)

Describe the consistency between resources, capabilities and objectives.

Justify in detail the proposed budget (personnel, supplies and travel) so as the purpose.

Maximum 5 pages for 15 groups

Below, details for the total budget for both, the proposed Research and Training Programmes as well as for Coordination are provided. The total budget is broken down in subheadings for the Coordinating Group and for each of the remaining eleven Research Groups, and additionally for each of the four years of the Programme proposed for the network. Moreover, the budget is also broken down for personnel costs as well as mobility and training for each group.

The budget assigned to the Coordinating Group, include subheadings for personnel to be hired for the group, mobility and training, platforms for the group and for the network as a whole, as well as per the Training Programme of the RETICs and for Coordination of the network.

As will be noted, no specific budget is assigned for equipment and supplies. Although a certain amount of resources for these two concepts will be required, all Research Groups agree to set as a priory the appointment of full-time researcher personnel to each Research Groups, including the Coordination of the project as a whole. Thus, aligned to that decision, almost all resources will be dedicated to that goal. In the following paragraphs, the reasons why this decision was taken, and also why such a decision will by no means compromise the consistency between resources and objectives of both the Research and Training programmes. it is justified,

The decision to dedicate almost all requested resources to appoint researchers is easy to understand, if one is aware of the conditions affecting the Research Groups within the different institutions of the Spanish Health Systems. All Research Groups are part of hospitals of one of the 17 Spanish Health Systems, in which no protected time is set for research apart from clinical tasks. Thus, clinicians form obstetrical and paediatric services need to perform some research tasks by delegation to full-time researches pay by this project. Furthermore, those clinicians included as the staff researchers in the different Research Group, do not have the technical skills to perform certain research tasks like biostatistics, laboratory determinations, etcetera.

On the other hand, the decision to dedicate all requested resources to appoint external researches to the Research Groups will not affect the exit of the Research and Training programmes because enough equipment and disposable supplies are and will continue to be available to Research Groups and to the Network as a whole. All Groups have a long-standing record on research, as shown in several sections of this application, especially in that dedicated to the “Scientific and technological Background of the Participating Groups”, as explained in the following two paragraphs, and thus have access to the equipment needed.

1. Most Research Groups are not only large and high quality health agents but also have well established research structures, as Research Institutes fully recognised and that have receive or are in process to obtain accreditation from the ISCiii. Some of this institutions also are part of network of 40 hospital included in the ISCiii´s CAIBER network (Spanish Platform for the Performance of Clinical Trials). The few Groups that do not belong to those institutions, do have well equipped Research Units. Thus, no additional equipment is required to assure the fulfilment of the objectives of this Research Program.

Partner’s institutions have equipment in the following areas: biochemical and haematological determinations, including measurement of drugs and toxic substances, hormonal and enzyme assays, metabolomics and proteomics, cellular differentiation studies, tissue culture, imaging techniques and all molecular biology procedures. Furthermore, five institutions have also facilities to perform animal studies both in rodents as well as in larger and foetal and juvenile animal models.

2. Regarding supplies and other disposables, the ongoing research grants that all Research Groups have, been mainly related to the same topics as on this proposal, also guaranty that the set goals will be achieved. In the case that as the Research Programme’s progresses in the following years, the structure of the budget will be rearrange to cover those

needs.

3. Moreover, all Research Groups have agree to seek additional funds to complement the resources assigned to this Research Programme, to be dedicated to cover and achieve new objectives that might appear along the line as this program develops.

For all this fore mention reasons, it can be assured the consistency between the resources requested and the objectives, tasks and outputs proposed and to be completed.

Justification_for_the_requested_budget.

A detailed justification of all the items included in the total budget for the Research and Training Programmes (personnel, travel and training, coordination and platforms) is given. Latter, justification of resources to each Research groups is also described.

1. Personnel. The appointment of a researcher to each Research Group is requested. Its justification as been already provided earlier on this section. For the Coordinating Group additional resources are requested to cover specific research tasks related to epidemiological and biostatistics special skills to be provided to all participating Research Groups, in relation to the design, performance and analysis of the results of epidemiological studies and clinical trials to be perform within the network, with the participation of other Affiliated Clinical Groups, mainly in cage of patient recruitment and data gathering.

Justification_of_resources_requested_for_each_Research_Group.
For each of the 12 Research Groups, including the Coordinating Group, funds to appoint one research assistant are requested. The amount ask for is in accordance to the recommendations set by the ISCiii. Each Group will determine the specific background and skills needed, and according to that, an appropriate candidate will be hired. To complement the stipend, each Group might dedicate additional resources, if available from other sources, usually of own or local funds. Stipends will be increased annually as per local, regional or national recommendations, and so, the annual budget will modified accordingly. The fact that all Research Groups are given equal resources, but the Coordinating Group has been agreed upon by all Groups, and accordingly tasks will be divided also evenly, also according to their knowhow and research capacities.

2. Mobility and training. A small amount is requested for each Research Group to minimally cover the expenses needed to attend the annual network´s Workshop and other face-to-face meetings to design, coordinate and analyse ongoing and planned future collaborative studies. These resources could also be used to pay expenses to attend other scientific meeting to which results of ongoing research projects are to be presented or for short stays with any of the other Research Groups for training in specific skills.

The limitation of those resources assigned will be complemented by each Research Group from other sources to make sure that sufficient prudential personal interaction does take place among Groups in other to

3. Equipment and disposable supplies. The specific reasons for not requesting any resources for these two concepts has been previously described and justified, to reassure that it will not be a limitation to fulfil the objectives of the Research and Training Programmes.

Justification_of_resources_requested_for_the_Coordinating_Group.

For the Coordinating Group additional recourses are requested, since not only will have similar research responsibilities and tasks, but also will take the coordinating role for both, the research and Training programmes. Moreover, it coordinates all administrative issues as well as the auto-evaluation process to assure the timely development of both programmes, and all dissemination efforts and other aspects related to organisation and management, and interim and final scientific and technical reports for the funding agency, the ISCiii.

Coordination. Specific request to appoint a Project Manager is included in the Budget. This seems fully justified by large number of Research and Clinical Affiliated Groups included in the Network as well as for the need to coordinate the numerous objectives, tasks and outputs, and assure its achievement at the preset times, according to the timetable of the Scientific Programmes' workplan.

Mobility and training. Resources allocated for this topic is the double to that assigned of all other Research Groups, because of the larger number of researches on the Croup, and also since the number of coordinating and evaluation meetings is larger.

Training programme. Resources are also allocated to the Coordinating Group to pay for annual the Workshop, that includes costs of lodging an a subsistence of a total of 60 persons, between staff and assistant researches, and other invited scientists. It pays also for costs of travel to attend other 2-4 coordination meetings, with all or part of the research Groups´ representatives.

Platforms. Other that to appoint a Project Manager, the Coordinating Group is funded to appoint a research assistant, like the rest of Research Groups. Additionally, it is budgeted to appoint two additional researches to cover the epidemiological and biostatistics need for the clinical studies, as described in the previous section

Finally, it should be noted that the coordination efforts not only involve the Research Groups but also the already recruited Affiliated Clinical Groups and those to be recruited as need arises for ongoing and future studies.

Proposed_Budget_2013_–_2016

Coordinator_Group

Year	2013	2014	2015	2016
Personnel_(1_doctor_researcher)	35.000,00	36.750,00	38.587,50	40.516,88
Mobility_and_Training	5.000,00	6.000,00	7.200,00	8.640,00
Platforms_(2_doctor_researchers)	70.000,00	73.500,00	77.175,00	81.033,75
Coordination_(included_an_Project_Manager)_	35.000,00	40.250,00	46.287,50	53.230,63
Training_Programme	10.000,00	11.500,00	13.225,00	15.208,75
Subtotal	155.000,00	168.000,00	182.475,00	198.630,00
Overhead	23.250,00	25.200,00	27.371,25	29.794,50
Total_Coordinator_Group	178.250,00	193.200,00	209.846,25	228.424,50

The_other_11_groups:

Year	2013	2014	2015	2016
Personnel_(1_doctor_researcher)	35.000,00	36.750,00	38.587,50	40.516,88
Mobility_and_training	4.000,00	4.800,00	5.760,00	6.912,00
Subtotal	39.000,00	41.550,00	44.347,00	47.428,88
Overhead	5.850,00	6.232,50	6.652,13	7.114,33
Total_each_group	44.850,00	47.782,50	50.999,63	54.543,21

TOTAL_NETWORK_(annual)	671.600,00	718.807,50	770.842,13	828.399,77

TOTAL 2.989.649,39 euros

RETIC CODE:
RD12/0026/0001

IMPACT AND TRANSFER

Describe the potential impact of the porposal activities and the expected scientific and technological contributions.

Detail the adequacy of the dissemination plan and the transfer of technology strategy

Maximum 2 pages

1. Potential impact of research of the proposed activities.

Our project plans to bring together the major Spanish clinical research groups in obstetric and paediatric subspecialist in neonatology, nutrition, metabolism, and neurology as well as paediatric psychologist and basic researches on aspects related to Maternal and Child Health and Development within our network and beyond. We have already planned to involve clinical researches from other groups not included in our project, but that have collaborated in the past, as Associated Clinical Groups (we have 25 groups already). This will potentiate the ability to perform epidemiological studies and above all randomised clinical trials (RCT). Research efforts will be integrated through attention to standards and interoperability to leverage resources and enhance meta-analyses.

We will continue the design and conduct RCT (7 now in progress) to potentiate our capacity and disseminate our research initiatives. This process of integration, with the possibility of adding new groups funded via competitive calls for proposals, at national, European, and even at International level. In fact, most members of the network either lead or collaborate in European-funded research projects that should enhance the international impact of our network achievements. To further maximize its impact in the areas concerned, the project will try to link and collaborate on key initiatives in the field.

The establishment of our research network will facilitate active collaborations between partners and add value to their current research activities. In addition, collaborations with other research public and private partnerships will be actively pursued. It can be anticipated that we could have a catalyst effect on relevant research activities, and thereby enable closer integration of programmes in Spain and Europe.

2. Improving the health status of Spanish population.

Our project will have a positive impact on health through the provision of information leading to cause a better short- and long-term clinical outcomes for preterm and term babies, and thus on adults both this will improve health as initially sick babies recover and grow, and by reducing psychological stress and uncertainly experienced by the parents and families of such babies, as well as that of the health care professionals involved in their care. Due to research and education, the risk of serious maternal complications during pregnancy and at the time of delivery is very low in industrialised countries such as Spain. However, there is always a fear that the baby might be born with health problems, especially if it is born prematurely.

Premature birth and intrauterine growth restriction (IUGR) are among the greatest health hazards of humankind. In fact, prematurity is the single most common cause of sickness and death among newborn babies worldwide. In addition, it imposes major financial costs on the family, health care system, society, and economy. The frequency of preterm births is rising in the developed world, potentially driven by less healthy lifestyles and diets. Spain has one of the highest levels of preterm births in the EU, of about 10 IUGR also affects mortality and morbidity, and in fact sets the early basis for adult diseases, like obesity and the metabolic syndrome.

The improvement in health, learning ability and mental capacity of the Spanish population will reduce the ongoing health and welfare costs associated with these lifetime disabilities or handicaps resulting from premature birth. Apart from that actions on prevention and management of obesity in Spanish children, having one of the highest prevalence rates among European countries, should be expected to contribute to control its epidemic increase.

3. Expected scientific and technological contributions.

The previous and ongoing scientific relationship and cooperation between the Research Groups, has involved mainly

but not exclusively, the study of the different aspects on two key areas on paediatric growth and development: 1) neonatal and post-neonatal risk factors for brain injury and abnormal neurodevelopment (ND) and 2) the early nutritional factors related to the latter development of the metabolic syndrome (MS) in preadolescent children.

It should be expected that results from the project will contribute in the following areas: 1) diagnosis, evaluation of risks and prediction and prevention of adverse consequences for foetus with IGR and hypoxia; and 2) improving neurodevelopment outcome and description of early biomarkers on term neonates with hypoxic-ischemic brain damage, and premature infants with either hyperoxia or hypoxia; 3) infants and children with multi-aetiological cerebral injury, and 4) diagnosis and prevention of nutritional factors for obesity, type 2 Diabetes and the metabolic syndrome.

4. Dissemination Strategy

An effective dissemination strategy will ensure that the rationale behind the current proposal (and ultimately the results themselves) is rapidly understood by the wider community, increasing the likelihood of adoption and thus impact on the health of Spanish citizens. The dissemination efforts will be directed to all major stakeholders as general public and parents associations (the Coordinator, Valls-i-Soler has a special interest in involving parents and greater public in the research process, as well as the research community and other stakeholders)

Moreover, some partners are also involved in European and International scientific societies. So, all partners will be actively encouraged to help disseminate our findings at national and international meetings, and we anticipate arranging special sessions on the project to be linked to international conferences such as the European Society for Paediatric Research/Society of Neonatology (ESPR/ESN), European Association of Prenatal Medicine (EAPM), and other European Societies of Paediatric Subspecialties, like Intensive Care, Surgery, Metabolism….

Website www.redsamid.net. Our website will be the central source of information for parents, public in general as well as other researchers and stakeholders. In addition to general dissemination, a section of the website will also be developed to specifically engage target industry. The site will be updated frequently with information about the status of the project, interesting news and stories, six monthly newsletters and publications generated by the project.

Dissemination will involve approaches that are specific to each WP underpinned by generic approaches that apply to the whole project. WP-specific dissemination will be targeted to the relevant research community, taking account of the nature of the results to be disseminated. Dissemination is planned to run throughout the project and will devote its efforts to adequate and its results to attract the interest of different stakeholders.

Dissemination activities have consequences in terms of both financial and time expenditure. The dissemination agenda includes the design of a communication plan, the development of communication tools, and the execution of dissemination activities in order to raise awareness of the project as a whole, and specifically of its results, among different stakeholders. Coordination will focus initially on developing a communication plan for publicizing the project and its results, thereby establishing a consistent strategy for maximizing the impact and efficiency of the communication efforts. This will fully define and formalize the four basic pillars of the communication strategy: 1) Definition of the communication objectives; 2) Identification of the target audiences; 3) Description of the dissemination actions to be tackled; 4) Specific tools to be developed in order to support effective communication.

Subsequently, the communication tools identified by the communication plan will be developed as needed, keeping in mind the actions, audiences and objectives to which these tools should serve as supporting materials. The bulk of these dissemination undertakings will entail primarily, though not exclusively, scientific interactions that will include, at least:
- Publication of scientific papers. Preference will be given to the generation of publications related with the project activities and results, submitted to Spanish and mainly international scientific journals of high impact factor and citation index.
- Presentations at relevant events (Congresses, Workshops, etc.). Participation in the organization of relevant events to present the project´s approaches and results will be promoted,
- Individual presentations and meetings with key stakeholders. To raise interest and gain support of key actors in the field, such as regulatory authorities, researchers and pharmaceutical companies, individual contacts will be established as needed. This task will provide an important connection with the study of future use of the project results.

Taken together, the expected innovations summarised above will represent significant steps in various fields of current biomedical research and are of high relevance to the goals of Spanish and European Health research. Moreover, it all seems to guaranty the adequacy of the dissemination plan and the transfer of technology strategy will have a high

impact on stakeholders.

Governance.

It is noteworthy that achievement of some of our objectives is subject to a number of risks. To ensure that challenges are effectively managed and mitigated risks, our work plan comprises a strong project management that will specifically include active risk-management that will specifically include, an active risk-management and performance assessment, continually reviewing the scientific progress achieved and by measuring/measure it, against the predefined goals. A governance structure with the capacity to obtain and analyse effort and output for relevance and quality, is an essential part of the proposal, and designed to both monitor activity and recommend corrective action plans to ensure that the awarded funds and any additional collaborative funding is well managed.

RETIC CODE:
RD12/0026/0001

SCHEME OF EVALUATION OF THE PROGRAMME

Description of indicators for external evaluation, timeframe and proposed evaluation scheme

Maximum 2 pages

Besides the annual evaluation of the project development by the standardized reports and oral presentations to the ISCiii (the funding agency), we will perform a self-evaluation process both, internally and by the External Committee, as described below.

A systematic appraisal will be designed to assure the quality of both, methods and results. Each partner will be required to formally report to the different WP Leaders on progress and achievement of specific tasks and outputs, in compliance with the work programme every six months (Partner Progress Reports, PTR). These will include at least the following items: 1) short description of activities; 2) percentage completion; 3) estimated time completion; 4) milestones achieved; and 5) deviations from the objectives and incidents. WP Leaders will be responsible for summarizing the latter reports in the WP Progress Report, also to be completed every six months. These documents will be evaluated by the Management Committee (Adolf Valls I Soler, Luis Cabero, Luis Alberto Moreno Aznar, Maximo Vento Torres y Oriol Vall Combelles) in order to monitor the state of the project and arrange the adequate corrective actions, if needed.

The general objective of the self-evaluation is to maintain a continuously active process allowing identifying and reporting any deviation from the expected path of the project in order to react efficiently as soon as any problem is detected. For that purpose, the specific objectives are: 1) development of an agreed evaluation strategy that involves all partners, 2) definition of a evaluation procedure based in a pyramidal sequence of validations, and information flows, from the self-evaluation of each partner activities, to the periodic evaluation of the overall project execution at the management meetings, and 3) the continuous evaluation based on the previous strategy and procedures.

The self-evaluation will be focused in two main issues: 1) the execution of the project, measuring continuously the advancement in relation with the original work-plan, and 2) the appropriateness of developments done for the consecution of project objectives. For that purpose the suggested working process is based in the periodic reporting of each partner organization activities to the WP Leader and the periodic reporting of each WP leader to the project leader. In these periodic report previously mentioned issues shall be evaluated. This way each WP leader has the ability to react against any local incidence and the project leader maintains a continuous view of project situation. In parallel to this day-to-day evaluation, high level evaluations will be done during the project management meetings. The project leader will have the responsibility to prepare a summary of the project overall situation in order to jointly evaluate the main questions of the project.

Related to quantifiable indicator, we consider that success of the project cannot be measured in terms of numeric indicators, therefore these will be only used as an evaluation measure. Another evaluation procedure relies on the quality control of the data. For each specific objective an indicator is established to evaluate its quality and timing, from its design to the impact on the target groups and stakeholders, and for the quantifiable ones, target values will be set. Ultimately, evaluation of the project will be performed by the relative achievement of all indicators listed on WP

Referring to the control and evaluation process, the suggested policy will be the followed. Each partner will be required to formally report to the WP Leader on progress and achievement of specific deliverables in compliance with the work programme every three months (Partner Technical Progress Reports). These will include at least the following: 1) Short description of activities. 2) Percentage completion. 3) Estimated time completion. 4) Milestones achieved, and 5) Deviations from the objectives and incidents. The WP Leader will be responsible for summarizing the latter reports in the WP Progress Report also every three months. The coordinator should receive this document from each WP Leader and document the Project Technical Progress Report 7?). This document will be evaluated by the Management Committee in order to monitor the state of the project and arrange the adequate corrective actions.Near the completion of each WP, each WP Leader will be required to develop a first version of the Deliverables of the WP. This first version will be distributed to all the other WP Participants in order to improve the document. The WP Leader will develop and distribute new version of the deliverables in an iterative process. When all WP participants agree with the document, it will be saved in the Generated Knowledge Pile. It is a centralized store of generated knowledge and documentation and it is controlled by the PM.

Near the fixed reporting due dates, the Project Manager (PM) will develop a first version of the Fixed Term Reports. These first versions will be distributed to the Management Committee in order to obtain their agreement. The PM will develop new improved versions of these documents with the comments from the Management Board in an iterative process. When the Board agrees with the documentation, it will be stored in the Generated Knowledge Pile and the PM is the responsible for the delivery to EC and other partners.

TH PM will deliver a copy of the document to all the partners. In the case of Fixed Term Reports they will be delivered to EC and all the partners at the established fixed periods every 6 months). The management of any actualization of this delivered documentation will also be responsibility of the PM Related to quantifiable indicator. These we consider that success of the project cannot be measured in terms of numeric indicators, therefore these will be only used as an evolution measure. The main indicator will be the number of newborns included in the study by each partner unit as a measure for the statistical validation of comparative overall studies.

Specific indicators. For evaluation of all research groups as well as tythe network as a whole, the following indicators will be used:

Groups. Results (publications, translation activities and transfer), sources obtained and Connectivity with other groups.
1.Results.
1.1. Scientific publications. The 5 best publications, related to the research program topics and all Publications on the 1st and 2nd quartile.
1.2 Transfer activities. Number of clinical trial, contracts with health authorities, clinical guidelines, patents…
2.External funding. Total amount per group and year. National and International projects.
3.Interaction of groups. Collaborative publications and projects, databases…
4.Integration index. Compelimp all previous indicators.

Network: 1. Cohesion (of the network), 2. Internationalization, 3. (Network) Training Plan 4. Development of shared platforms, 5. Cooperative activity (within Network), and 6. Management, organization, planning and reporting the activities (of the Network)

STRENGTHS (How to improve, in brackets).

1. Potential participation and leadership in European and International projects. (More international dissemination of the achievements of the network)

2. Leadership in clinical trial design. (Improve the ability to carry out these EC funded proyects)

3. Capacity national leadership in different areas of the strategic plan. (Proposal of a perinatal / neonatal / pediatric network conducting EC).

4. Ability to provide experts in different research areas of network. (Disseminate this capacity in the professionals involved in each area or subspecialty)

5. Ability of several groups to perform experimental and genetic studies, genomic. (Dissemination of this information and organization of appropriate courses)

WEAKNESSES (Actions to be taken, in brackets)

1. Real integration on common goals.(More leadership of the steering committee).

2. Inability to spread the powerful research of network. (Disseminate properly the potential of the network).

3. Reduced number of groups for some projects (EC). (Stabilize and expand the clinical groups associated).

4. Network internationalization.(Encourage participation in more European projects).

5. Level of impact and citation of common publications. (Establish a strategy for upgrading the number and quality of publications)

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Add an image as annexe (if you wish) (formats: gif, jpg)

Maximum 1 image