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PRODEX Programme – Annex 4

Project Reporting

This file has to be sent back by **electronic means** to the appointed administrator(s) at ESA (specified in the PEA) and to the responsible administrator at BELSPO (listed in section 3 of the Guidelines).

A. Identification of the project.

- Title/Acronym: **IMpulSE (IMMUNO-2, MoCISS, SPHEROIDS)**
- Identification of the overall project selected/endorsed by ESA (AO or none):
  IMMUNO-2 (PI: Dr. A. Choukèr, Munich, Germany);
  MoCISS (PI: Dr. A. Choukèr, Munich, Germany);
  SPHEROIDS (PI: Dr. D. Grimm, Aarhus, Denmark).
- Possible role of the BPI and of each Bco-I in the overall project selected/endorsed by ESA (PI, co-I, other): **S. Baatout: BPI, M. Moreels: Bco-I, R. Quintens: Bco-I.**
- Satellite(s) or flight opportunity(ies) (+ date(s)) selected/endorsed by ESA: **ISS flight for IMMUNO-2 (scheduled for end 2015). ISS flight for MoCISS (scheduled for end 2015). ISS flight for SPHEROIDS (BIOBOX Increment #6) (scheduled for end-2015).**
- PEA (reference, starting and ending dates): **MOSAIC (C90-380): 01/05/2009 to 30/04/2011; MOSAIC2 (42-000-90-380): 01/05/2011 to 31/12/2012; MOSAIC3: 01/01/2013-31/12/2013 (42-000-90-380)**
- Period covered by this *Project Reporting*: **01/01/2014 - 31/12/2014**

B. Identification of the BPI.

- Title, surname, name: **Prof. Dr. Sarah BAATOUT,** Head of Radiobiology Unit
- List of the team members involved in the project: Marjan Moreels, Roel Quintens, Kevin Tabury
- Institute/University: SCK•CEN
- Department/Laboratory: Radiobiology Unit, Molecular and Cellular Biology
- Address: Boeretang 200, BE-2400 MOL
- Tel.: +32-14-33 27 29
- Fax: +32-14-32 10 49
- E-mail: sbaatout@sckcen.be

- Website: http://www.sckcen.be
- Institute/Department Head, endorsing this Project Proposal: Professor Eric van Walle, general manager

C. Identification of the Bco-I's (if applicable).

- Title, surname, name: **Dr. Marjan MOREELS, PhD**
- Institute/University: SCK•CEN
- Department/Laboratory: Molecular & Cellular Biology, Radiobiology Unit
- Address: Boeretang 200, BE-2400 MOL
- Tel.: +32-14-33 28 16
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- E-mail: mmoreels@sckcen.be
- Website: http://www.sckcen.be
- Institute/Department Head, endorsing this Project Proposal: Professor Eric van Walle, general manager

- Title, surname, name: **Dr. Roel QUINTENS, PhD**
- Institute/University: SCK•CEN
- Department/Laboratory: Molecular & Cellular Biology, Radiobiology Unit
- Address: Boeretang 200, BE-2400 MOL
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- Fax: +32-14-32 10 49
- E-mail: rquinten@sckcen.be
- Website: http://www.sckcen.be
- Institute/Department Head, endorsing this Project Proposal: Professor Eric van Walle, general manager

D. Describe the results obtained since the last reporting and compare with the original objectives foreseen at this stage (see section G of the original *Project Proposal* (annex 2)). (max. 2 pages)

1. Introduction

General topic

During spaceflight, astronauts are exposed to different stress challenges of physical and psychological nature – the so-called **space stressors -** which can all affect the normal functioning of the human body:

- **Microgravity**: It is well known that the strongly reduced gravity in space can change the balance of the mechanical forces acting on different cell types, resulting in the triggering of specific cellular responses thereby leading to loss/change of functionality and/or programmed cell death (apoptosis).
- **Cosmic radiation:** Ionizing radiation can interact with biological tissues by inducing (in)direct damage to cells. Gaining more insight into the effects of cosmic radiation at the cellular level is of critical importance especially for long-term space flights and interplanetary missions. In this context, it will be interesting to identify biomarkers for radiation exposure and for predicting individual sensitivity towards radiation-induced damage.
- **Psychological stress**: There is no doubt that astronauts suffer from mental stress during space flight which can be caused by various parameters (confinement, isolation, heavy workload, disturbed sleep pattern …). Mental stress triggers several pathways within the brain, resulting amongst others in the release of stress hormones which in turn affect several organ systems including the immune system.

Purpose of the contract: Within IMPULSE, three different ESA accepted flight experiments will further evaluate the impact of the stress challenges described above. **IMMUNO-2** will perform a follow-up study of astronauts' health that stay for longer periods on the ISS. **MoCISS** includes an *in vitro* study onboard the ISS that will monitor the cellular immunity of astronauts *ex vivo* by use of the *in vitro* delayed type hypersensitivity (DTH) assay. Within **SPHEROIDS**, *in vitro* experiments on the ISS will further investigate the impact of microgravity on human endothelial cells.

Study	ESA Call	PI	Full Title
1. IMMUNO-2	ESF ILSRA 2009	Dr. A. Choukèr, Munich, Germany	Consequences of Stress Challenges on Stress Response systems and immunity in Space: a multidisciplinary approach.
2. MoCISS	ESF ILSRA 2009	Dr. A. Choukèr, Munich, Germany	Monitoring the Cellular Immunity by *in vitro* delayed type hypersensitivity assay on the ISS.
3. SPHEROIDS	ESA-AO-2004-006	Dr. D. Grimm, Aarhus, Denmark	Effects of weightlessness on tube formation, differentiation, and the mechanisms of apoptosis in human endothelial cells.

2. Achieved results

IMMUNO-2 (Consequences of Stress Challenges on Stress Response systems and immunity in Space: a multidisciplinary approach).

This project on the ISS is an integrative study protocol to provide a more holistic approach to become more conscious of, and to increase the knowledge on the complex physiological adaptation of humans during long-term space missions. Using a multidisciplinary approach, consequences of space stress challenges on stress response systems and immunity will be investigated. This perspective study will include 8-10 cosmonauts who are exposed to life in space and to the living conditions on the ISS in the course of long duration missions (up to 1 year).

In the frame of the IMMUNO-2 flight experiment, SCK-CEN is responsible for performing gene expression analyses on blood samples from astronauts at different time points before, during and after their flight. As a preparatory step, ground-based experiments have been performed in 2014 on a number of other cohorts (including volunteers who stayed for a prolonged period at the Concordia station in Antarctica as well as the subjects who participated to the MARS-520 isolation experiment). Data analysis for both these groups is still ongoing but results point to changes in genes related to the circadian rhythm as well as genes which have previously been shown to be deregulated in socially isolated individuals. We also observed some changes in the expression of genes related to different immunological pathways which may explain the observed transient activation of the immune response of these individuals during the winter period of their stay in Antarctica. Further analysis and validation of results is still needed. Several papers related to these experiments are currently under preparation and expected to be submitted in 2015.

In 2014, SCK•CEN performed several ground-based experiments for identification of gene expression biomarkers of exposure and individual sensitivity to low- and high-LET radiation. The effects of different radiation qualities (X-irradiations performed at SCK•CEN and carbon, nickel and iron ions irradiation experiments performed at GSI, Darmstadt, Germany) in human peripheral blood mononuclear cells were compared using several end points such as trascriptomic response (microarrays) and DNA double strand breaks repair kinetics (γH2AX assay). As a result, we identified a gene expression signature which is suitable for biodosimetry purposes following exposure to both low- and high-LET radiation. Interestingly, some of the genes identified in our studies as robust dose predictors, were also previously shown to allow discrimination of ionizing radiation response profiles from those induced by inflammation. Importantly, as the design of the microarrays allowed us to do so, we studied the radiation response of the above mentioned genes panel at the exon level and identified the most sensitive exons. All our microarray results were confirmed by qRT-PCR.

In 2014 also, in an attempt to find the genes suitable for individual radiosensitivity assessment we performed an iron ions irradiation experiment (highly relevant for Space conditions) combining the two above-mentioned techniques on the samples from the same healthy volunteers. This allowed us to integrate the data on individual DNA repair kinetics following heavy ions exposure with genome-wide gene expression response. Overall, we could see a more persistent up-regulation of the DNA repair and cell cycle regulation genes when compared to X-ray exposure, reflecting the complexity of DNA damage caused by high-LET particles and, as a consequence, slower rate of DNA repair. Our ground-based experiments allow us to build a strong experimental background for the Space flight experiments. Moreover, all the microarray experiments carried out so far with the use of heavy ions can also be used for preliminary studies of the radiation response of

immunity-related genes.

One paper concerning the identification of gene and exon signatures for X-ray exposure is under final preparation and expected to be submitted in February 2015. A second paper, concerning the comparison in transcriptional response to low- and high-LET radiation is foreseen to be submitted by the end of the year 2015.

In 2014 as well, after a few rounds of modifications and adaptations to space technical constraints, the Experiment Science Requirements (ESR) documents have been finalized and are now under final discussion between ESA and the Russian Space Agency (IBMP). IMMUNO-2 will likely fly end 2015. The design and the choice in the various necessary control tests (on blood, heart and brain function, urine, breathe) to be performed on the Earth based control groups was finalised in 2014

MoCISS (Monitoring the Cellular Immunity by *in vitro* delayed-type hypersensitivity assay on the ISS).

The aim of MoCISS is to monitor cellular immunity *ex vivo* from ISS crew members subjected to a multitude of stressful conditions during long duration missions. Using the *in vitro* delayed type hypersensitivity (DTH) test, the rationale of this assay is to monitor cellular immune (dys-) function in space and to investigate the role of stress hormones on the antigen/mitogen dependent immune responses. In addition, the *in vitro* incubation conditions onboard the ISS allow to comparatively test for the effects of gravitation (microgravity vs. 1G – incubation/centrifugation in the KUBIK module). Part of the work is including parallel ground-based studies performed by SCK•CEN.

In 2014, in preparation for the MoCISS flight experiment a number of optimization experiments were performed at SCK•CEN. The influence of the use of closed tubes (no gas-exchange) as well as the simulated microgravity condition (using the 3-D RPM device available at SCK•CEN) and radiation exposure were investigated in a set of viability experiments. Our results indicate that the use of closed tubes and microgravity simulation do not remarkably affect cell viability up to 48 h. After X-ray irradiation, our first results show only mild effects for doses ranging from 0 to 1 Gy.

In addition, experiments were performed to evaluate the effect of simulated microgravity and radiation exposure on the cellular immune response. The *in vitro* DTH assay was performed under *1 x g* and simulated microgravity conditions. Low basal cytokine levels (no challenge) were measured under both gravity conditons. In the normal 1 x g environment, pro-inflammatory cytokine concentrations increased significantly after 24 h stimulation with bacterial antigens. However, the rise in cytokine levels after challenge was clearly inhibited during microgravity simulation. Preliminary results show no distinct effect of X-ray irradiation doses up to 1 Gy on the plasma cytokine concentrations in both *1 x g* and simulated microgravity environment.

The flight experiment will be performed in collaboration with the American National Space Agency (NASA). The study will include 8-10 astronauts who are exposed to life in space and to the living conditions on the ISS in the course of long durations missions (5-7 months).

MoCISS is currently in the third and final implementation phase: the ESA revised ESR documents have been finalised in 2014 and SCK-CEN provided consequent help in the writing. To note, the ESR and preliminary design underwent a few rounds of ESA SPOT review (between Nov 2013 and Nov 2014). Thereafter, end 2014, it was sent to NASA for verification from their side. In 2014 and since the final approval of the ESR documents by ESA, the design of the necessary hardware have been started. It is expected that MoCISS will fly early 2016.

Remark 1: In 2013 ESA launched an Announcement of Opportunity for Life Science Research using the spaceflight analogue "Bed Rest" (AO-13-BR). In response to this particular call, SCK•CEN participated in two proposals out of which one has been succesfully selected for a definition phase in 2014.

*The selected proposal is "**BCR- Effect of bed rest on the creation of B lymphocyte antigen receptor repertoire and evaluation of the benefits of a nutritional supplementation with anti-inflammatory and anti-oxidant substances**" (coordinator: Prof J.-P. Fripiat) in January 2013.*

Remark 2: End 2013 ESA also launched an Announcement of Opportunity for Medical, Physiological and Psychological Researsh Using Concordia Antarctic Station as Human Exploration Analogue (AO-13-Concordia). In response to this particular call, SCK•CEN participated in one proposal which was selected for a definition phase in 2014.

*The selected proposal is "**Consequence of long-term confinement and hypobaric hypoxia on immunity in the antarctic Concordia environment (CHO2ICE II-study) from observations to mechanisms**" (coordinator: Prof Alexander Choukèr)*

SPHEROIDS (Effects of weightlessness on tube formation, differentiation, and the mechanisms of apoptosis in human endothelial cells)

This project focuses on the impact of microgravity on human endothelial cells *in vitro*. In the context of the previous MOSAIC and MOSAIC-2 contracts, extensive studies have been performed on cultured endothelial cells (EA.hy926, human endothelial cell line) using the Random Positioning Machine (RPM) by the group of Daniela Grimm (Aarhus, Denmark) in collaboration with SCK•CEN. This research has led to 8 joint publications so far (with 2 publications in 2014). These studies have shown that human endothelial cells are highly sensitive to simulated microgravity.

In parallel, additional work was also performed at SCK•CEN on the specific biological and molecular effects of acute and chronic low dose (cosmic) radiation on endothelial cells. This work resulted in two PhD theses (Michaël Beck, fully covered by BELSPO/PRODEX/ESA and Charlotte Rombouts who defended her PhD thesis in March 2014) as well as 6 publications. 3 other publications have been published in 2014 in Int J Mol Med (Rombouts et al, Int J Radiat Biol; Beck et al, Int J Mol Med; Beck et al, Int J Mol Med).

In 2013 and in 2014, hardware was developed by RUAG Space (Zurich, Switzerland). The bread board model of the SPHEROIDS hardware was tested according to the RUAG document IC-129.64-10 (Feb, 2013). This testing included functionality test of the

hardware (photo documentation of hardware) as well as elucidating the best storage temperature of fixed samples (RNA concentration), and the determination of the best cell number for the 7 and 14 day experiments (living cell number). All tests were performed in close contact with RUAG and ESA and are still ongoing. In addition, several meetings between ESA, RUAG and the coordinator were held. It is foreseen that the SPHEROIDS experiment will fly mid-2016. This experiment will enable the science team to distinguish the effects caused by simulated microgravity (RPM) from those, which are due to the influence of real microgravity or from other space conditions since part of the samples will be placed in two separate parts of the BIOBOX (0G and 1G).

In 2014, further optimization tests will still be performed concerning cell survival and function changes, resistance to vibration when cells are cultivated within the SPHEROIDS hardware.
A final step in the SPHEROIDS study is to expose these human endothelial cells to real space flight conditions in 2016.

E. Describe the tangible outputs of the project; include separately what is still to be expected.

Hardware, software, equipment (+ give an evaluation of its performance)

The Luminex platform at SCK•CEN is currently used for different projects within IMPULSE in view of the precise measurement of secreted proteins (cytokines/chemokines) in a small sample volume (<100 µL of biological fluid).

The genomic platform at SCK•CEN is currently used for the monitoring of 50,000 genes per sample (Affymetrix Human Gene 2.0 ST arrays).

Two Random Positioning Machines (Dutch Space, the Netherlands) and 4 Rotating Wall Vessels (RWV) are available at SCK•CEN to perform ground-based experiments for microgravity simulation.

- An irradiation facility (head: Dr F. Vanhavere) is available at SCK-CEN for irradiation of cells under X-rays or simulated LET radiation space conditions (gamma and neutrons).

- In April 2014, SCK-CEN has inaugurated a new and up-to-date animal facility that can host rodents. The facility is now available for research.

International publications (peer-reviewed) in 2014

- Arena C, De Micco V, Macaeva E, Quintens R. *Space radiation effects on plant and mammalian cells*. Acta Astronautica. 2014 Nov;104(1):419-31.

- Beck M, Rombouts C, Moreels M, Aerts A, Quintens R, Tabury K, Michaux A, Janssen A, Neefs M, Ernst E, Dieriks B, Lee R, De Vos WH, Lambert C, Van Oostveldt P, Baatout S. *Modulation of*

gene expression in endothelial cells in response to high LET nickel ion irradiation. Int J Mol Med. 2014 Oct;34(4):1124-32.

- Beck M, Moreels M, Quintens R, Abou-El-Ardat K, El-Saghire H, Tabury K, Michaux A, Janssen A, Neefs M, Van Oostveldt P, De Vos WH, Baatout S. *Chronic exposure to simulated space conditions predominantly affects cytoskeleton remodeling and oxidative stress response in mouse fetal fibroblasts*. Int J Mol Med. 2014 Aug;34(2):606-15.

- Feuerecker M, Crucian B, Salam AP, Rybka A, Kaufmann I, Moreels M, Quintens R, Schelling G, Thiel M, Baatout S, Sams C, Choukèr A. *Early adaption to the antarctic environment at dome C: consequences on stress-sensitive innate immune functions*. High Alt Med Biol. 2014 Sep;15(3):341-8.

- Pani G., De Vos W., Samari N., de Saint-Georges L., Baatout S., Van Oostveldt P., Benotmane MA, MorphoNeuroNet: An automated method for dense neurite network analysis, Cytometry, Volume 85 2014 (2), 188–199.

- Rombouts C., Aerts A., Quintens R., Baselet B., El Saghire H., Harms-Ringdahl M., Haghdoost S, Janssen A., Michaux A., Yentrapalli R., Benotmane M.A., Van Oostveldt P. and Baatout S.- Transcriptomic profiling suggests a role for IGFBP5 in premature senescence of endothelial cells after chronic low dose rate irradiation.- In: International Journal of Radiation Biology, 90:7(2014), p. 560-574

- Yi B, Rykova M, Feuerecker M, Jäger B, Ladinig C, Basner M, Hörl M, Matzel S, Kaufmann I, Strewe C, Nichiporuk I, Vassilieva G, Rinas K, Baatout S, Schelling G, Thiel M, Dinges DF, Morukov B, Choukèr A. *520-d Isolation and confinement simulating a flight to Mars reveals heightened immune responses and alterations of leukocyte phenotype*. Brain Behav Immun. 2014 Aug;40:203-10.

– Participation to congresses: distinguish between invited speaker, with oral presentation, with poster presentation and without contribution obtained in 2014

Invited speaker in 2014

- Baatout S.- Biomarkers in radiobiology.- 2nd workshop of the Belgian hadrontherapy consortium – Namur, Belgium, 25 May 2014

Oral presentations in 2014

- Macaeva E., Quintens R., De Vos W., Moreels M., Tabury K., Michaux A., e.a.- *Gene and exon signatures as high-potential biomarkers of exposure and individual radiosensitivity to low- and high-LET radiation*.- 41st Annual Meeting of the European Radiation Research Society ERR2014.- Rhodes, Greece, 14-19 September 2014.

- Quintens R., Suetens A., Macaeva E.- *Cellular and molecular effects of different beam qualities on cancer and blood cells*.- BHTC workshop "Hadrontherapy: from cell to patient".- Namur, Belgium, 23-23 May 2014.

- Quintens R.- *CHOICE: the transcriptome perspective*.- ESA Topical Team meeting.- Palermo, Italy, 3-5 February 2014.

- Schokaert T.- Possible scenarios to cultivate cyanobacteria on the Moon for life support.- presentation given for the Odissea prize ceremony, 16 January 2014

- Van Walleghem M.- *Animal models in space research*.- 1st workshop "Drawing lessons from stem cells and animal models outside the radiation field".- Mol, Belgium, 13-13 June 2014.

- Van Walleghem M.- *Consequences of space stressors on immunity: evaluation of immunological changes using in vitro space analogs on Earth*.- RDB Seminar.- Mol, Belgium, 27 January 2014.

Poster presentations in 2014

- Macaeva E., Quintens R., De Vos W., Moreels M., Tabury K., Michaux A., e.a.- *Gene and exon signatures as biomarkers of exposure and individual radiosensitivity to low- and high-LET radiation*.- Day of the PhD's.- Mol, Belgium, 23-23 October 2014.

- Macaeva E., Quintens R., De Vos W., Moreels M., Tabury K., Michaux A., e.a.- *Gene and exon signatures as high-potential biomarkers of exposure and individual radiosensitivity to low- and high-LET radiation*.- 41st Annual Meeting of the European Radiation Research Society ERR2014.- Rhodes, Greece, 14-19 September 2014.

- Verslegers M., Pani G., De Vos W., Samari N., Quintens R., de Saint-Georges L., e.a.- *Combined exposure to simulated microgravity and acute or chronic radiation reduces neuronal network integrity and survival*.- 41st Annual Meeting - ERR2014.- Rhodes, Greece, 14-19 September 2014.

- Macaeva E., Quintens R., De Vos W., Moreels M., Tabury K., Michaux A., e.a.- *Gene and exon expression as biomarkers for low- and high-LET radiation exposure*.- DoReMi's 3rd Periodic Meeting.- Munich, Germany, 8-10 July 2014.

- Van Walleghem M., Moreels M., Tabury K., Feuerecker M., Choukèr A., Baatout S.- *Consequences of space stressors on immunity: evaluation of immunological changes using in vitro space analogs on Earth*.- Day of the PhD's.- Mol, Belgium, 23 October 2014.

- Van Walleghem M., Moreels M., Tabury K., Feuerecker M., Choukèr A., Baatout S.- *Impact of simulated microgravity on cell-mediated immunity using the in vitro DTH assay*.- 6th International Congress of Medicine in Space and Extreme Environments (ICMS).- Berlin, Germany, 16-19 September 2014.

- Verslegers M., Pani G., De Vos W., Samari N., Quintens R., de Saint-Georges L., e.a.- *Combined exposure to simulated microgravity and acute or chronic radiation reduces neuronal network integrity and survival*.- 9th FENS Forum of Neuroscience.- Milan, Italy, 5-9 July 2014.

– Education and training activities in 2014

- Baatout S.- Space health effects.- University College of London, Mol, Belgium, February 2014 - (European Master in Radiation Biology). (International Course)

- Baatout S.- Radiation-induced effects with particular emphasis on genetics, development and space-related health issues.- University College of London, Mol, Belgium, February 2014.- (European Master in Radiation Biology). (International Course)

- Baatout S.- Introduction on Life Science Programmes at ESA.- KULeuven-UGent, Leuven, Belgium, November 25, 2014.- (B-KUL-G0G06a : Life Sciences and Biology in Space). (National Course)

- Baatout S.- Chapter 1: What are Life Sciences in Space? Chapter 2: General introduction on the challenges to human physiology in space; Chapter 3: Animal experiments in Space; Chapter 4: From body to molecular biology.- KULeuven-UGent, Leuven, Belgium, December 2, 2014.- (B-KUL-G0G06a : Life Sciences and Biology in Space). (National Course)

- Baatout S.- Chapter 5: Space microbiology; Chapter 6: Life support systems in space.- KULeuven/UGent, Leuven, Belgium, December 9, 2014.- (B-KUL-G0G06a : Life Sciences and Biology in Space Course). [National Course]

- Baatout S.- Real space conditions (from a few seconds to months) for life science experimentation.- KULeuven-UGent, Leuven, Belgium, December 10, 2014.- (B-KUL-G0G06a : Life Sciences and Biology in Space). [National Course]

Baatout S.- Chapter 7: Plant biology in space; Chapter 8: Developmental biology in space.- KULeuven/UGent, Leuven, Belgium, December 16, 2014.- (B-KUL-G0G06a : Life Sciences and Biology in Space Course). [National Course]

Baatout S.- Chapter 9: Space analogs on Earth for human (in vivo) studies. Chapter 10: Environmental monitoring aboard the ISS.- KULeuven/UGent, Leuven, Belgium, December 17, 2014.- (B-KUL-G0G06a : Life Sciences and Biology in Space Course). [National Course]

- Macaeva E.- *Measurement of gamma H2AX foci formation as a marker of ionizing radiation induced DNA damage*.- UGent/KU Leuven/SCK•CEN, Mol, Belgium, November 18, 2014.- (Master in Space Sciences. Course in Life Sciences in Space. Site visit to SCK•CEN).

- Macaeva E.- *Measurement of gamma H2AX foci formation as a marker of ionizing radiation induced DNA damage*.- University of Namur/SCK•CEN, Mol, Belgium, November 7, 2014.- (Cours SPHYM201 Travaux pratiques cours "Interactions des radiations avec la matière").

- Macaeva E.- *Radiation biomarkers*.- SCK•CEN, Mol, Belgium, August 18, 2014.- (Summer school in radiobiology).

- Macaeva E.- *Radiation biomarkers: an overview*.- SCK•CEN, Mol, Belgium, February 25, 2014.- (Two-week training course on radiation-induced effects with particular

emphasis on genetics, development, teratology, cognition as well as space-related health issues).

- Moreels M., Baatout S.- Space health effects.- SCK•CEN, Mol, Belgium, February, 2014.- (European Master in Radiation Biology). (International Course)

- Moreels M., Baatout S.- Impact of (cosmic) radiation on immune cell signalling.- SCK•CEN, Mol, Belgium, February, 2014.- (European Master in Radiation Biology). (International Course)

- Moreels M., Baatout S.- Space research programs at SCK•CEN.- SCK•CEN, Mol, Belgium, February, 2014.- (European Master in Radiation Biology). (International Course)

- Quintens R.- Introduction to analysis of data by means of systems biology.- SCK•CEN, Mol, Belgium, February, 2014.- (Two-week course on radiation-induced effects with particular emphasis on genetics, development, teratology, cognition as well as space-related health issues). (International Course)

- Quintens R.- PRACTICAL: Molec Biol – Radiation-induced gene expression in PC3 cells: quantitative PCR of DNA damage response genes.- SCK•CEN, Mol, Belgium, February, 2014.- (Two-week course on radiation-induced effects with particular emphasis on genetics, development, teratology, cognition as well as space-related health issues). (International Course)

- Tabury K., Van Walleghem M., Moreels M., Baatout S.- *Space-simulated effects on the cytoskeleton of monocytes*.- Radiobiology, Mol, Belgium, October 10, 2014.

- Van Walleghem M., Moreels M., Baatout S.- *Health Space Effects*.- SCK•CEN, Mol, Belgium, August 14, 2014.- (Summer School in Radiobiology).

- Van Walleghem M., Moreels M., Baatout S.- *Immunology in space*.- SCK•CEN, Mol, Belgium, August 14, 2014.- (Summer School in Radiobiology).

- Promoted works: Bachelor/Master/PhD theses in 2014

Master theses

Koninckx H.- Measures counteracting the radiation health risks on a manned lunar outpost.- Leuven, Belgium: KUL-UGent Master in Space Studies, 2014.- 77 p.- Master thesis

PhD theses

- Rombouts C.- The vascular endothelial cell response following exposure to low doses of ionizing radiation.- Gent, Belgium: Universiteit Gent, 2014.- 222 p.- PhD thesis.- ISBN 978-90-5989-692-5.

- Awards related to space biology

- Student Bursary Award to attend the 6th International Congress of Medicine in Space and Extreme Environments (ICMS 2014), Berlin, Germany, 16-19 September 2014.

- Young Investigator Award for participation to the 41st Annual Meeting of the European Radiation Research Society (ERRS 2014), Rhodes, Greece, 14 - 19 September 2014.

– Membership of relevant committees related to the project and participation to major project reviews

- Guest professorship, Faculty of Bioengineering Sciences, Gent University (S. Baatout)
- Guest professorship, Faculty of Sciences, Namur University (S. Baatout)
- Board member of the Belgian Society for Analytical Cytology (S. Baatout)
- Secretary, treasurer and board members of the European Radiation Research Society (S. Baatout, M. Moreels)
- Member of APECS (Association of Polar Early Career Scientists in Belgium) (M. Moreels)
- Nominated expert (by the Belgian minister of health) of the High Council for Health, Belgium, active participation (S. Baatout)
- Member of the expert panel for the evaluation of the scientific proposals submitted to GANIL for beam time
- Expert of the evaluation committee of FNRS for the evaluation of scientific proposals
- Expert of the evaluation committee of ANR (Agence nationale de la recherche, France) for the evaluation of scientific proposals

The group is also member of the following associations:
– Vlaamse Ruimtevaart Industrie (VRI)
– European Low GRavity Association (ELGRA)
– Association of Polar Early Career Scientists (APECS), Belgium http://www.facebook.com/apecs.belgium; https://sites.google.com/site/sciencefairnederlands/home

The group belongs to the following networks:
– YouSpace LinkedIn: http://www.linkedin.com/groups/YouSpace-4921809/about
– beSPACE LinkedIn: http://www.linkedin.com/groups?gid=4851172
– Member of the Working Group "Space" of the Belgian Senate

F. List your Belgian and international scientific and industrial collaborators within this reporting period, and summarize their contribution to the project.

Collaborations within Belgium :

- SCK•CEN is a founding member of the Belgian Hadrontherapy Consortium (BHTC) that involves the foundation against cancer and the main radiotherapeutical centers in Belgium. Hadrontherapy is a type of radiotherapy using heavy ions for cancer treatment. Within the BHTC, SCK-CEN is mainly collaborating with UCL, FUNDP and KUL.

Collaborations outside Belgium :

- The group actively collaborates with different European groups involved in ESA research projects: IMMUNO-1, IMMUNO-2, CHOICE, MoCISS projects: PI: Dr Alexander Choukèr (LMU, Munich, Germany); 8 European partners

- ESA funded expert team – the Topical Team "Stress and Immunity in Space" – coordinator: Dr Alexander Choukèr, (LMU, Munich, Germany); 8 European partners

- Collaboration with the laboratory of Daniela Grimm (Aarhus, Denmark) for research on endothelial cells submitted to microgravity is currently performed with this group and led to 8 joint publications so far.

- Collaboration with the group of Jean-Pol Frippiat (Université de Nancy, France) concerning immunological experiments in hyper- and micro-gravity (4 joint publications so far).

- Collaboration on heavy ion irradiation with the Biophysics group of the accelerator facility GSI (Darmstadt, Germany) – Dr Nicole Averbeck, Dr Michael Scholz, Prof Dr Marco Durante

- Collaboration for heavy ion experiments at the GANIL facility (Caen, France) – Dr Amine Cassimi, Dr Florent Durantel and Dr Isabelle Testard

- Collaboration with Dr Ulrich Giesen (PTB, Braunschweig, Germany) for microbeam irradiation experiments

G. Describe possible problems encountered, their origin and the solutions adopted or proposed. (max. 2 pages)

- Scientific, technical, administrative, personnel, ...;
- Budget management (*e.g.* cost overruns);
- Cooperation within the consortium (scientific and industrial partners);
- Resulting time delays;
- Remaining risks.

Cooperation within the consortium: a lot of ground-based experiments related to IMPULSE have been conducted in order to better decipher the effects of specific space stressors (namely, radiation and microgravity) on various cell types. However, in the context of the flight experiments (for MOCISS, IMMUNO-2, SPHEROIDS) preliminary work still needs to be performed before the actual flight experiments can take place. Part of this work is due to the intrinsic interindividual variability between human donors.

Resulting time delays: All the ground-based experiment with space-simulated devices have

a low risk, in that sense that these devices are already available at SCK•CEN, and have been used in previous Prodex contracts (RADCELL, CORALS, MOSAIC-1/2).

The flight schedule of the three studies is getting more concrete. IMMUNO-2 and MOCISS will likely fly end 2015, whereas SPHEROIDS will likely fly in 2016. A long delay has been caused by the delay in the hardware development of SPHEROIDS.

For MOCISS and IMMUNO-2, potential time delays can still be caused amongst others by delays in hardware development as well as by the various clearances that might need to be provided by the various instances within ESA, NASA and the Russian Space Agency.

Budget management: Since November 2013, a PhD student (Merel Van Walleghem) has been engaged and has joined the SCK-CEN radiobiology unit.

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