PROJECT FINAL REPORT

("**Publishable**"
or
"**Use and dissemination of foreground**"
or
"**societal implications**")

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1. FINAL PUBLISHABLE SUMMARY REPORT

Executive Summary (1 page).

The new **EU Directive** on the protection of animals used for scientific purposes (2010/63/EC) foresees various animal protection and welfare measures. EUPRIM-Net II has contributed ideally to some of them through its different activities.

For example **Article 28** of the Directive requires the Member States to ensure "that staff be adequately **educated, trained and competent**". EUPRIM-Net II regularly offered established courses for scientists, veterinarians, technical and animal care personnel on various topics such as General Primate Biology, Behaviour, Diseases and more. A web-based exchange module for veterinarians and other personnel working with NHPs was developed and implemented. European veterinarians were offered specialised training in NHP requirements in a rotation and training program. Last but not least an NHP-specific laboratory animal science course was developed according to the new (2014) FELASA guidelines. Certification of the course is anticipated before the end of this year (2015). This course is now offered without European funding.

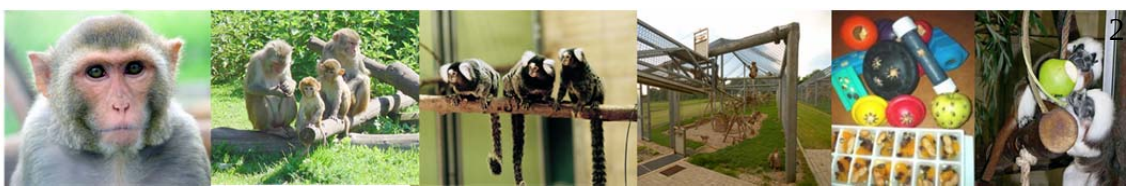
"Psychological wellbeing", allowing the animals to express natural behaviours and gain a measure of control over their environment, is addressed through the field of **Animal Behavioural Management (ABM)** as well as **Positive Reinforcement Training (PRT)**. Training is now offered in eight different lectures by the EUPRIM-Net ABM/PRT **seminar group**. What makes this concept unique is that the lectures have been standardised and translated into six European languages meeting the demand for training by local trainers in the mother tongue. The seminar group was supported by research activities to scientifically evaluate the effectiveness of ABM/PRT through behavioural observations by trained ethologists and the assessment of physiological effects.

Knowledge exchange between experts is the basis for advancement in science. EUPRIM-Net II organised a series of workshops and conferences on relevant topics around primate research and keeping, this included events especially targeting the industry as well as non-European institutes in order to maximise outreach.

Although for the time being the total replacement of NHPs *in vivo* experiments by *in vitro* models is far from feasible, ethical considerations compel the development of alternative methods. Consequently, with **Article 10** the Directive 2010/63/EC "seeks to facilitate and promote the advancement of alternative approaches", and (the validation of) alternative methods are subject of Articles 46 and 47. EUPRIM-Net II has developed *in vitro* technologies to replace, reduce and refine NHPs studies within neuroscience / neuroimmunology and vaccine research.

Biobanking is another approach to reduce the number of animals in experiments. Article 27 of Directive 2010/63/EC states that "Member States should, where appropriate, facilitate the establishment of programmes for sharing the organs and tissue of animals that are killed". The EUPRIM-Net BioBank has provided access to primate materials from different NHP species.

The research projects also developed and improved **assays for the health monitoring** of NHP. As important refinement **cage-based testing systems** were developed and advanced, reducing the stress of animals in experiments.



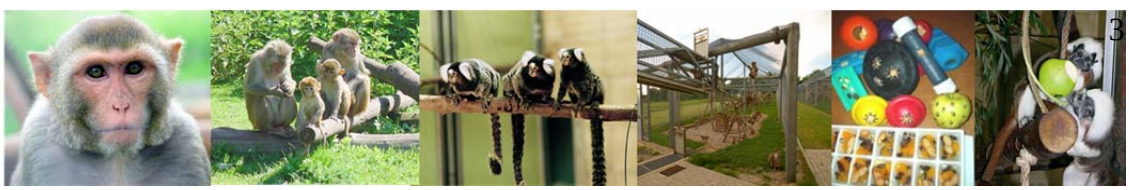
Summary Description of the project context and the main objectives (4 pages).

The development of alternative technologies promises to replace testing on animals. However, for the foreseeable future until valid alternatives exist, biological and biomedical research as well as toxicological safety testing depends on the use of relevant animal models. In some cases the animal model of choice are non-human primates (NHP). Although this group forms less than 0.1% of all animals used in research, NHP play a special role in providing critical insights that are central for many areas of research owing to their highly developed sensory and cognitive abilities. At the same time research with NHP underlies particularly high ethical (and legal) standards, and a responsible application of the 3Rs concept of Refinement, Reduction, and Replacement is mandatory.

The EU and its national states have instituted a large number of measures to ensure the best welfare of NHP used for scientific purposes. Besides legislative and regulatory efforts (Directive 2010/63/EC on the protection of animals used for scientific purposes) the EU has provided funding to EUPRIM-Net, a network of nine European primate centres from six countries which was established as a Research Infrastructure in 2006 and has now just completed its second round of funding by the Commission (FP7 GA262443).
In this project the primate centres' infrastructures and expertise were integrated in order to provide critical services, training and advice to scientific institutions in Europe conducting primate research and to zoological gardens that keep primates. The Network-, Access- and Research Activities all aimed at advancing animal welfare and the 3Rs for NHP in experiments and procedures.

Best Practice in Husbandry and Experimental Procedures. Knowledge exchange and networking is probably one of the most important activities for researchers in order to advance their science and progress. What better occasions can yield opportunities than workshops and conferences on topics in their field? EUPRIM-Net's aim was to provide a series of workshops on relevant topics all around primate keeping, handling and research. The target audience were primate veterinarians and scientists working in primate research, including the industry and non-European primate centres as important partners and stakeholders.
Veterinarians specialised on non-human primates are rare and require a specialised education before being able to assess the special requirements and needs of NHP. EUPRIM-Net II aimed at contributing to the education of veterinarians in becoming NHP-specialists by giving European veterinarians the opportunity to work hands-on with monkeys. Implementation of an electronic exchange module was aimed to facilitate communication between veterinarians from different primate centres.

ABM/PRT. Behavioural Management techniques and Positive Reinforcement Training (PRT) of laboratory NHPs for participation in procedures has been developed and implemented within EUPRIM-Net to minimise the stress level for the animals, promote more reliable experimental results, and lead to an increased safety, both for animals and personnel. "Psychological wellbeing", allowing the animals to express natural behaviours and gain a measure of control over their environment is a core aim within EUPRIM-Net. Psychological wellbeing is addressed through the field of Animal Behavioural Management (ABM), involving ethological aspects of captive animal



husbandry as well as PRT. In EUPRIM-Net II the aim was to establish an ABM/PRT seminar group in order to spread knowledge and understanding about ABM and PRT of laboratory primates to as many primate facilities as possible in Europe and around the world. The seminar group should be supported by research activities to scientifically evaluate the effectiveness of ABM/PRT through behavioural observations by trained ethologists and the assessment of physiological effects.

Education. Article 28 of the Directive requires the Member States to ensure "that staff be adequately educated, trained and competent". Therefore, education and training of staff working hands-on with NHP was one of the most important aims of EUPRIM-Net II. For veterinarians and scientists courses were planned on different subjects (modules): General Biology, Behaviour, Husbandry, Diseases and Parasites, Ethics; animal caretakers and technicians have a more difficult time than scientists to find suitable CPD courses. EUPRIM-Net II planned to provide an opportunity for animal caretakers and technicians in primate research to continue their education and improve their skills. For animal caretakers and technicians it may be necessary to provide courses in their mother tongue as they may not be as proficient in English as scientists. To guarantee standardisation and high quality of the courses, certification of the courses by the Federation of European Laboratory Animal Science Associations (FELASA) was aspired.

International Cooperation. In order to maximise outreach EUPRIM-Net aspired to establish a comprehensive exchange programme between important international key players in primate research. EUPRIM-Net aimed to offer a platform of international collaborations linking the centres' expertise in all relevant areas and resulting in manifold benefits for all participating centres, including EUPRIM-Net.

Co-operation with industrial/commercial partners. In addition to primate centres functioning as public bodies several commercial companies use primates to an extensive degree and thus should be involved in the ongoing discussion and development of the use of primate for research and other purposes. One of EUPRIM-Net II's objectives was to intensify the collaboration with these industrial partners to exchange and learn from the industry's experience as well as let them participate in the activities of EUPRIM-Net.

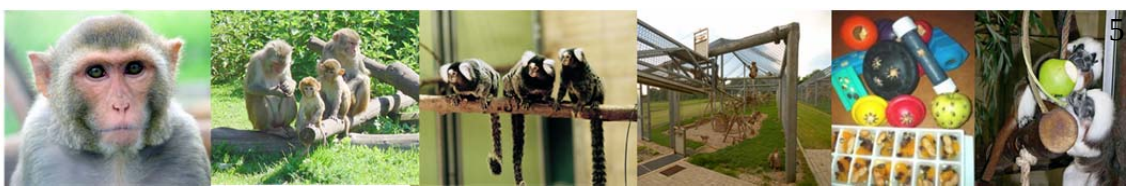
PRIMOCID. With PRIMOCID the objective was to provide access to well-established disease models with the aim to facilitate studies on disease mechanisms and the development of new therapies. The aim was to offer Access to models for rheumatoid arthritis (in rhesus monkeys and marmosets), multiple sclerosis (in rhesus monkeys and marmosets), allograft rejection (skin, in rhesus monkeys), and (new to this project) to infectious disease models and neurodegenerative diseases. Projects aimed at the development of alternatives for animal testing, such as organotypic cultures or refinement of existing models was appreciated. Development of new disease models was also possible, but on a limited scale as this should fit within the limitations for access provided with regard to time and budget. In addition to the disease models access was to be given to the primate laboratories at the BPRC and the possibility to study primate behaviour.

BioBank. Tissue and genetic material obtained from primates represents a valuable resource as it can be used in specific studies in biomedical research. However, the provision of primate material is

difficult and time demanding and hence, comparative studies involving primate research are often challenging or even impeded due to limited or non-availability of appropriate material. The aim of EUPRIM-Net II was to make available collections of diverse primate materials in three institutes of EUPRIM-Net (DPZ, BPRC, WWU) both for internal use and for external scientists. The idea behind the BioBank is to ensure the sharing of rare and valuable primate resources through more efficient access to specific types of samples available to researchers for biomedical research as well as for conservation studies. The EUPRIM-Net II BioBank aimed to: 1) accelerate progress in the solution of biomedical and other scientific problems that depend on supply of primate biological materials; 2) contribute to the 3R-concept (reduce, refine, replace) by reducing the numbers of primates needed through efficient resource sharing; 3) substantially enhance various European research fields through access to restricted primate materials, such as non-invasively collected DNA samples from endangered species, RNA and cDNA samples from a variety of healthy and diseases tissues; 4) provide genetically characterized and, therefore, certified primate material. The EUPRIM-Net II BioBank consists of: A) a tissue bank representing both normal and diseased tissues of primates including blood and serum samples (DPZ, BPRC, WWU); and B) a gene bank with DNA, RNA, cDNA.

Tools to Measure Infection and Diseases. Further EUPRIM-Net aimed to develop and apply new technologies for the detection and validation of diagnostic and prognostic markers of viral and bacterial diseases in NHP. The specific objectives were: 1) to develop multiplex assays for detection of pathogens, and for the determination of immune responses and cytokine levels; 2) to develop transcript-analysis assays for the identification of diagnostic and prognostic RNA markers of disease progression; 3) to explore the use of non-invasive, or less-invasive sampling in these assays, 4) to standardise protocols and exchange data between partners.
The implementation of the new technologies in NHP research has a high merit to strongly contribute to the 3R principle. Use of archival tissue samples, or non-, or less-invasively obtained samples further contributes to the 3R's. Importantly, all techniques established in course of this research project can easily be adapted and applied to other pathogens or diseases of NHP. The techniques developed in this Research Activity will have considerable impact on future research in the EU involving NHP. This will not be limited to the field of infectious diseases, as they can be widely used in research on animal models for human diseases.

Cage-based Systems. Recording of physiological data, especially invasively, but also non-invasively, often requires that animals are handled and restrained in their movements during the experimental procedures. In system neuroscience, for example, constraining the animal's head movements is the standard procedure for microelectrode recordings from the animal's brain, while the animal performs cognitive tasks. The interaction with the animal bears the potential to induce stress, which should be avoided, might be detrimental to the behavioural learning progresses, and can have confounding effects on the physiological parameters in question. If physiological data is not collected for research purposes, but to monitor animal welfare in a colony, such stress leads to the paradoxical situation that attempts to optimize animal welfare might actually reduce it. The objective of this research activity was to develop and implement procedures for remotely



monitoring physiological and behavioural data from monkeys in their housing environments. Telemetry systems were combined with behavioural test systems for integrated and automated data collection. The expected impact is a considerable reduction of potential stress for monkeys in experimental situations, and improved possibilities to continuously monitor animal welfare. These developments help to identify sources of stress and to reduce stress in research monkeys. Induced stress is a confounding factor for many research questions. Reduction of stress contributes to the refinement of studies by improving the quality of the collected data. As a consequence the number of animals needed for a study is reduced and animal welfare in experimental conditions is improved.

***In vitro* Technologies (Alternative Methods).** Another important aim of this project was to develop and apply new *in vitro* technologies leading to Replacement, Reduction and Refinement (the 3Rs) regarding the use of NHP in biomedical research. The specific objectives were:

1) to develop *in vitro* model systems for research on the central nervous system;
2) to develop *in vitro* test methods for vaccine research.

Studies on the CNS that use NHP often go accompanied with moderate to severe discomfort for the animals. This is often due to the invasive nature of the studies or to the very long preclinical incubation times of e.g. transmissible neurodegenerative diseases. Moreover, the negative public perception of CNS studies provides an extra motivation for the development of alternatives. The development and validation of *in vitro* primary cell cultures, transgenic cells and specified cell culture systems can provide researchers with the possibility to predict the outcome of *in vivo* experiments and to screen compounds or therapeutics that directly target resident CNS cells as a pre- *in vivo* test phase, reducing the number of NHP needed for *in vivo* studies. The development and validation of slice culture techniques can be used to address even more complex research questions, further reducing animal numbers for *in vivo* studies.
In HIV vaccine research, controlled prime-boost regimen strategies followed by experimental exposure (challenge) to simian or human/simian immunodeficiency viruses (SIV or SHIV) is, as yet, only feasible in NHP. The protective outcome of SIV vaccination can only be measured *in vivo*, leading to studies where NHP are kept under experimental conditions for extended periods of time. The aim was to develop and validate *in vitro* methods to predict the clinical outcome of vaccination *ex vivo*, ideally rendering the experimental *in vivo* challenge with virus unnecessary leading to a considerable reduction of the duration of *in vivo* experiments. One of the major obstacles in the development of vaccines is the selection of potent adjuvants that are safe and licensed for human application.
Adjuvants and vaccine formulations are tested in various animal models, including NHP, causing significant degrees of discomfort in the form of unwanted side-effects. The objective was to develop and employ *in vitro* technology to select and develop new adjuvants with good adjuvating potential, but with minimal side-effects. Although this project contributes mainly to refinement, the topic is so general and involves so many animals that even slight improvements will generate considerable effects regarding animal welfare.

Description of the main S & T results/foregrounds (max25 pages).

Best practice and harmonisation in husbandry and experimental procedures with NHP.
Knowledge exchange and networking is probably one of the most important activities for researchers in order to advance their science and progress. To this end, twelve workshops were organised targeting veterinarians and scientists and one also addressing regulatory authorities as well as the public.

Connections to other European organisations focusing on non-human primates [European Primate Veterinarians (EPV)] and professional animal training experts [AnimalConcepts] were exploited. The NHP-using industry and non-European primate centres are valuable exchange- and collaborative partners, thus five workshops were especially targeted towards these groups. One workshop in Nairobi, Kenya included a minisymposium that was attended by the German Ambassador in Kenya. All in all the workshops were visited by more than 400 participants. EUPRIM-Net II workshops between 2011 and 2015 – brief summaries:

"General techniques and best practice using NHP": This workshop was co-hosted by EPV and focused on minimal invasive techniques to be used in both research centres and zoos. Besides presentations and discussions, training on endoscopic techniques by the experts in a "dummy system" and more detailed information on thermographic techniques were provided.

"Primate Welfare & Training Workshop": A summary of the workshop has been published in "Enrichment Record" with both EUPRIM-Net members (Marit Vernes) and AnimalConcepts (Sabrina Brando) as co-authors. [Brando S, Vernes M (2014). Primate Welfare and Training Workshop. Enrichment Records, Winter 2014]

"Food-and-fluid control": The workshop was co-hosted by AnimalConcepts; the aim was to share knowledge on training methods to refine the use and care of NHP in neuroscience research. Veterinary care of these animals, the possibilities to prevent or diminish food and fluid control and behavioral management were discussed.

"Primate nutrition and its implications in research and on animal health": The workshop was co-hosted by EPV and included effects of primate nutrition on various aspects of animal welfare and behavioral management. In addition, several case reports discussing practical aspects were presented and discussed. These discussions included topics on food supplements, food restriction, obesity, and skin problems.

"Workshop on the microbiome and animal health": A one-day workshop on the microbiome and animal health, specifically aimed at non-human primates. The discussions included practical aspects on analysis and more detailed effects of changes in the microbiome and health aspects.

"Non-invasive imaging in non-human primates": A workshop on non-invasive imaging in non-human primates was conducted including Refinement of infectious disease studies using advanced imaging; SPECT in non-human primates; Optical imaging in preclinical research; Hyperpolarized

MRI – Potential and perspectives; Structural and functional cardiac imaging; Research in non-human primates – role of in vivo imaging; Anatomical and functional MRI in awake marmosets; Diffusion weighted imaging: Basic concepts and recent technological advances; Arterial spin labeling: Noninvasive perfusion measurements and beyond; Neurotransmission and brain metabolism – Advanced magnetic resonance spectroscopy.

"Methods and Practices for professional banking of tissues and material": One of the main issues was the visibility and how to reach the general researchers. From this point of view, much input was provided by the users and the external speakers.

"Alternative methods for the use of non-human primates in biomedical research": The workshop included lectures by key scientists in the field of alternatives as well as by experts from governmental and non-governmental organizations. Furthermore, parallel sessions were organised to stimulate discussion on the challenges of advancing the use of alternative methods for NHP. Subgroups voted on four statements and together composed a list with opportunities and priorities. [ALTEX. 2014;31(4):520-9. doi: http://dx.doi.org/10.14573/altex.1406231. Epub 2014 Jul 24.]

Workshops conducted together with industrial and/or non-European partners:

"Positive Reinforcement Training (PRT) and Animal Welfare" & "Practical training and implementation of environmental enrichment": These two workshops were conducted at the Institute of Primate Research (IPR) in Nairobi, Kenya. The Basics of PRT were taught and the possibilities of implementing enrichment practically demonstrated. One of the workshops was accompanied by a minisymposium attended by the German Ambassador.

"Novel Insights into Primate Genomics: Impact for Biomedical Research": This workshop was initiated by our industrial partner and co-hosted by EUPRIM-Net because species selection and suitability of an individual experimental animal may depend on the genetic background, which may not always be known. [Trends Genet. 2014 Nov;30(11):482-7. doi: 10.1016/j.tig.2014.05.004]

"Refinement of non-human primate use in research": This workshop was initiated by our industrial partner as satellite workshop at the symposium of the International Primatological Society and co-hosted by EUPRIM-Net because an important part of this workshop was on education of staff working with NHP.

"Workshop on the use and the advantages of marmosets in translational biomedical research":
Genetically modified marmosets most likely will become exceptionally relevant in academic and industrial research in Europe, the US, and Japan. However, since important biological characteristics of this NHP species may be affected in genetically modified marmosets, it is of utmost importance to proactively consider possible effects of the modifications on the monkeys' well-being and housing. In this context, the 3R (Reduction, Refinement, Replacement) and 4R (3Rs plus) principles were discussed.

Education & Training. Article 28 of the Directive requires the Member States to ensure "that staff be adequately educated, trained and competent". To this end one of the most important aims of EUPRIM-Net II was to provide education to staff working hands-on with primates, including all occupations involved from animal care takers, animal trainers and technicians to scientists and veterinarians. Participants came from ten different European countries and four non-European countries.

Animal care takers, animal trainers, technicians:

This group has a more difficult time than scientists to find suitable Continued Professional Development (CPD) courses. EUPRIM-Net II provided a highly appreciated opportunity for animal caretakers and technicians in primate research to continue their education and improve their skills. For them it may be necessary to provide courses in their mother tongue as they may not be as proficient in English as scientists. This was taken into consideration. More than 125 participants took part in six courses carried out in Germany and the UK. Content of the courses were general primate biology, diseases and parasites, husbandry, handling, and its challenges (e.g. zoonses), communication of primate research (problems, strategies and suggestions).

Veterinarians:

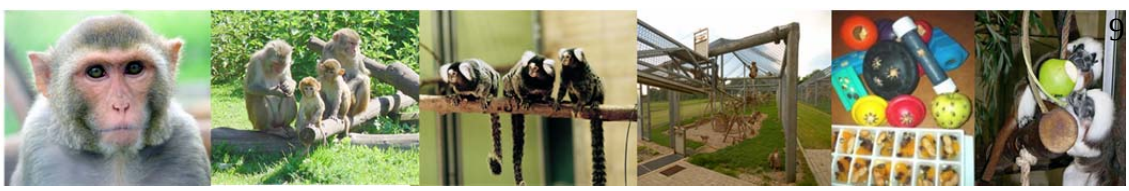
The rotation system for training of veterinarians and assistants/technicians was planned to foster species-specialisation of veterinarians with regard to non-human primates. The programme admitted six veterinarians who were trained in two-week training visits at the BPRC visits. After each training period, participants received a training certificate.

Veterinarians and scientists:

Ten CPD courses were offered to veterinarians and scientists that were in total attended by 210 participants. Course contents were offered in modules on general biology; primate sociobiology, husbandry, and nutrition; primates in biomedical research; primate husbandry, medical aspects, security, advanced methods and ethics; general primatology, behaviour, cognition and neurophysiology; marmosets as animal models. The course language was English or French.
In the beginning of 2014 FELASA (Federation of European Laboratory Animal Science Associations) revised their recommendations for the accreditation of education and training courses in laboratory animal science. According to the new system it became possible to introduce species-specific courses that could be certified by FELASA. This opened up the way for EUPRIM-Net II to develop primate– specific Laboratory Animal Science (LAS) courses according to FELASA guidelines, function A+B, the highest recognised certification in Europe and address Continued Professional Development as mentioned in Annex I. The first course was held within the term of EUPRIM-Net II. This course was divided in two parts, encompassing an e-learning phase that was specifically developed for this course as well as practical parts. The accreditation process of the primate-specific Laboratory Animal
Science course is ongoing beyond the term of EUPRIM-Net II. Nevertheless, development of this course would not have been possible without the support of the EU Commission.

All staff working hands-on with monkeys:

A Seminar Group has been formed, consisting of veterinarians, ethologists, and animal trainers.



Together, this group has created eight lectures on topics regarding Animal Behaviour Management (ABM), ranging from breeding laboratory primates to enrichment and problem solving. The group now offers to come to facilities keeping NHP and present these lectures as in-house training. They can customise a combination of lectures according to the needs of the facility; for instance, the facility might be interested in learning more about how to conduct behavioural studies and how to start training their primates. All lectures are 3-4 hours long and the target audience is animal technicians; however all personnel involved in managing the colony, including scientists, will benefit from attending. During the EUPRIM-Net II term (2011-2015) 19 seminars with one or more lectures were given to NHP-keeping facilities within and outside Europe of which only a basic number was subsidised by the EU; since then the in-house trainings have become well-known and popular and requests have already come in for the time beyond EU-funding for EUPRIM-Net II. A short description of the different lectures can be found below.

Lectures offered by the ABM/PRT Seminar Group (www.euprim-net.eu/network/ABMseminars.html):

Ecology and behaviour of primates - In this lecture natural including social behaviour of common laboratory primates is described - important knowledge when housing a particular species.

How to optimize laboratory primate housing and cages - An empty cage is useless to the animals. This lecture gives ideas of how to plan and improve the animals' living quarters. Improved welfare may improve the quality of the science!

An introduction to primate training - This lecture gives the basic tools to start training animals to collaborate in procedures, facilitate housing and handling, and improve human-animal relationships!

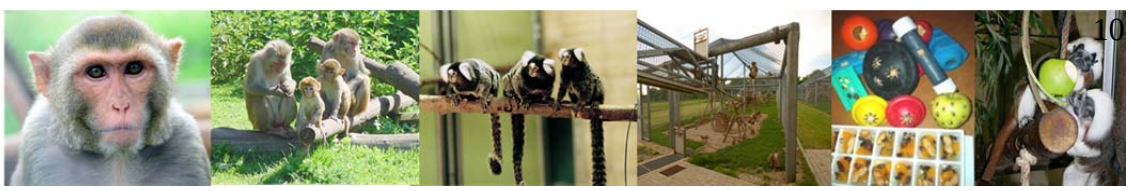
Environmental enrichment in primate facilities - Why and how a modern enrichment program may be implemented is presented in this lecture in a structured approach.

Breeding laboratory primates - How can breeding success be optimised? This lecture gives ideas with regards to primate breeding, incorporating veterinary, behavioural and practical perspectives.

Solving behavioural problems - Animals don't always behave the way we want them to. In this lecture, structured approach is presented to solving common behavioural problems in primate facilities.

How to observe and measure behaviour - Did the enrichment programme work? Which individuals are compatible for pair housing? From a management perspective observing and measuring behaviour is capital. This lecture addresses those issues.

Why stress matters - In this lecture, we argue that we need to be concerned with reducing stress both to improve welfare and the quality of the science.



Outreach & Dissemination. The EUPRIM-Net consortium takes serious interest in providing the public community with solid information about the keeping and wellbeing NHP used for research purposes in the primate centres of the Infrastructure and their benefit for health research. This is especially important in the current setting, where recently various ways (European citizens' initiative, European Parliament resolutions, petitions, and parliamentary questions) have been attempted to call into question the value of Directive 2010/63/EU, to try and repeal it and ban the use of animals in research and development.

To this end factual reporting and information sharing on research with and on NHP is more crucial than ever. Therefore, a virtual tour was designed and developed that was regarded an appropriate approach to inform a broad audience about the breeding and housing facilities and the way nonhuman primates are bred, kept and handled for research purposes in primate centres. For the virtual tour (www.dpz.eu/en/info-center/mediacenter/virtual-tour.html) the premises of the German Primate Center (DPZ) were chosen as an applicable example also reflecting the work of the other EUPRIM-Net institutions.

BioBanking. Over the recent years the value of biobanking and its contribution to the 3Rs (replacement, reduction, refinement) has become more and more obvious. This has been recognised by European legislation and put in writing with Directive 2010/63/EU on the protection of animals used for scientific purposes: Article 18 urges member states to facilitate where appropriate, the establishment of programmes for the sharing of organs and tissues of animals killed. And in fact one such programme has been established by the EU-funded infrastructure EUPRIM-Net with the EUPRIM-Net BioBank.
Over its 54 months duration EUPRIM-Net II has provided 97 organ- and tissue samples of non-human primates to 21 research projects. Since maximally 20% of the total infrastructure can be subsidised by the EU that means that at least 485 organ- and tissue-samples have been distributed by the EUPRIM-Net institutes involved. It is actually more likely that all in all close to 600 samples have been provided by the consortium over the EUPRIM-Net II duration, as one institute was not involved in the EUPRIM-Net BioBank at the time of proposal submission but since then have established a biobank and have distributed non-human primate samples. One institute was involved but did in fact not distribute samples via the EUPRIM-Net biobank due to the complexity of the administration.
The number of samples distributed via the EUPRIM-Net BioBank reflects the ratio of non-human primates versus other species, especially rodents, used for research purposes. Considering this niche the number of distributed samples is actually quite impressing, especially with respect to the 3Rs and the number of animals which may have been spared. The research projects that were provided with organ- and tissue samples were in the fields of immunology, oncology, endocrinology, neuro- and eye anatomy, neurophysiology, drug screening, genetics and epigenetics, and HIV research. Gene samples from non-human primates are rare and yet a variety of scientific disciplines can make good use of them. Whether used in research on conservation issues, evolution and epigenomics,

genetic backgrounds of social behaviours or for conducting medical research like finding cures for diseases like B-cell-malignancies or HIV: DNA or RNA of different NHP species, from Rhesus or Cynomolgus macaque to chimpanzee and bonobo from the EUPRIM-Net II BioBank have contributed to scientific progress during the past 54 months and were much appreciated by the scientists.
All in all, the EUPRIM-Net Genebanks provided 80 samples that were funded by the European Commission via EUPRIM-Net II to 17 research projects. As maximally 20% of the total infrastructure can be reimbursed by the EU that means that over the 54 months of EUPRIM-Net II funding at least 400 gene samples were provided to the European scientific community.

PRIMOCID. With PRIMOCID (Non-Human Primate Models of Chronic Immune Disorders) Transnational Access was provided to eight research projects, supporting scientists from six different European countries with experimental animals and expertise. The projects were in the fields of Multiple Sclerosis, Tuberculosis, Malaria, Alzheimer Disease, DNA vaccines, arthritis, and behaviour.

Deviation in Transnational Access. Various BioBanks have been established over the last years with a strong emphasis on human BioBanks in order to provide invaluable recourses to the scientific community. The service of Animal BioBanks allocating biological material of animals to scientist is additionally driven by the aim of reducing animal experiments. This argument is notably valid for the Primate BioBanks of EUPRIM-Net.
Partly Primate BioBanks are in competition with the Human BioBanks but they can also be characterised as “niche BioBanks” providing material for particular studies. Thus, the estimate of demand scientist requesting material from the EUPRIM-Net BioBank is very challenging and variable over the time. For the enhancement of primate material in scientific studies several measures have been conducted to make the Primate BioBank well known (flyers, posters and talks at conferences) and will be continued to increase the visibility of these valuable material.
To some extent, the EUPRIM-Net II BioBank suffered from the EU frame for TNA which was devised mainly for large equipment infrastructures and not for sample distribution. The administrative effort for receiving a tissue sample was seen very burdensome for both sides the provider and the users. Therefore it was difficult to convince both scientists and users to undergo the complex administrative procedures for small and comparatively inexpensive biomaterial samples: So, although a tremendous successful number of samples were provided, not all could receive EUPRIM-Net II funding, because the administrative prerequisites were not fulfilled. One EUPRIM-Net partner institute intended to participate in the BioBank activity and did indeed distribute several samples over the project lifetime; however, owing to the complexity of the administrative procedures as well as the transnationality constraint prevented this partner from giving away samples with EUPRIM-Net II funding. A simplification of the procedure providing samples to scientist would probably increase the willingness to request material from the EUPRIM-Net Primate BioBank.

Also, sample demand varied over the project lifetime. At least part of this phenomenon was linked to the revision of Directive 86/609/EEC. The new Directive 2010/63/EU "on the protection of animals used for scientific purposes" has by now been transposed into National Law by all member states; however implementation is still ongoing and many details are still not fully clear to scientists (and authorities). On the providers' side e.g., although Article 18 requests that "Members States shall facilitate, where appropriate, the establishment of programmes for the sharing of organs and tissues of animals killed", in practice the rules according to which this must occur are just becoming clearer now. On the users' side, including animal biomaterial into their research plans for grant application has become more difficult.
Some PRIMOCID and BioBank users had to be denied funding because although not part of the EUPRIM-Net II participating institutes, they formally belonged to the beneficiaries through their affiliations (e.g. CNRS in France).

Tools to measure Infection and Disease in NHP. The 3R concept implies that more data are obtained from minimal numbers of animals, and from small samples that are preferably collected using non- or less-invasive sampling techniques. To this end several assays have been developed in EUPRIM-Net II:

When working with NHP, there is always the possibility of anthropo-zoonotic transfer from humans to NHP and vice versa. To better assess the risk of infection a multiplex assay for the detection of respiratory pathogens in NHP was developed and validated. Using this assay, infections with respiratory viruses could be detected in colonies of NHP. For the direct detection of different viruses, a Luminex-based multiplex assay, the so called Respiratory Luminex assay (RLA), was developed and validated. The same technology platform has been used to identify cytokine signatures in materials from macaques infected with Mycobacterium tuberculosis (Mtb) and evaluate their potential to provide diagnostic indicators.

Characterisation of the gut microbiome from the colony of healthy rhesus macaques at the BPRC was started and feces of animals of different age groups and sex were sampled. Libraries of 16S-rRNA were prepared and further sequenced. At least three new bacterial species were identified and have been or will be submitted to the German Collection of Microorganisms and Cell Culture (Leibniz- Institute DSMZ) for further in-depth characterisation and inclusion in their collection. Currently, a new Peptococcus strain has been identified in the rhesus macaques (proposed name: *Peptococcus simiae*), and has been submitted to this collection. Several other new bacterial strains will also be sent out to the DSMZ for in depth analysis soon. This work will be continued to better understand the reciprocity of the immune system with the microbial community of the gut. Alternative approaches to dissecting immune responses in GBV-B-infected tamarins were explored (GBV-B is the tamarin counterpart of the hepatitis C virus). The GBV-B detection system was improved by using an extensive archive of a range of biological materials from naive and infected animals as well as new animal studies where appropriate.

More assays were developed for the identification of diagnostic and prognostic markers of viral and bacterial diseases in NHP. These apply transcript analysis and have a potential to improve health

surveillance programs in NHP-keeping facilities. E.g. MPXV-regulated miRNAs could be detected in samples from infected macaques and cell cultures. Moreover, Herpes B Latency associated transcript (LAT) could be detected and eight new miRNAs identified in herpes B virus (BV)-infected cells.

Complementing this assay, a quantitative Polymerase Chain Reaction (qPCR) assay for the detection of BV-specific nucleic acids in ganglia of rhesus macaques could be established. A peptide microarray technique was used to develop an assay to measure antibodies against the two immunodominant glycoproteins B (gB) and D (gD). This should avoid “false negative” results possibly obtained by the commercially available HSV-1-ELISA.

Dedicated mRNA signatures from Mtb-infected macaques could be validated that are prognostic RNA markers of disease progression and miRNAs associated with the pathology of viral hepatitis were explored as a result of GBV-B infection in tamarins.

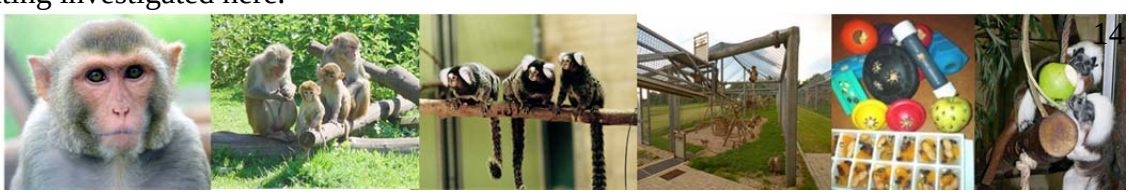
Non-invasive or less-invasive sampling for use in multiplex or transcript-based assays was explored and the development of non-invasive sampling procedures for routine virus surveillance was initiated. This work has not been completed; nevertheless, in total more than 400 swabs have been collected from the BPRC colony animals and stored at -80°C.

Proof of concept was established for the use of dried blood spots for evaluation of cytokines using a Luminex multiplex immunoassay. Exploring the use of non-invasively sampled materials for the detection of miRNA has started. Literature suggests that miRNA can be detected in urine, and thus urine samples taken at termination have been stored in order to perform comparisons with assays undertaken on serum and liver when these are fully analysed.

Cage-based wireless recordings in unrestrained monkeys. Recording of physiological data, especially invasively, but also non-invasively, often requires that animals are handled and restrained in their movements during the experimental procedures. The interaction with the animal bears the potential to induce stress, which should be avoided, might be detrimental to the behavioural learning progresses, and can have confounding effects on the physiological parameters in question. If physiological data is not collected for research purposes, but to monitor animal welfare in a colony, such stress leads to the paradoxical situation that attempts to optimise animal welfare might actually reduce it.

The research reported here had two major goals. First, comparison of stress levels in different experimental procedures in primates, particularly testing for the effect of a cage-based behavioral testing approaches compared to approaches which require handling the animals; second, development of a cage-based behavioral testing and training procedures for rhesus monkeys suitable for neuroscientific research.

The major finding of this reporting period and WP9 as a whole supports a cascade of stress level increments one may have expected: Cage-based testing can have an enrichment effect in socially healthy groups in housing colonies of baboons, which may be considered to be the least stress imposing setting investigated here.

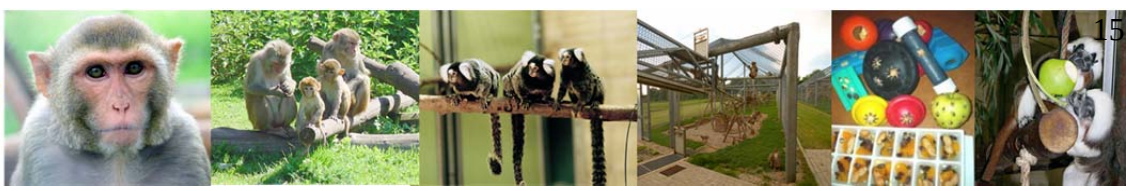


How a cage-based test system in a lab environment and in different species compares to that remains to be investigated. In a laboratory environment, using cage-based approaches compared to lab-based approaches including animal handling, in marmoset monkeys preliminarily show lower acute stress responses in cage-based approaches compared to lab-based approaches. Yet, lab-based approaches with regular handling in marmosets did not lead to sustained increased stress levels which would show in sleep or other physiological stress-associated parameters measured remotely. Results were partly obtained from different NHP species and may not transfer to other species. But if cage-based approaches also reduce stress in other NHP species and settings then the cage-based behavioral testing and automated training procedure developed for rhesus monkeys in neuroscientific context in EUPRIM-Net II could mark a first step towards a refined experimental approach in this field.

***In vitro* technologies to replace, reduce, and refine NHP studies.** For the time being biological and biomedical research as well as toxicological safety testing depends on the use of relevant animal models. In some cases the animal model of choice are NHP. Nevertheless, the number of animals used in experiments ought to be as small as possible. To this end EUPRIM-Net II has conducted research to develop in vivo technologies that can deliver (preliminary) results necessitating fewer NHP in the experiment.
This research was able to validate primary in vitro glia cell cultures as pre in vivo screening method.

Some tissue-specific findings in this research project might be therapeutically exploitable in neuroinflammatory and neurodegenerative diseases. Furthermore organotypic brain slice cultures from rhesus macaques were characterised: Although these slices were demonstrated to be responsive to neuro-inflammatory stimuli, exposure to neurotoxic agents resulted in massive cell death and general loss of viability. Whereas the organotypic slice cultures thus represent a valuable new tool to study (innate) neuro-inflammatory responses, their use as models for neurotoxicity is limited.

For the study of BSE and transmissible neurodegenerative diseases in NHP in general, there is a lack of an appropriate in vitro system. The strategy was the establishment of transgenic rabbit kidney (RK13) cell lines which overexpress full-length prion protein. Established transgenic cell lines expressing PrPc of either squirrel monkey (*Saimiri sciureus*) or cynomolgus monkey (*Macaca fascicularis*) BSE did support prion propagation and therefore could not be used for the diagnosis of macaque-adapted BSE; however RT-QuIC could be established and adapted for the ultrasensitive detection of prion activity in various specimens. With this new technique prion replication in peripheral tissues of BSE-inoculated macaques can be assessed. The detection of prions in different clinical specimens (e.g. CSF, lymph nodes, blood), that can be obtained routinely and/or by mildly invasive methods and even before the occurrence of clinical manifestations is of high importance. Those clinical specimens in combination with ultrasensitive methods, like RT-QuIC, can be used to predict disease outcome in vivo thereby significantly reducing the time necessary for the keeping of prion-inoculated macaques. We therefore consider the establishment of RT-QuIC for specific and



highly sensitive detection of macaque-adapted BSE as equivalent to the anticipated deliverable to produce BSE-susceptible cell lines.

Although infection rates are declining due to improved education and enhanced worldwide access to antiretroviral medication, HIV-infection remains a global health problem. However, an AIDS vaccine is still lacking and NHP research remains a necessity to reach that goal. An *in vitro* test that delivers early prediction of AIDS vaccine efficacy in human or macaques, which represent the major species for preclinical AIDS vaccine trials, could contribute to vaccine development as well as to refinement and reduction of studies conducted in NHP. We therefore aimed at developing predictive *in vitro* protocols in the monkey model of AIDS. To do so, we primarily analysed samples from three different experiments. Extending the original application, we used four approaches to refine the macaque model of AIDS:

1) We validated and/or detected other prognostic marker for the macaque model of AIDS;

2) As a potential additional prognostic marker, we quantified expression of innate immunity genes and identified correlates of protection that can be used to determine AIDS vaccine efficacy ex vivo within 48 h post vaccination.

3) We found that a single nucleotide polymorphism (SNP) in DCSIGN/CD209 - that is similar to a human SNP - can be used as a further prognostic marker to distribute animals evenly into the various experimental groups (as means of standardization) to reduce number of experimental animals without losing statistical significance (manuscript in preparation).

4) We investigated antiviral non-cytolytic activity of CD8 cells in an attempt to identify a novel prognostic marker that can serve as standardization of experiments. While we did not find strong evidence that this activity influenced susceptibility to SIV-infection, candidate genes linked to this activity were detected by transcriptional profiling.

Adjuvants are formulations, which upon administration lead to non-specific immune stimulation. They are used to induce immune responses directed against pathogens (as for vaccination purposes) or to generate immune responses against components of the body itself (as in experimental animal models of human auto-immune diseases like e.g. multiple sclerosis, diabetes or rheumatoid arthritis). However, some of the more potent adjuvants are notorious for their adverse effects. Complete Freund's Adjuvant (CFA) for example is known for the development of granulomatous skin lesions, hampering application in humans and causing various degrees of discomfort to NHP. There is therefore an urgent need for new and safe adjuvants for human use and a particular need to develop new, cleaner adjuvants for use in experimental animals. With the recent discovery of a family of molecules that form part of the innate immune system, the Toll-like and NOD-like receptors (TLR and NLR resp.), important progress was made in our understanding of how adjuvants work on a molecular level. Upon activation these receptors deliver a potent non-specific activating signal to the immune system, much like adjuvants do. We have used this knowledge to develop in vitro systems to model the adjuvating effects, in the form of TLR and NLR bioassays, as well as in vitro systems to model the adverse effects, in the form of in vitro granuloma models. Both

assay types have been developed and extensively used to both identify new adjuvant candidates with good adjuvating potential as well as to characterise the granuloma-inducing potential of new adjuvant candidates.
Moreover alternative approaches to CFA have been developed using mycobacterial strains that specifically lack the expression of sets of proteins inducing less lung granulomas than CFA. Second, as a bottom-up approach, we have characterised the overall innate immune responses evoked by *M. butyricum*, both qualitatively and quantitatively, and used this information to compose an entirely new adjuvant (MiMyc) that mimics these responses.

Scientific evaluation of Animal Behavioural Management (ABM) and Positive Reinforcement Training (PRT). Research was carried out within EUPRIM-Net II to investigate effects of ABM/PRT measures or experimental refinement methods. In this context the impact of voluntary cognitive testing on captive group-housed long-tailed macaques' (*Macaca fascicularis*) stress level and social behavior was examined. There are two opposing views on the potential impact of experimental testing: Separation from the group and/or frustration during the experiment might cause an increased stress level. Alternatively, experimental testing might serve as enrichment for captive individuals and thus contributes to the animals' welfare. When data collection will be finished (September 2015), we will pool the data to enhance sample size for the planned paper "The impact of cognitive testing on stress levels in captive long-tailed macaques (*Macaca fascicularis*)". Overall, the results strongly suggest that cognitive testing is neither detrimental to the participating individuals nor to the group as a whole, in terms of agonistic interaction rates.

Moreover decision making in animal trainers was analysed as a function of training frequency and a paper finalised that has recently been submitted for publication. A textbook chapter was written on laboratory primate training that will shortly be submitted for publication in an online, open access format. During EUPRIM-Net II at least seven papers and five additional manuscripts in the field of ABM/PRT were produced in different stages of publication. Note that two papers also explore intricate uses of negative reinforcement training (NRT) in combination with PRT. An interesting finding was that NRT may indeed be used to reduce fear and give animals more control over their situation. Data collection has started on the impact of early socialization on laboratory primates. This project has stalled but we're hoping to relaunch it during 2016. Blood cortisol data was analysed from animals in different stages of training. However, the results were inconclusive and we've decided not to pursue a publication elaborating on that issue.

Please provide a description of the potential impact (including the socio-economic impact and the wider societal implications of the project so far) and the main dissemination activities and the exploitation of results. The length of this part cannot exceed 10 pages.

For the foreseeable future until valid alternatives exist, biological and biomedical research as well as toxicological safety testing depends on the use of relevant animal models. In some cases the animal model of choice are non-human primates (NHP). Understanding the biology of nonhuman primates helps us to understand our own biology. That is why NHP play an important role in biological and biomedical research. This group of animals provides models which are essential for research in genomics and biotechnology for health. The successful development of new strategies against human diseases like infectious (e.g. HIV, hepatitis) and neurological diseases (e.g. Alzheimer´s or Parkinson Disease) or cancer depends on the availability of NHP or biological material of NHP origin.

This also holds true for the development of new therapeutics (vaccines, gene therapy) and transplantation research. Although this group forms less than 0.1% of all animals used in research, NHP play a special role in providing critical insights that are central for many areas of research owing to their highly developed sensory and cognitive abilities. At the same time and for the same reasons research with NHP underlies particularly high ethical (and legal) standards, and a responsible application of the 3Rs concept of Refinement, Reduction, and Replacement is mandatory.

This is especially important in the current setting, where recently various ways (European citizens' initiative, European Parliament resolutions, petitions, and parliamentary questions) have been attempted to call into question the value of Directive 2010/63/EU on the protection of animals used for scientific purposes, to try and repeal it and ban the use of animals in research and development. To this end factual reporting and information sharing on research with and on NHP is more crucial than ever.

The EU and its national states have instituted a large number of measures to ensure the best welfare of NHP used for scientific purposes. Besides legislative and regulatory efforts (Directive 2010/63/EU) the EU has provided funding to EUPRIM-Net, a network of nine European primate centres from six countries which was established as a Research Infrastructure in 2006 and has now just completed its second round of funding by the Commission (FP7-GA-262443).

Outreach. With EUPRIM-Net II the EU has continued support to a virtual European Primate Centre where standards are high, best practices are used and all NHP-keeping facilities in Europe and worldwide can benefit. Owing to their highly developed sensory and cognitive abilities, it is important to exchange and network for the welfare of the NHP in experiments. If the experimental animal is stressed this may have confounding effects to the physiological parameters in question and thus detrimental to the advancement of biological and biomedical research. EUPRIM-Net II facilitated networking and mutual knowledge transfer by offering high-end workshops on significant topics around the keeping of NHP for research purposes or advanced technology in

primate research, not only for its consortium members, but also outreaching to industrial stakeholders and researchers outside Europe. Important collaborations have been initiated that show how important animal welfare issues are also to these groups and joint efforts will contribute to advancement of animal welfare and thus biological and biomedical science beyond the state of the art. Last but not least the workshops provided opportunities for exchange on state-of-the-art technologies, contributing on the best research with NHP in Europe.

EUPRIM-Net II not only addressed scientists but outreached also to non-professionals. This is of particular importance because for the common public it may be difficult to understand why and how NHP are used in experiments and to what extent they may suffer distress during procedures. In the virtual tour through a European Primate Centre that has been produced by EUPRIM-Net II one can learn about research with NHP and how the animals are kept, with the aim to increase acceptance of NHP research among European citizens (http://www.dpz.eu/en/info-center/media-center/virtualtour.html). Especially in times of European Citizen's Initiatives and Petitions against research with animals, it is important to disseminate solid information on NHP research and how animals are kept and handled. Owing to this climate, EUPRIM-Net II has hosted a workshop "Alternative methods for the use of non-human primates in biomedical research" bringing together key scientists working on alternatives to animal research with experts from governmental and non-governmental organisations. During this workshop parallel sessions were organised to stimulate discussion on the challenges of advancing the use of alternative methods for NHP. Subgroups voted on four statements and together composed a list with opportunities and priorities regarding implementation of all 3Rs alternatives, stem cells, NHP *in vivo* models, and communication. The white paper that resulted from of the Workshop [ALTEX (31)4: 520-529; DOI: http://dx.doi.org/10.14573/altex.1406231] can serve as guiding document for future activities.

Education. Article 28 of the Directive on the protection of animals used for scientific purposes (2010/63/EC) requires the Member States to ensure "that staff be adequately educated, trained and competent". Even before the revision of the European Directive, EUPRIM-Net II had designed a strong programme for continued professional development of staff working with and on NHP. Workshop-like courses on different topics with international experts offered high-end education for scientists and veterinarians, while moreover courses were offered in their local language to animal trainers and care takers as well as technicians, in many instances a rare opportunity for them to receive customised education. Moreover, these courses have represented a very important opportunity for Continued Professional Development (CPD) for all 335 participants from ten different European and four non-European countries and have given NHP staff a chance to exchange with colleagues without the fear of resentments which they may encounter at mixed events.

Developed from scratch was an NHP-specific course meeting FELASA (Federation of laboratory animal science associations) guidelines for the accreditation of laboratory animal science (LAS) courses. This course comprises theoretical and practical contents and a comprehensive E-Learning

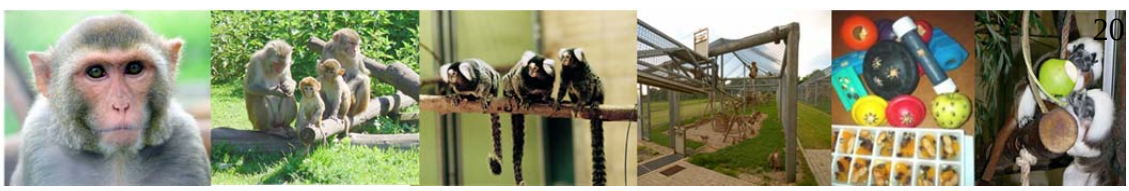
part was developed especially for this course. The course will probably be accredited before the end of this year (2015) and will then be the first NHP-specific course in Europe certified by FELASA, revolutionising basic education of new staff working with NHP and contributing to harmonisation of NHP-staff education in Europe.

Thirdly, a EUPRIM-Net Seminar Group was formed with participation of ethologists, veterinarians, animal trainers and scientists who created and now offers eight standardised lectures on different topics around NHP keeping and handling to NHP-keeping facilities as in-house trainings (www.euprim-net.eu/network/ABM-seminars.html). These trainings are extremely important because the EUPRIM-Net expert inspects the on-site conditions and can customise the training according to the needs of the facility. Even beyond the EUPRIM-Net II term, Seminar Group members have been asked to give trainings to academic and industrial laboratories.

BioBanking has a high merit for the 3Rs as the sharing of tissues and organs implies the reduction of experimental animals sacrificed for scientific purposes. Over its 54 months duration EUPRIM-Net II has provided 97 organ- and tissue samples of NHP to 21 research projects. All in all, the EUPRIM-Net Genebanks provided 80 samples that were funded by the European Commission via EUPRIM-Net II to 17 research projects. Since maximally 20% of the total infrastructure can be subsidised by the EU that means that at least 485 organ- and tissue-samples (actually, close to 600 samples are more likely) and at least 400 gene samples have been distributed by the EUPRIM-Net institutes involved. These samples have contributed to progress of European research, at the same time sparing animals that would otherwise have been sacrificed especially for the research project in question. Apart from the number of distributed samples it should be emphasised that the EUPRIM-Net BioBank is a unique and valuable resource in Europe for access to characterised, high quality NHP biomaterial used by researchers in biological and biomedical research accelerating progress in the solution of biomedical and other scientific problems that depend on supply of NHP biomaterial.

PRIMOCID. In some cases NHP is the only appropriate animal model that can give answers to specific scientific questions. Experimentation with NHP requires expert knowledge and specialised facilities.
Through PRIMOCID (Transnational Access to Non-Human Primate Models of Chronic Immune Disorders) the infrastructure project EUPRIM-Net II has offered expert knowledge, facilities and animals to European researchers. Over the 54 months eight projects have been funded by the European Commission. Since maximally 20% of the total infrastructure can be subsidised that means that at least 40 excellent projects in the fields of Multiple Sclerosis, Tuberculosis, Malaria, Alzheimer Disease, DNA vaccines, arthritis, behaviour and more have been conducted that would not have been possible without the kind of expert service offered by the EUPRIM-Net consortium, or only under conditions not optimal for the research or the animals.

Tools to measure Infection and Disease in NHP. When working with NHP, there is always the possibility of anthropo-zoonotic transfer from humans to NHP and vice versa. Moreover, the 3R



concept implies that more data are obtained from minimal numbers of animals, and from small samples that are preferably collected using non- or less-invasive sampling techniques. Particularly, New World monkeys (NWM), like marmosets and tamarins, are progressively used in biomedical research. A serious drawback of using NWM is the limited blood sample volume that can be collected. Flow cytometric methods (e.g. Luminex platform), or the analysis of cellular transcripts using microarrays or quantitative RT-PCR assays were developed during the EUPRIM-Net II term to enable researchers to analyse multiple parameters from a single small sample. Here, specific emphasis was laid on the development and application of the above mentioned technologies to monitor biomarkers in NWM and macaques. The implementation of the new technologies in NHP research has significantly contributed to the 3R principle. Use of archival tissue samples, or non-, or less-invasively obtained samples further contributed to the 3Rs, enhancing 1) the quality of life of the animals used in research, and 2) responding to the increasing demand of data by scientists. Importantly, all techniques established in the course of this research project can easily be adapted and applied to other pathogens or diseases of NHP.

Monkey "home office". Induced stress is a confounding factor for many research questions. Reduction of stress contributes to the refinement of studies by improving the quality of the collected data. As a consequence the number of animals needed for a study is reduced and animal welfare in experimental conditions is improved. An important finding during the EUPRIM-Net II term was that cage-based testing can have an enrichment effect in socially healthy groups in housing colonies of baboons, which may be considered to be the least stress imposing setting investigated here. In a laboratory environment, using cage-based approaches compared to lab-based approaches including animal handling, marmoset monkeys preliminarily show lower acute stress responses. Yet, lab-based approaches with regular handling in marmosets did not lead to sustained increased stress levels.

Results were partly obtained from different NHP species and may not transfer to other species. But if cage-based approaches also reduce stress in other NHP species and settings then the cage-based behavioral testing and automated training procedure developed for rhesus monkeys in neuroscientific context could mark a first step towards a refined experimental approach in this field.

Development of *in vitro* (alternative) technologies. European citizens call for the use of alternative methods replacing animal experiments and testing. In reality, molecular or cell-culture-based methods need validation that is time-consuming. Nevertheless, the development of *in vitro* methods is a refinement with high potential to reduce the number of animals needed or to even replace an animal experiment and should be pursued. Sometimes an *in vitro* method can help to alleviate discomfort for the animal undergoing experimental procedures. For these reasons *in vitro* technologies should be expedited.

Biomedical research that focuses on the central nervous system (CNS) in general goes accompanied with moderate to severe discomfort for animals involved in such research. Still relatively large numbers of NHP are used in in vivo CNS studies, and there is an urgent need to develop alternative

in vitro models for NHP CNS studies. The methods developed during the EUPRIM-Net II term are all initiated from 'left-over' material from other experiments. We are currently applying these techniques as a pre *in vivo* test phase, enabling colleagues with valuable information leading to a reduction of animals necessary before the start of in vivo experiments. Not only does this lead to better science with fewer animals, it also makes more complete use of the animals from which the cultures are initiated.

HIV vaccine research requires NHP to be kept under experimental conditions for extended periods of time. The *in vitro* methods developed within EUPRIM-Net II have the potential to contribute to refinement in HIV vaccine research by reducing the time the animal has to spend in the experimental setting and by helping to distribute animals evenly into the various experimental groups (as means of standardisation) which may even reduce number of experimental animals without losing statistical significance.

Adjuvants are enhancing the immunisation effect but may also cause discomfort to humans but also to research animals in the form of unwanted side-effects. In EUPRIM-Net II in vitro assays were developed to both identify new adjuvant candidates with good adjuvating potential as well as to characterise the granuloma-inducing potential of new adjuvant candidates.

Scientific evaluation of Animal Behavioural Management (ABM) and Positive Reinforcement Training (PRT). Adaptation and training of laboratory primates for participation in procedures are generally accepted as methods to reduce the stress level for the animals and promote more reliable experimental results. However, there is a limited amount of scientific literature within this area and thus little solid information on the effectiveness of measures such as ABM or PRT. EUPRIM-Net II contributed with research in this area and seven articles and a book chapter have been published or are in preparation.

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National Institute for Biological Standard and Control (NIBSC), South Mimms, United Kingdom

Westfälische-Wilhelms-Universität (WWU) with
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2. USE AND DISSEMINATION OF FOREGROUND

Section A (public)

EURPIM-Net II's main objective was the advancement of animal welfare and the 3Rs in research and testing with non-human primates. These efforts occurred in the different areas making up/necessary for NHP research: from breeding, housing and handling of the animals, educating staff, providing expert support for experiments with NHP and biomaterial, to health monitoring, development of refined stress-reducing experimental designs or alternative *in vitro* methods.

Owing to the variety of different approaches it is impossible to weigh the importance of one against another. Order of appearance in the following table is corresponding to the EUPRIM-Net II Work Packages.

TABLE A1: LIST OF SCIENTIFIC (PEER REVIEWED) PUBLICATIONS

NO.	Title	Main author	Title of the periodical or the series	Number, date or frequency	Publisher	Place of publication	Year of publication	Relevant pages
1	EU CONTINUES SUPPORT OF EUROPEAN NETWORK ON PRIMATE RESEARCH (EUPRIM-NET)	Björg Pauling	BOLETÍN DE LA ASOCIACIÓN	Volumen 18, Número 2 Julio, 2011			2011	4
2	EU Continues Support of European Network on Primate Research (EUPRIM-Net)	Björg Pauling	Laboratory Primate Newsletter	50[4] 01/10/2011			2011	19
3	Evaluation of ultrasonic vocalizations in common	Jaco Bakker , Tessa J.M. van	Lab Animal	Vol. 43/Issue 9 20/08/2014	Nature America Inc.	United States	2014	313-320

	marmosets (Callithrix jacchus) as a potential indicator of welfare	Nijnatten, Annet L. Louwerse , Guus Baarends , Saskia S. Arndt , Jan A.M. Langermans						
4	Physiological and behavioural stress responses in cynomolgus macaques (Macaca fascicularis) to noise associated with construction work	K. Westlund , A.-L. Fernstrom , E.-M. Wergard , H. Fredlund , J. Hau , M. Spangberg	Laboratory Animals	Vol. 46/Issue 1 01/01/2012	Royal Society of Medicine Press Ltd	United Kingdom	2012	51-58
5	Can conditioned reinforcers and Variable-Ratio Schedules make food- and fluid control redundant? A comment on the NC3Rs Working Group's report	Karolina Westlund	Journal of Neuroscience Methods	Vol. 204/Issue 1 01/02/2012	Elsevier	Netherlands	2012	202-205
6	Questioning the necessity of food– and fluid regimes: Reply to Prescott and colleagues' response	Karolina Westlund	Journal of Neuroscience Methods	Vol. 204/Issue 1 01/02/2012	Elsevier	Netherlands	2012	210-213
7	Training is enrichment—And beyond	Karolina Westlund	Applied Animal Behaviour Science	Vol. No 152; 01/03/2014	Elsevier	Netherlands	2014	1-6
8	Training pair-housed Rhesus macaques (Macaca mulatta) using a combination of negative and positive reinforcement	Eva-Marie Wergård , Hans Temrin , Björn Forkman , Mats Spångberg ,	Behavioural Processes	Vol. 113 01/04/2015	Elsevier	Netherlands	2015	51-59

		Hélène Fredlund , Karolina Westlund						
9	Genome typing of nonhuman primate models: implications for biomedical research	Tanja Haus , Betsy Ferguson , Jeffrey Rogers , Gaby Doxiadis , Ulrich Certa , Nicola J. Rose , Robert Teepe , Gerhard F. Weinbauer , Christian Roos	Trends in Genetics	Vol. 30/Issue 11 01/11/2014	Elsevier Limited	United Kingdom	2014	482-487
10	Genotyping of non-human primate models: perspectives andchallenges for the implementation of the "three R's"	T. Haus, K. Prinz, B. Pauling, and C. Roos	Primate Biology	1; 15/10/2014	Copernicus Publications		2014	1-9
11	The EUPRIM-Net Primates Biobank	Valeska Stephan; Björg Pauling	Biopreservation and Biobanking	Vol. 13/Issue 4 01/08/2015	Mary Ann Liebert Inc.	United States	2015	301-302
12	Rhesus Macaques (Macaca mulatta) Are Natural Hosts of Specific Staphylococcus aureus Lineages	Sanne van den Berg , Willem J. B. van Wamel , Susan V. Snijders , Boudewijn Ouwerling , Corné P. de Vogel , Hélène A. Boelens , Rob J. L. Willems , Xander W. Huijsdens , Frank	PLoS One	Vol. 6/Issue 10 20/10/2011	Public Library of Science	United States	2011	e26170

		A. W. Verreck , Ivanela Kondova , Peter J. Heidt , Henri A. Verbrugh , Alex van Belkum						
13	Multiple Antibody Targets on Herpes B Glycoproteins B and D Identified by Screening Sera of Infected Rhesus Macaques with Peptide Microarrays	Sven-Kevin Hotop , Ahmed Abd El Wahed , Ulrike Beutling , Dieter Jentsch , Dirk Motzkus , Ronald Frank , Gerhard Hunsmann , Christiane Stahl-Hennig , Hans-Joachim Fritz	PLoS One	Vol. 9/Issue 1 31/01/2014	Public Library of Science	United States	2014	e86857
14	Retrospective Serology Study of Respiratory Virus Infections in Captive Great Apes	Hester Buitendijk , Zahra Fagrouch , Henk Niphuis , Willy Bogers , Kristin Warren , Ernst Verschoor	Viruses	Vol. 6/Issue 3 01/03/2014	MDPI	Switzerland	2014	1442-1453
15	Changes in immune cell populations in the periphery and liver of GBV-B-infected and convalescent tamarins (Saguinus labiatus)	Simon P. Hood , Edward T. Mee , Hannah Perkins , Ori Bowen , Jessica M. Dale , Neil M. Almond , Peter Karayiannis , Helen Bright , Neil J. Berry , Nicola J. Rose	Virus Research	Vol. 179 01/01/2014	Elsevier	Netherlands	2014	93-101

16	ACUTE-PHASE RESPONSES IN HEALTHY AND DISEASED RHESUS MACAQUES (MACACA MULATTA)	Anne K. H. Krogh , Jo F. H. Lundsgaard , Jaco Bakker , Jan A. M. Langermans , Frank A. W. Verreck , Mads Kjelgaard-Hansen , Stine Jacobsen , Mads Frost Bertelsen	Journal of Zoo and Wildlife Medicine	Vol. 45/Issue 2 01/06/2014	American Association of Zoo Veterinarians	United States	2014	306-314
17	Baboons' Response Speed Is Biased by Their Moods	Yousri Marzouki , Julie Gullstrand , Annabelle Goujon , Joël Fagot	PLoS One	Vol. 9/Issue 7 25/07/2014	Public Library of Science	United States	2014	e102562
18	Assessment of Social Cognition in Non-human Primates Using a Network of Computerized Automated Learning Device (ALDM) Test Systems	Joël Fagot , Yousri Marzouki , Pascal Huguet , Julie Gullstrand , Nicolas Claidière	Journal of Visualized Experiments	Issue 99 01/01/2015	MYJoVE Corporation	United States	2015	1-7
19	Effects of freely accessible computerized test systems on the spontaneous behaviors and stress level of Guinea baboons (Papio papio)	Joël Fagot , Julie Gullstrand , Caralyn Kemp , Céline Defilles , Mourad Mekaouche	American Journal of Primatology	Vol. 76/Issue 1 01/01/2014	John Wiley and Sons Inc.	United States	2014	56-64
20	Cognitive control under social influence in baboons.	Pascal Huguet , Isabelle Barbet , Clément Belletier , Jean-Marc	Journal of Experimental Psychology: General	Vol. 143/Issue 6 01/01/2014	American Psychological Association Inc.	United States	2014	2067-2073

		Monteil , Joël Fagot						
21	Recovery time after intra-abdominal transmitter placement for telemetric (neuro) physiological measurement in freely moving common marmosets (Callitrix jacchus)	Jaco Bakker, Rianne Klomp, Milene WM Rijnbeek, Saskia S Arndt, Ingrid HCHM Philippens and Jan AM Langermans	Animal Biotelemetry	20142:10 17/01/2014	Springer		2014	2-10
22	Optimization of the input impedance of a low-noise unipolar powered amplifier	L. Rafflenbeul , M. Schäck , R. Werthschützky	Procedia Engineering	Vol. 25 01/01/2011	Elsevier BV	Netherlands	2011	1293-1296
23	Statins amplify TLR-induced responses in microglia via inhibition of cholesterol biosynthesis	Céline Van Der Putten , Hedwich F. Kuipers , Ella A. Zuiderwijk-Sick , Linda Van Straalen , Ivanela Kondova , Peter J. Van Den Elsen , Jeffrey J. Bajramovic	Glia	Vol. 60/Issue 1 01/01/2012	John Wiley and Sons Inc.	United States	2012	43-52
24	Inflammasome-Induced IL-1 Secretion in Microglia Is Characterized by Delayed Kinetics and Is Only Partially Dependent on Inflammatory Caspases	S. M. Burm , E. A. Zuiderwijk-Sick , A. E. J. 't Jong , C. van der Putten , J. Veth , I. Kondova , J. J. Bajramovic	Journal of Neuroscience	Vol. 35/Issue 2 14/01/2015	Society for Neuroscience	United States	2015	678-687

EUPRIM-Net II offered services and expertise around the 3Rs of refinement, reduction and replacement in research with and on non-human primates, including a fourth "R" for "responsibility". The dissemination activities listed here raised awareness of the EUPRIM-Net II project or certain activities, contributing to EUPRIM-Net being perceived as a leading voice in Europe with regards to animal welfare of NHP in research.

TABLE A2: LIST OF DISSEMINATION ACTIVITIES

NO.	*Type of Activities*	*Main leader*	*Title*	*Date/Period*	*Place*	*Type of Audience*	*Size of Audience*	*Countries Addressed*
1	Press releases	DEUTSCHES PRIMATENZENTRUM GMBH	EU supports international network on primate research	23/11/2010	Germany and Europe	Scientific community (higher education, Research) - Industry - Civil society - Policy makers - Medias	9999	Europe
2	Oral presentation to a scientific event.	DEUTSCHES PRIMATENZENTRUM GMBH	Monkey "home office" - telemtry for distance monitoring and minimal invasive investigation in primate research EUPRIM-Net Meeting	24/11/2010	EUPRIM-Net II KickOff Meeting, Göttingen, Germany	Scientific community (higher education, Research)	50	Europe
3	Publication	STICHTING BIOMEDICAL PRIMATE	PRIMOCID Dissemination:	01/01/2011	Europewide	Scientific community	20	Europe

		RESEARCH CENTER	Direct Mailings to colleagues (repeated regularly)			(higher education, Research)		
4	Flyers	STICHTING BIOMEDICAL PRIMATE RESEARCH CENTER	PRIMOCID Dissemination: Distribution of Flyers at National & International Meetings (repeated regul)	01/01/2011	Europe	Scientific community (higher education, Research)	300	Europe and worldwide
5	Web sites/Applications	DEUTSCHES PRIMATENZENTRUM GMBH	The EUPRIM-Net Project	17/01/2011	global	Scientific community (higher education, Research) - Industry - Civil society - Policy makers - Medias	500	global
6	Flyers	DEUTSCHES PRIMATENZENTRUM GMBH	Courses on General Primatology	19/05/2011	EFPIA (European Federation of Pharmaceutical Industries and Associations)	Industry	500	Europe
7	Posters	DEUTSCHES PRIMATENZENTRUM GMBH	European Primate Network: Specialised infrastructures and procedures for biological and biomedical r	25/05/2011	ScandLas Meeting, Frederiksberg, Denmark	Scientific community(higher education, Research) - Industry	500	Europe
8	Flyers	DEUTSCHES PRIMATENZENTRUM	Courses on General	25/05/2011	ScandLas Meeting, Frederiksberg, Denmark	Scientific community	500	Europe

		GMBH	Primatology			(higher education, Research) - Industry		
9	Presentations	DEUTSCHES PRIMATENZENTRUM GMBH	EUPRIM-Net: Ensuring best practice and advancing the 3Rs in primate research	26/05/2011	ScandLas Meeting, Frederiksberg, Denmark	Scientific community (higher education, Research) - Industry	500	Europe
10	Presentations	DEUTSCHES PRIMATENZENTRUM GMBH	European Primate-Network (EUPRIM-Net): Advancing 3Rs and International Standards in Biological and B	27/05/2011	JRC, Ispra, Italy (ESTAF)	Scientific community (higher education, Research) - Industry - Civil society - Policy makers	20	Europe
11	Publication	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE	A new method to assess the behavior of nonhuman primates	06/06/2011	30ème ASTAL meeting, Marseille, France	Scientific community (higher education, Research)		France
12	Presentations	CONSIGLIO NAZIONALE DELLE RICERCHE	EUPRIM-Net - European Primate Network: Advancing 3Rs and International Standards in Biological and B	13/06/2011	ICLAS Symposium, Istanbul, Turkey	Scientific community (higher education, Research) - Industry	300	Europe, Mediterranean
13	Publication	STICHTING BIOMEDICAL PRIMATE	PRIMOCID Dissemination:	01/07/2011	Europe and worldwide	Scientific community	300	Europe and worldwide

		RESEARCH CENTER	LinkedIn announcements July 2011 in 3 groups (repeated regularly)			(higher education, Research)		
14	Presentations	DEUTSCHES PRIMATENZENTRUM GMBH	Visit of Professor Carlos Burmann, President of APE 2006-2008	19/07/2011	German Primate Centre	Scientific community (higher education, Research)	3	Spain
15	Publication	DEUTSCHES PRIMATENZENTRUM GMBH	EU CONTINUES SUPPORT OF EUROPEAN NETWORK ON PRIMATE RESEARCH (EUPRIM-NET)	31/07/2011	BOLETÍN DE LA ASOCIACIÓN PRIMATOLÓGICA ESPAÑOLA	Scientific community (higher education, Research)	300	Spain and other Spanish-speaking countries
16	Organisation of Conference	DEUTSCHES PRIMATENZENTRUM GMBH	EUPRIM-Net: Ensuring best practice and advancing the 3Rs in primate research	08/08/2011	Primate symposium August 7 to August 11, 2011 in Sochi-Adler, Russia	Scientific community (higher education, Research)	100	Russia
17	Posters	HEALTH PROTECTION AGENCY HPA	Characterisation of immune cell population changes during GBV-B infection	08/09/2011	18th International symposium on HCV and related viruses, Seattle 2011	Scientific community (higher education, Research)	200	global
18	Publication	DEUTSCHES PRIMATENZENTRUM GMBH	EU Continues Support of European Network on	01/10/2011	Laboratory Primate Newsletter	Scientific community (higher education,	1000	USA and worldwide

			Primate Research (EUPRIM-Net)			Research)		
19	Oral presentation to a scientific event	SMITTSKYDDSINSTITUTET	EUPRIM-Net II, the European Primate Network	02/10/2011	Annual Enrichment Symposium, San Diego, USA	Scientific community (higher education, Research)	200	international, especially USA
20	Publication	DEUTSCHES PRIMATENZENTRUM GMBH	Website of the month - www.euprim-net.eu	15/10/2011	Lab Animal Europe	Scientific community (higher education, Research)	9999	Europe
21	Flyers	STICHTING BIOMEDICAL PRIMATE RESEARCH CENTER	PRIMOCID	19/10/2011	ACTRIMS/ACTRIMS meeting Amsterdam	Scientific community (higher education, Research)		Europe
22	Flyers	DEUTSCHES PRIMATENZENTRUM GMBH	PRIMOCID	26/10/2011	ISNI meeting, Barcelona, Spain	Scientific community(higher education, Research)		Europe
23	Organisation of Workshops	STICHTING BIOMEDICAL PRIMATE RESEARCH CENTER	Best Veterinary Practice	04/11/2011	Biomedical Primate Research Centre	Scientific community (higher education, Research)	300	mainly Europe
24	Presentations	DEUTSCHES PRIMATENZENTRUM GMBH	Training von Primaten in der Versuchstierhaltung mittels positiver Verstärkung	07/11/2011	German Primate Centre	Scientific community (higher education, Research)	50	Germany

			(PRT)					
25	Presentations	DEUTSCHES PRIMATENZENTRUM GMBH	Visit of George Omondi und Recoi Hilter of IPR, Kenya	17/11/2011	DPZ, Göttingen	Scientific community (higher education, Research)	5	Germany, Kenya
26	Publication	DEUTSCHES PRIMATENZENTRUM GMBH	PRIMOCID/EUPRIM-Net	17/11/2011	The EUROPRISE Annual meeting November 17, 2011, Prague Czech Republic	Scientific community (higher education, Research)		Europe
27	Oral presentation to a scientific event mainly	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE	Automated testing of cognitive performance in semi-free ranging baboons (Papio papio).	29/11/2011	NC3Rs Primate Welfare Meeting, London, UK	Scientific community (higher education, Research) - Industry	100	Europe
28	Posters	DEUTSCHES PRIMATENZENTRUM GMBH	EUPRIM-Net - European Primate Network Advancing 3Rs and International Standards in Biological and Bi	29/11/2011	NC3Rs Primate Welfare Meeting, London, UK	Scientific community (higher education, Research)	150	Europe
29	Posters	DEUTSCHES PRIMATENZENTRUM GMBH	The EUPRIM-Net course series an activity of the European Primate Network	29/11/2011	NC3Rs Primate Welfare Meeting, London, UK	Scientific community (higher education, Research)	150	Europe
30	Posters	DEUTSCHES PRIMATENZENTRUM GMBH	The EUPRIM-Net course series an activity of the	06/12/2011	VIII Göttinger Freilandtage, 06.-09. December 2011	Scientific community (higher		worldwide

			European Primate Network			education, Research)		
31	Oral presentation to a scientific event	WESTFAELISCHE WILHELMS-UNIVERSITAET MUENSTER	Le primate comme "modèle animal" en psychologie cognitive: Illzstration des Méthodes et de quelques thèmes de recherche	10/01/2012	EFOR Conference, Paris, France	Scientific community (higher education, Research)	100	mainly France, Europe
32	Exhibitions	DEUTSCHES PRIMATENZENTRUM GMBH	The EUPRIM-Net course series an activity of the European Primate Network	29/01/2012	Primadaption workshop and networking, 29. Jan. 03. Feb. 1212 Immokalee, FL, USA	Scientific community (higher education, Research)		USA
33	Oral presentation to a scientific event	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE	A new method to assess the behaviour of nonhuman primates	06/06/2012	30th ASTAL Meeting, Marseilles, France	Scientific community (higher education, Research)	100	mainly France, Europe
34	Organisation of Workshops	SMITTSKYDDSINSTITUTET	Workshop _ Positive Reinforcement Training	24/09/2012	Nairobi, Kenya	Scientific community (higher education, Research)	20	Europe, Kenya
35	Organisation of Conference	DEUTSCHES PRIMATENZENTRUM GMBH	Initiating Collaboration between Kenyan IPR and EUPRIM-Net	26/09/2012	Nairobi, Kenya	Scientific community (higher education, Research)	40	Europe, Kenya
36	Organisation	DEUTSCHES	Novel Insights into	24/10/2012	Göttingen, Germany	Scientific	30	mainly

	of Workshops	PRIMATENZENTRUM GMBH	Primate Genomics: Impact for Biomedical Research			community (higher education, Research) - Industry		Europe, USA
37	Flyers	DEUTSCHES PRIMATENZENTRUM GMBH	European Primate Network (EUPRIM-Net II) "Advancing 3Rs and International Standards in Biological and Biomedical Research"	15/11/2012	Keio University, Central Institute for Experimental Animals, Kawasaki, Japan	Scientific community (higher education, Research)	30	Japan
38	Oral presentation to a scientific event mainly	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE	L'intelligence acquise	24/01/2013	AFSTAL Meeting, Comtech, Paris, France	Scientific community (higher education, Research) - Industry	100	France, Europe
39	Flyers	DEUTSCHES PRIMATENZENTRUM GMBH	"European Primate Network (EUPRIM-Net II)	28/02/2013	Keio University, Central Institute for Experimental Animals, Kawasaki, Japan	Scientific community (higher education, Research)	100	mainly Japan
40	Posters	DEUTSCHES PRIMATENZENTRUM GMBH	European Primate Network (EUPRIM-Net II)	28/02/2013	Keio University, Central Institute for Experimental Animals, Kawasaki, Japan	Scientific community (higher education, Research)	100	mainly Japan
41	Posters	DEUTSCHES PRIMATENZENTRUM	The EUPRIM-Net Project and the	11/03/2013	Neurobiology Meeting, Göttingen, Germany	Scientific community	300	mainly Germany,

		GMBH	Monkey Home Office			(higher education, Research)		Europe
42	Oral presentation to a scientific event	STICHTING BIOMEDICAL PRIMATE RESEARCH CENTER	Ultrasonic vocalisation is only present in a limited vocal repertoire of common marmosets (Callithrix jacchus)	08/05/2013	International Conference on Diseases of Zoo and Wild Animals, Vienna, Austria	Scientific community (higher education, Research)	100	mainly Europe, global
43	Posters	DEUTSCHES PRIMATENZENTRUM GMBH	EUPRIM-Net European Primate Network Advancing 3Rs and International Standards in Biological and Biomedical Research	10/06/2013	12th FELASA - SECAL Congress, Barcelona, Spain	Scientific community (higher education, Research) - Industry - Civil society - Policy makers - Medias	1000	mainly Europe, Global
44	Posters	DEUTSCHES PRIMATENZENTRUM GMBH	The EUPRIM-Net Course Series: Upgrading personnel to support animal welfare	10/06/2013	12th FELASA - SECAL Congress, Barcelona, Spain	Scientific community (higher education, Research) - Industry - Civil society - Policy makers - Medias	1000	mainly Europe, Global
45	Oral presentation to a scientific	STICHTING BIOMEDICAL PRIMATE RESEARCH CENTER	Macaque breeding management:	12/06/2013	12th FELASA SECAL Congress, Barcelona, Spain	Scientific community (higher	1000	mainly Europe, Global

	event		introduction, success rate and tenure length of alpha males.			education, Research) - Industry - Civil society - Policy makers - Medias		
46	Oral presentation to a scientific event	KAROLINSKA INSTITUTET	Negative and Positive Reinforcement - A way to avoid unnecessary suffering	12/06/2013	12th FELASA SECAL Congress, Barcelona, Spain	Scientific community (higher education, Research) - Industry - Civil society - Policy makers - Medias	1000	mainly Europe, Global
47	Oral presentation to a scientific event	STICHTING BIOMEDICAL PRIMATE RESEARCH CENTER	Non-human primates in biomeidcal research: baöance between animal welfare and biosafety	19/06/2013	16th Annual Conference of the European Biosafety Association, Basel, Switzerland	Scientific community (higher education, Research) - Industry	150	Europe
48	Oral presentation to a scientific event	DEUTSCHES PRIMATENZENTRUM GMBH	Welfare and Cognition in primates	01/07/2013	Basel Declaration Conference "Transparency in Animal Research"	Scientific community (higher education, Research) - Industry - Civil society - Policy makers - Medias	100	Europe
49	Posters	STICHTING	Determination of	01/08/2013	Institute for Animal	Scientific	100	mainly UK,

		BIOMEDICAL PRIMATE RESEARCH CENTER	recovery period after intra-abdominal transmitter and EEG electrode placement in common marmosets (Callithrix jacchus)		technology (IAT) Congress, UK	community (higher education, Research)		Europe
50	Oral presentation to a scientific event	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE	Keynote Lecture: Visual Cognition in Baboons: Assessment with innovative self-testing procedures	10/09/2013	European Federation of Primatology (EFP) Annual Meeting, Antwerp, Belgium	Scientific community (higher education, Research)	200	mainly Europe, global
51	Organisation of Workshops	DEUTSCHES PRIMATENZENTRUM GMBH	Workshop - Animal Welfare	23/09/2013	Nairobi, Kenya	Scientific community (higher education, Research)	30	Europe, Kenya
52	Organisation of Workshops	STICHTING BIOMEDICAL PRIMATE RESEARCH CENTER	3-day workshop on primate welfare and training	30/09/2013	BPRC; Rijswijk, Netherlands	Scientific community (higher education, Research)	30	Europe
53	Flyers	CONSIGLIO NAZIONALE DELLE RICERCHE	European Primate Network (EUPRIM-Net II) Primate BioBank	13/10/2013	8th Combined Meeting Of Orthopaedic Research Societies, San Servolo, Venice, Italy	Scientific community (higher education, Research)	300	International
54	Posters	DEUTSCHES PRIMATENZENTRUM	The "monkey home office"	04/11/2013	NC3Rs Primate Welfare Meeting, London, UK	Scientific community	150 l	mainly Europe,

		GMBH				(higher education, Research) - Industry		globa
55	Oral presentation to a scientific event	STICHTING BIOMEDICAL PRIMATE RESEARCH CENTER	Cortisol in haren als parameter voor chronische stress (hair cortisol as paramenter to determine chronic stress)	12/11/2013	Egmond aan Zee, The Netherlands	Scientific community (higher education, Research)	100	mainly The Netherlands , Europe
56	Posters	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE	Bien être du babouin en situation de tests informatisés	19/11/2013	Colloque Sfeca, Dijon, France	Scientific community (higher education, Research) mainly	100	France, Europe
57	Flyers	STICHTING BIOMEDICAL PRIMATE RESEARCH CENTER	EUPRIM-Net II - BioBank	21/11/2013	HandsOn: BioBaking, Den Haag	Scientific community (higher education, Research) - Industry	100	mainly Netherlands , Europe
58	Organisation of Workshops	STICHTING BIOMEDICAL PRIMATE RESEARCH CENTER	Workshop on BioBanking	27/11/2013	Deutsches Primatenzentrum Göttingen, Germany	Scientific community (higher education, Research)	30	mainly Europe, USA
59	Oral presentation to a scientific	DEUTSCHES PRIMATENZENTRUM GMBH	EUPRIM-Net and the EUPRIM-Net BioBank	28/11/2013	EPV Annual Meeting, Göttingen, Germany	Scientific community (higher	150	mainly Europe, USA

	event					education, Research) - Industry		
60	Flyers	DEUTSCHES PRIMATENZENTRUM GMBH	*CPD Courses for NonHumanPrimate Staff*/in Spanish/	01/12/2013	for distribution through EFPIA	Scientific community (higher education, Research) - Industry	50	Europe
61	Flyers	DEUTSCHES PRIMATENZENTRUM GMBH	The European Primate Network - EUPRIM-Net II	03/12/2013	IX. Göttinger Freilandtage, Göttingen, Germany	Scientific community (higher education, Research)	300	Worldwide
62	Oral presentation to a scientific event	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE	Lessons from six years of research using automated cognitive testing procedures with monkeys	13/02/2014	EFOR meeting, Paris, France	Scientific community (higher education, Research)		Europe, mainly French-speaking
63	Organisation of Workshops	STICHTING BIOMEDICAL PRIMATE RESEARCH CENTER	Alternative methods for the use of non-human primates in research	27/02/2014	Rijswijk, The Netherlands	Scientific community (higher education, Research) - Industry - Civil society - Policy makers	50	mainly Europe
64	Oral presentation to a wider public	DEUTSCHES PRIMATENZENTRUM GMBH	The Monkey "Home Office"	27/02/2014	Symposium on alternatives to animal experiments in research. BPRC. Rijswijk, The Netherlands	Scientific community (higher education,	50	Europe

						Research) - Civil society - Policy makers		
65	Oral presentation to a scientific event	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE	Cognition du primate non-humain	22/03/2014	XIII forum des Sciences Cognitives, Paris, France	Scientific community (higher education, Research)		Europe, mainly France
66	Oral presentation to a scientific event	DEUTSCHES PRIMATENZENTRUM GMBH	Cage- versus lab-based experiments: A test case for severity assessment in neuroscience research with non-human primates	28/03/2014	Symposium on Innovative Strategies for Severity Assessment in Laboratory Animals, Medizinische Hochs	Scientific community (higher education, Research)		Europe, mainly Germany
67	Posters	DEUTSCHES PRIMATENZENTRUM GMBH	Towards a cognitive neuroscience with less restrained animals	01/05/2014	7th Primate Neurobiology Meeting, Tübingen, Germany	Scientific community (higher education, Research) mainly	100	Germany
68	Exhibitions	DEUTSCHES PRIMATENZENTRUM GMBH	Presentation of XBI "monkey home office" (WP9)	17/05/2014	Open Day Federal Council, Berlin, Germany	Civil society	18000	Germany
69	Organisation of Workshops	STICHTING BIOMEDICAL PRIMATE RESEARCH CENTER	Primate food and fluid control workshop: Sharing knowledge on	23/05/2014	Rijswijk, The Netherlands	Scientific community (higher education, Research) -	30	mainly Europe

			training methods to refine the use and care of these animals.			Industry		
70	Oral presentation to a scientific event	DEUTSCHES PRIMATENZENTRUM GMBH	Towards a cognitive neuroscience without restrained animals	23/05/2014	Primate food & water control workshop, Rijswijk, The Netherlands	Scientific community (higher education, Research) - Industry		Europe
71	Press releases	DEUTSCHES PRIMATENZENTRUM GMBH	Council President Weil shakes robot hand	02/06/2014	www.dpz.eu/en/news/news/single-view/news/ratspraesident-weil-schuettelt-roboterhand.html	Civil society		mainly Germany
72	Oral presentation to a scientific event	DEUTSCHES PRIMATENZENTRUM GMBH	Towards a cognitive neuroscience without restrained animals	13/08/2014	International Primatological Society Congress, Hanoi, Vietnam	Scientific community (higher education, Research)		worldwide
73	Posters	DEUTSCHES PRIMATENZENTRUM GMBH	9th World Congress on Alternatives and Animal Use in the Life Sciences	24/08/2014	Prague, Czech Republic	Scientific community (higher education, Research) - Industry - Civil society - Policy makers - Medias	1000	worldwide
74	Posters	DEUTSCHES PRIMATENZENTRUM GMBH	A cage-based behavioural testing system for	24/08/2014	9th World Congress on Alternatives and Animal Use in the Life Sciences, Prague,	Scientific community (higher		worldwide

			NHP		Czech Republic	education, Research) - Industry - Civil society - Policy makers - Medias		
75	Organisation of Workshops	STICHTING BIOMEDICAL PRIMATE RESEARCH CENTER	Primate nutrition and its implication in research	20/11/2014	Sevilla, Spain	Scientific community (higher education, Research)	70	worldwide
76	Oral presentation to a scientific event	DEUTSCHES PRIMATENZENTRUM GMBH	Cage-based and wireless approaches for neuroscience research in non-human primates	26/11/2014	EUPRIM Course on General Primatology - Behaviour, Cognition and Neurophysiology, German Primate Cent	Scientific community (higher education, Research)	50	Europe
77	Flyers	DEUTSCHES PRIMATENZENTRUM GMBH	Deutsches Biobanken Symposium	03/12/2014	Berlin, Germany	Scientific community (higher education, Research) - Industry mainly	300	Germany
78	Oral presentation to a scientific event	DEUTSCHES PRIMATENZENTRUM GMBH	Towards a cognitive neuroscience with less restrained animals	16/03/2015	Primate Neurobiology Meeting, Goettingen, Germany	Scientific community (higher education, Research)		Europe, mainly Germany
79	Posters	DEUTSCHES PRIMATENZENTRUM GMBH	Towards a cognitive neuroscience with less restrained	18/03/2015	12th Goettingen Meeting of the German Neuroscience Society, Göttingen, Germany	Scientific community (higher education,		Europe, mainly Germany

			animals			Research)		
80	Oral presentation to a scientific event	Department of Health	miRNAs as biomarkers of GBV-B, a tamarin model of Hepatitis C	30/03/2015	UK Society for General Microbiology Annual Meeting, Birmingham	Scientific community (higher education, Research)	300	mainly UK
81	Oral presentation to a scientific event	Department of Health	Production of recombinant tamarin antibodies targeting GBV-B proteins to characterise the humoral immune response of GBV-B infection in tamarins	30/03/2015	UK Society for General Microbiology Annual Meeting, Birmingham	Scientific community (higher education, Research)	300	mainly UK
82	Oral presentation to a scientific event	Department of Health	miRNAs as biomarkers of GBV-B, a tamarin model of Hepatitis C	14/05/2015	UK meeting on the biology and pathology of hepatitis C	Scientific community (higher education, Research)		mainly UK, Europe
83	Oral presentation to a scientific event	Department of Health	Production of recombinant tamarin antibodies targeting GBV-B proteins to characterise the humoral immune response of GBV-B infection in tamarins	14/05/2015	14th UK meeting on the biology and pathology of hepatitis C	Scientific community (higher education, Research)		mainly UK, Europe
84	Organisation	STICHTING	Workshop The	10/06/2015	BPRC, Rijswijk, Netherlands	Scientific	30	Europe,

	of Workshops	BIOMEDICAL PRIMATE RESEARCH CENTER	Microbiome - Health and Disease			community (higher education, Research) Mainly		USA
85	Organisation of Workshops	WESTFAELISCHE WILHELMS-UNIVERSITAET MUENSTER	Course on marmoset as an animal model	22/06/2015 Münster, Germany	Scientific community (higher education, Research)		60	European
86	Organisation of Workshops	DEUTSCHES PRIMATENZENTRUM GMBH	Workshop on in vivo imaging of non-human primates	29/06/2015	Göttingen, Germany	Scientific community (higher education, Research) - Industry	60	European
87	Organisation of Workshops	DEUTSCHES PRIMATENZENTRUM GMBH	Workshop on the use and the advantages of marmosets	10/06/2015	DPZ, Göttingen, Germany	Scientific community (higher education, Research)	16	Europe, Japan
88	Oral presentation to a scientific event	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE	Lessons from five years of ALDM testing in social groups of baboons	10/06/2015	Neurex "Primate Cognition" meeting, Strasbourg, France	Scientific community (higher education, Research)		Europe
89	Oral presentation to a scientific event	DEUTSCHES PRIMATENZENTRUM GMBH	Telemetry systems in neurobiology	18/06/2015	Laboratory Animal Science Course, German Primate Center, Goettingen, Germany	Scientific community (higher education, Research)	18	Europe, mainly Germany
90	Web sites/Applicatio	DEUTSCHES PRIMATENZENTRUM	Virtual Tour Through Primate	30/06/2015	www.dpz.eu/en/info-center/media-center/virtual-	Civil society		worldwide

	ns	GMBH	Husbandry		tour.html			
91	Oral presentation to a scientific event	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE	The study of primate cognition : novel approach, novel findings	13/06/2015	1st Pheno-workshop Congress, ICM, Paris, France	Scientific community (higher education, Research)		Europe

Section B (confidential)

EUPRIM-Net II laid the basis for good scientific practice in industries using NHP (e.g. pharma toxicology). The project was not itself involved in the application for patents, etc.; however, attitudes, handling techniques, training and education services etc. disseminated by EUPRIM-Net II paved the grounds to ethically sound products that can be exploited in a commercial way.

TEMPLATE B1: LIST OF APPLICATIONS FOR PATENTS, TRADEMARKS, REGISTERED DESIGNS, ETC.

Type of IP Rights: Patents, Trademarks, Registered designs, Utility models, etc.	Application reference(s) (e.g. EP123456)	Subject or title of application	Applicant (s) (as on the application)

TEMPLATE B2: OVERVIEW TABLE WITH EXPLOITABLE FOREGROUND

Exploitable Foreground (description)	Exploitable product(s) or measure(s)	Sector(s) of application	Timetable, commercial use	Patents or other IPR exploitation (licences)	Owner & Other Beneficiary(s) involved
In-house Training for NHP staff	*EUPRIM-Net Seminar Group Lectures*	*Academic and Commercial NHP-keeping facilities*	*Not applicable; available since 2015*	*Not applicable*	*Beneficiary 1 (DPZ) Beneficiary 2 (BPRC) Beneficiary 6 (CNR-IBCN) Beneficiary 7 (UdS-CdP) Beneficiary 8 (CNRS) Beneficiary10 (KI)*
NHP-specific FELASA course function A, B, and C	*Development of an NHP-specific laboratory science course*	*Academic and Commercial NHP-keeping staff*	*Not applicable; available since 2015*	*Not applicable Accreditation by FELASA end 2015 or beginning 2016*	*Beneficiary 1 (DPZ)*
EUPRIM-Net BioBank: NHP biomaterial sample distribution	*EUPRIM-Net Office as mediator for sample requests*	*Academic and Commercial NHP researchers*	*Not applicable; available since 2006*	*Not applicable*	*Beneficiary 1 (DPZ) Beneficiary 2 (BPRC) Beneficiary 5 (WWU-CeRA) Beneficiary 8 (CNRS-SdP)*
Virtual Tour through the primate husbandry of the DPZ	*Website: http://www.dpz.eu/en/info-center/media-center/virtual-tour.html*	*Common public (Europe and worldwide)*	*Not applicable; available since 2015*	*Not applicable*	*Beneficiary 1 (DPZ)*
Generation of an assay for the detection of Herpes B Latency associated transcript (LAT) in samples	*Improved assay to detect herpes B virus infections*	*Academic and Commercial NHP researches*	*Not applicable; available since 2014*	*Not applicable*	*Beneficiary 1 (DPZ)*
Spreading of in-cage behavioural testing system	*The "Monkey Home-Office"*	*Behavioral and neuroscientific primate research*	*Not applicable; abailable since 2014*	*Not applicable*	*Beneficiary 1 (DPZ) Beneficiary 2 (BPRC) Beneficiary 8 (CNRS)*
In vitro assays for innate immune responses	*State of the art assays for qualitative and semi-quantitative assessment of innate immune responses*	*Academic and commercial researchers*	*Not applicable; available since 2014*	*Not applicable*	*BPRC, technology is accessible for interested researchers and companies*
In vitro replacement or	*Primary dissociated*	*Academic and*	*Not applicable;*	*Not applicable*	*BPRC, technology is accessible*

TEMPLATE B2: OVERVIEW TABLE WITH EXPLOITABLE FOREGROUND					
Exploitable Foreground (description)	**Exploitable product(s) or measure(s)**	**Sector(s) of application**	**Timetable, commercial use**	**Patents or other IPR exploitation (licences)**	**Owner & Other Beneficiary(s) involved**
reduction technology	*microglia and astrocyte cell cultures*	*commercial researchers*	*available since 2013*		*for interested researchers and companies*

In-house Training for NHP staff:

Its purpose: A EUPRIM-Net Seminar Group was formed with participation of ethologists, veterinarians, animal trainers and scientists who created and now offers eight standardised lectures on different topics around NHP keeping and handling to NHP-keeping facilities as in-house trainings (www.euprim-net.eu/network/ABM-seminars.html). These trainings are extremely important because the EUPRIM-Net expert inspects the on-site conditions and can customise the training according to the needs of the facility.

How the foreground might be exploited, when and by whom: Even beyond the EUPRIM-Net II term, Seminar Group members have been asked to give trainings to academic and industrial laboratories. These trainings have now to be paid by the requester on a full-cost basis.

IPR exploitable measures taken or intended: not applicable

Further research necessary, if any: Further development of the lectures in regular intervals is recommended to uphold the best quality and state-of-the-art.

Potential/expected impact (quantify where possible): Better keeping and handling of NHP with respect to the 3Rs has been proposed to yield better scientific outcomes. Furthermore, better handling of animals may enhance public acceptance of NHP research and testing.

NHP-specific FELASA course function A, B, and C:

Its purpose: Basic education enabling new staff to work with NHP under supervision and contributing to harmonisation of NHP-staff education in Europe by accreditation by FELASA (Federation of Laboratory Animal Science Associations).

How the foreground might be exploited, when and by whom: New staff at NHP-keeping facilities (academia and industry) earn certificate enabling them to work with NHP under supervision (as recommended by FELASA: "FELASA 2015. Recommendations for the Accreditation of Education and Training Courses in Laboratory Animal Science. http://www.felasa.eu/media/uploads/E&T_Recommendations_Accreditation_Revised_20150223.pdf)". Since the end of EUPRIM-Net II one additional course has already taken place, the next course being planned for April 2016. FELASA accreditation is in process and expected for end 2015 / early 2016. The course is paid by the student or its affiliation on a full-cost basis.

IPR exploitable measures taken or intended: not applicable

Further research necessary, if any: Updating of the course in regular intervals and in co-operation with the FELASA is recommended to guarantee best quality and state-of-the-art

Potential/expected impact (quantify where possible): Basic education in NHP-specific laboratory animal science is a prerequisite enabling new staff to work with NHP under supervision. This course will be the first NHP-specific FELASA course of its kind and can serve as template for the establishment of other NHP-specific FELASA courses in Europe.

EUPRIM-Net BioBank: NHP biomaterial sample distribution:

Its purpose: Share with and provide NHP biomaterial (e.g. DNA, RNA, tissues, organs, blood, and serum) to the European research community

How the foreground might be exploited, when and by whom: Biological and Biomedical scientists (academia and industry) needing NHP biomaterial for their research. Even beyond the term of EUPRIM-Net II, the EUPRIM-Net office is taking on requests and forwarding them to the appropriate providers.

IPR exploitable measures taken or intended: not applicable

Further research necessary, if any: Updating of protocols for sample preparation is recommended.

Potential/expected impact (quantify where possible): Reduce the number of NHP needed in biological and biomedical research; provide a rare and valuable resource to European researchers.

Virtual Tour through the primate husbandry of the DPZ:

Its purpose: Providing the public community with solid information about the keeping and wellbeing NHP used for research purposes in the primate centres of the Infrastructure and their benefit for health research.

How the foreground might be exploited, when and by whom: Inform the common public about NHP research and keeping, thereby raising awareness and acceptance for research on and with NHP (http://www.dpz.eu/en/info-center/media-center/virtual-tour.html; available since 2015)

IPR exploitable measures taken or intended: not applicable

Further research necessary, if any: Further development of the website is recommended if appropriate.

Potential/expected impact (quantify where possible): Providing solid information on NHP research and keeping to the common public is especially important in the current setting, where recently various ways (European citizens' initiative, European Parliament resolutions, petitions, and parliamentary questions) have been attempted to call into question the value of Directive 2010/63/EU, to try and repeal it and ban the use of animals in research and development.
To this end factual reporting and information sharing on research with and on NHP is more crucial than ever in order to raise awareness and acceptance.

Generation of an assay for the detection of Herpes B Latency associated transcript (LAT) in samples

Its purpose: To develop an assay which can clearly distinguish between infection of macaques with human herpes simplex virus or with the macaque herpes B virus. This is essential as infection of humans with monkey herpes B virus can be fatal.

How the foreground might be exploited, when and by whom: Scientists working with NHP or commercial labs performing viral diagnostics may use the published data to develop improved diagnostic assays

IPR exploitable measures taken or intended: not applicable

Further research necessary, if any: further validation using sera from nonhuman primates and humans is recommended.

Potential/expected impact (quantify where possible): To avoid human infections with herpes B virus

Spreading of behavioural testing system

Its purpose: Share device with and provide knowledge via publication(s) on how to implement and apply such devices to the European research community.

How the foreground might be exploited, when and by whom: all laboratories that do research on captive Primates, which comprises neuroscientific and ethological laboratories as well as it may be applicable for breeding facilities pre-training and pre-testing animals for their destination laboratories.

IPR exploitable measures taken or intended: not applicable

Further research necessary, if any: exploring further fields of application like automation of training protocols or animal selection profiling tests.

Potential/expected impact (quantify where possible): improving animal welfare by replacing potentially stressful laboratory based procedures by home-cage based procedures.

In vitro assays for innate immune responses

Its purpose: To provide the research community with animal-free, cell reporter models that allow for the qualitative and semi-quantitative assessment of innate immune responses. These models include libraries of cell lines that are transfected with so-called pathogen pattern recognition receptors (e.g. Toll-like receptors and NOD-like receptors) and/or engineered to express luciferase in response to NF-kB or IFRE-mediated signal transduction. Although some of these individual lines are also commercially available by now, we have developed and validated a full library of lines that cover the breadth of innate immune responses. The combined use of these assays in a tiered testing strategy leads to rapid, semi-quantitative and detailed assessment of innate immune responses.

How the foreground might be exploited, when and by whom: Biological and Biomedical scientists from academia and/or industry are granted access to our library of cell lines. Technology is not sold, but access is. In the future access to the research community might be granted via e.g. transnational access programmes. As we will continue updating and expanding our library, technology will be kept state of the art. We receive requests for testing of biological materials (also to avoid testing in animals) > 5 times per year.

IPR exploitable measures taken or intended: not applicable

Further research necessary, if any: We will continue to add new lines if new receptors or transcription factors are identified that play a role in innate immune responses. Such new lines are rapidly embedded into the current library.

Potential/expected impact (quantify where possible): In the short term development of Refinement technology in the form of better adjuvants that can replace old adjuvants that are notoriouos for their adverse effect profile. In the long run our techniques might help reduce animal numbers needed for testing of biologicals in eg pyrogenicity assays.

In vitro replacement or reduction technology

Its purpose: (1) To provide the research community with technology and protocols to optimally use animals sacrificied for research purposes and (2) to provide the research community with access to primary cell culture technology enabling a *pre in vivo* test phase when biologicals or drugs are to be tested *in vivo*.

How the foreground might be exploited, when and by whom: Biological and Biomedical scientists from academia and/or industry are granted access to this technology. Technology is not sold –although protocols have been made publicly available by means of scientific publications-, but access to technology is. In the future access to the research community might be granted via e.g. transnational access programmes. We receive requests for the use of dissociated primary cell cultures about once a year.

IPR exploitable measures taken or intended: not applicable

Further research necessary, if any: We will continue to adapt protocols and to expand our technology by the addition of new cell types and new methodology to cultivate the cells (eg 3D and co culture systems and possibly organotypic slice cultures).

Potential/expected impact (quantify where possible): In the long run this technology might help to step-by-step phase out the use of animals in *in vivo* procedures. Short term we provide researchers with *pre in vivo* testing opportunities, leading to better science and to a reduction in animal numbers needed for testing of e.g. biologicals.

3. REPORT ON SOCIETAL IMPLICATIONS

Replies to the following questions will assist the European Commission to obtain statistics and indicators on societal and socio-economic issues addressed by projects. The questions are arranged in a number of key themes. As well as producing certain statistics, the replies will also help identify those projects that have shown a real engagement with wider societal issues, and thereby identify interesting approaches to these issues and best practices. The replies for individual projects will not be made public.

A General Information *(completed automatically when **Grant Agreement number** is entered.*

Grant Agreement Number:	262443
Title of Project:	European Primate Network: Advancing 3Rs and International Standards in Biological and Biomedical research
Name and Title of Coordinator:	Professor Dr. Stefan Treue

B Ethics

1. Did you have ethicists or others with specific experience of ethical issues involved in the project?	○ ✓	**Yes** **No**

2. Please indicate whether your project involved any of the following issues (tick box) :	***YES***
INFORMED CONSENT	
• Did the project involve children?	no
• Did the project involve patients or persons not able to give consent?	no
• Did the project involve adult healthy volunteers?	no
• Did the project involve Human Genetic Material?	no
• Did the project involve Human biological samples?	no
• Did the project involve Human data collection?	no
RESEARCH ON HUMAN EMBRYO/FOETUS	
• Did the project involve Human Embryos?	no
• Did the project involve Human Foetal Tissue / Cells?	no
• Did the project involve Human Embryonic Stem Cells?	no
PRIVACY	
• Did the project involve processing of genetic information or personal data (eg. health, sexual lifestyle, ethnicity, political opinion, religious or philosophical conviction)	no
• Did the project involve tracking the location or observation of people?	no
RESEARCH ON ANIMALS	
• Did the project involve research on animals?	yes
• Were those animals transgenic small laboratory animals?	no
• Were those animals transgenic farm animals?	no
• Were those animals cloning farm animals?	no
• Were those animals non-human primates?	yes
RESEARCH INVOLVING DEVELOPING COUNTRIES	
• Use of local resources (genetic, animal, plant etc)	no
• Benefit to local community (capacity building ie access to healthcare, education etc)	no
DUAL USE	
• Research having potential military / terrorist application	no

C Workforce Statistics

3 Workforce statistics for the project: Please indicate in the table below the number of people who worked on the project (on a headcount basis).

Type of Position	Number of Women	Number of Men
Scientific Coordinator	0	1
Work package leader	5	6
Experienced researcher (i.e. PhD holders)	15	19
PhD Students	2	0
Other	22	10

4 How many additional researchers (in companies and universities) were recruited specifically for this project?	**20**
Of which, indicate the number of men:	5
Of which, indicate the number of women:	15

D Gender Aspects

5 Did you carry out specific Gender Equality Actions under the project ?

○ Yes
✓ No

6 Which of the following actions did you carry out and how effective were they?

		Not at all effective				Very effective
❑	Design and implement an equal opportunity policy	○	○	○	○	○
❑	Set targets to achieve a gender balance in the workforce	○	○	○	○	○
❑	Organise conferences and workshops on gender	○	○	○	○	○
❑	Actions to improve work-life balance	○	○	○	○	○
✓	Other: Not applicable					

7 Was there a gender dimension associated with the research content – i.e. wherever people were the focus of the research as, for example, consumers, users, patients or in trials, was the issue of gender considered and addressed?

○ Yes- please specify

✓ No

E Synergies with Science Education

8 Did your project involve working with students and/or school pupils (e.g. open days, participation in science festivals and events, prizes/competitions or joint projects)?

✓ Yes- please specify: WP4 courses were open to university students

○ No

9 Did the project generate any science education material (e.g. kits, websites, explanatory booklets, DVDs)?

✓ Yes- please specify: lecture print outs; E-Learning available via internet

○ No

F Interdisciplinarity

10 Which disciplines are involved in your project? *[See drop –down menus]*

✓ Main discipline: 1.5 Biological sciences (biology, botany, bacteriology, microbiology, zoology, entomology, genetics, biochemistry, biophysics, other allied sciences, excluding clinical and veterinary sciences)

✓ Associated discipline: 4.2 Veterinary medicine

✓ Associated discipline: 3.3 Health sciences (public health services, social medicine, hygiene, nursing, epidemiology)

G Engaging with Civil society and policy makers

11a Did your project engage with societal actors beyond the research community? *(if 'No', go to Question 14)*

✓ Yes
○ No

11b If yes, did you engage with citizens (citizens' panels / juries) or organised civil society (NGOs, patients' groups etc.)?

- ○ No
- ○ Yes- in determining what research should be performed
- ○ Yes - in implementing the research
- ✓ Yes, in communicating /disseminating / using the results of the project

11c In doing so, did your project involve actors whose role is mainly to organise the dialogue with citizens and organised civil society (e.g. professional mediator; communication company, science museums)?	○	Yes
	✓	No

12 Did you engage with government / public bodies or policy makers (including international organisations)

- ○ No
- ○ Yes- in framing the research agenda
- ○ Yes - in implementing the research agenda
- ✓ Yes, in communicating /disseminating / using the results of the project

13a Will the project generate outputs (expertise or scientific advice) which could be used by policy makers?

- ○ Yes – as a **primary** objective (please indicate areas below- multiple answers possible)
- ✓ Yes – as a **secondary** objective (please indicate areas below - multiple answer possible)
- ○ No

13b If Yes, in which fields?

Agriculture		Energy		Human rights	
Audiovisual and Media		Enlargement		Information Society	
Budget		Enterprise		Institutional affairs	
Competition		Environment		Internal Market	
Consumers		External Relations		Justice, freedom and security	
Culture		External Trade		Public Health ✓	yes
Customs		Fisheries and Maritime Affairs		Regional Policy	
Development Economic and Monetary Affairs		Food Safety		Research and Innovation ✓	yes
Education, Training, Youth ✓	yes	Foreign and Security Policy		Space	
Employment and Social Affairs		Fraud		Taxation	
		Humanitarian aid		Transport	

13c If Yes, at which level?

- ○ Local / regional levels
- ○ National level
- ✓ European level
- ○ International level

H Use and dissemination

14	**How many Articles were published/accepted for publication in peer-reviewed journals?**	**24**
15	**How many new patent applications ('priority filings') have been made?** *("Technologically unique": multiple applications for the same invention in different jurisdictions should be counted as just one application of grant).*	**0**
16	**Indicate how many of the following Intellectual Property Rights were applied for (give number in each box).**	
	Trademark	**0**
	Registered design	**0**
	Other	**0**
17	**How many spin-off companies were created / are planned as a direct result of the project?**	**0**
	Indicate the approximate number of additional jobs in these companies:	

18 Please indicate whether your project has a potential impact on employment, in comparison with the situation before your project:

❑	Increase in employment, or	❑	In small & medium-sized enterprises
❑	Safeguard employment, or	❑	In large companies
❑	Decrease in employment,	❑	None of the above / not relevant to the project
✓	Difficult to estimate / not possible to quantify	❑	

19	**For your project partnership please estimate the employment effect resulting directly from your participation in Full Time Equivalent (*FTE = one person working fulltime for a year*) jobs:**	*Indicate figure:*
	Difficult to estimate / not possible to quantify	✓

I Media and Communication to the general public

20 As part of the project, were any of the beneficiaries professionals in communication or media relations?

○ Yes ✓ No

21 As part of the project, have any beneficiaries received professional media / communication training / advice to improve communication with the general public?

○ Yes ✓ No

22 Which of the following have been used to communicate information about your project to the general public, or have resulted from your project?

✓	Press Release	❑	Coverage in specialist press
❑	Media briefing	❑	Coverage in general (non-specialist) press
❑	TV coverage / report	❑	Coverage in national press
❑	Radio coverage / report	❑	Coverage in international press
✓	Brochures /posters / flyers	✓	Website for the general public / internet
❑	DVD /Film /Multimedia	❑	Event targeting general public (festival, conference, exhibition, science café)

23 In which languages are the information products for the general public produced?

✓	Language of the coordinator	✓	English
✓	Other language(s)		

Question 10: Drop down menu will include the Classification of Scientific Disciplines according to the Frascati Manual 2002 (Proposed Standard Practice for Surveys on Research and Experimental Development, OECD 2002):

FIELDS OF SCIENCE AND TECHNOLOGY

1. NATURAL SCIENCES

1.1 Mathematics and computer sciences [mathematics and other allied fields: computer sciences and other allied subjects (software development only; hardware development should be classified in the engineering fields)]

1.2 Physical sciences (astronomy and space sciences, physics and other allied subjects)

1.3 Chemical sciences (chemistry, other allied subjects)

1.4 Earth and related environmental sciences (geology, geophysics, mineralogy, physical geography and other geosciences, meteorology and other atmospheric sciences including climatic research, oceanography, vulcanology, palaeoecology, other allied sciences)

1.5 Biological sciences (biology, botany, bacteriology, microbiology, zoology, entomology, genetics, biochemistry, biophysics, other allied sciences, excluding clinical and veterinary sciences)

2 ENGINEERING AND TECHNOLOGY

2.1 Civil engineering (architecture engineering, building science and engineering, construction engineering, municipal and structural engineering and other allied subjects)

2.2 Electrical engineering, electronics [electrical engineering, electronics, communication engineering and systems, computer engineering (hardware only) and other allied subjects]

2.3. Other engineering sciences (such as chemical, aeronautical and space, mechanical, metallurgical and materials engineering, and their specialised subdivisions; forest products; applied sciences such as geodesy, industrial chemistry, etc.; the science and technology of food production; specialised technologies of interdisciplinary fields, e.g. systems analysis, metallurgy, mining, textile technology and other applied subjects)

3. MEDICAL SCIENCES

3.1 Basic medicine (anatomy, cytology, physiology, genetics, pharmacy, pharmacology, toxicology, immunology and immunohaematology, clinical chemistry, clinical microbiology, pathology)

3.2 Clinical medicine (anaesthesiology, paediatrics, obstetrics and gynaecology, internal medicine, surgery, dentistry, neurology, psychiatry, radiology, therapeutics, otorhinolaryngology, ophthalmology)

3.3 Health sciences (public health services, social medicine, hygiene, nursing, epidemiology)

4. AGRICULTURAL SCIENCES

4.1 Agriculture, forestry, fisheries and allied sciences (agronomy, animal husbandry, fisheries, forestry, horticulture, other allied subjects)

4.2 Veterinary medicine

5. SOCIAL SCIENCES

5.1 Psychology

5.2 Economics

5.3 Educational sciences (education and training and other allied subjects)

5.4 Other social sciences [anthropology (social and cultural) and ethnology, demography, geography (human, economic and social), town and country planning, management, law, linguistics, political sciences, sociology, organisation and methods, miscellaneous social sciences and interdisciplinary , methodological and historical S1T activities relating to subjects in this group. Physical anthropology, physical geography and psychophysiology should normally be classified with the natural sciences].

6. HUMANITIES

6.1 History (history, prehistory and history, together with auxiliary historical disciplines such as archaeology, numismatics, palaeography, genealogy, etc.)

6.2 Languages and literature (ancient and modern)

6.3 Other humanities [philosophy (including the history of science and technology) arts, history of art, art criticism, painting, sculpture, musicology, dramatic art excluding artistic "research" of any kind, religion, theology, other fields and subjects pertaining to the humanities, methodological, historical and other S1T activities relating to the subjects in this group] .