June 2021

# Project News

**Newsletter 4 — June 2021**

**Developing an Integrated Risk Management Framework for Nano-BioMaterials used in medical devices and advanced therapeutic medicinal products**

BIO RIMA

## Latest news from BIORIMA

Welcome to the fourth BIORIMA newsletter and the first one for 2021, which will give you a short overview of what has been achieved since the last edition and what is planned for the project's final year

"Uncertainty" is a never-ending story: omnipresent and continuously affecting life at various levels in different ways. The current pandemic has been a global test to show how well societies are prepared in terms of their capacity to meet unforeseen challenges that emerge from what we cannot control. In this way, uncertainty has always been a major driver of human development: opening up the way for ground-breaking research and discoveries, and for innovations that emanate with new insights and understanding. This is why the way we deal with uncertainties has ultimately paved the way towards more sustainable human wealth, health and safety.

A safe and sustainable society and environment are the two pillars on which our future stands, and both have to be continuously supported and protected by transparent, long-sighted and science-based regulation that is shared by all actors involved.

BIORIMA is contributing to these ongoing new regulatory needs by developing novel methodologies that help us to obtain the knowledge and tools to manage possible risks associated with emerging new materials, such as nano-biomaterials (NBM), when used in medical applications. The project has developed an extensive amount of scientific data that will not only help us to prevent, control or mitigate possible adverse effects that these materials may cause, but also strengthen the in-house compliance of end-users, such as material manufacturers, users or service providers, with the rapidly changing regulatory environment. In this way, it will expedite the journey through the "dead valley" - the time between a new innovation and its market entry.

As the project is in its final year, a main focus of the work is still to integrate the vast amount of knowledge, data and methodologies generated during the past three years into the BIORIMA Risk Management Framework (RMF) and Decision Support System (DSS), which are the core results of the project.

These are the 'go-to' platforms for end-users to find the most appropriate measurement and testing tools, techniques and routes to handle the possible risks of nano-biomaterials along the product life cycle, in relation to expected benefits and as part of their registration and authorization protocols.

Case studies have been performed to demonstrate the applicability of the RMF/DSS for particular NBM using local and remote validation exercises underpinned by industrial partners from within the consortium, and by consulting with stakeholders outside the project. Comprehensive regulatory-related technical, organizational and market-relevant information was collected, evaluated and used to assess the performance of the tools developed in the project and integrated into the IRM framework. Results from these surveys will help to ensure that NBM can be managed in a safe and sustainable way, and possible risks reduced or avoided when used in MD and AMTP.

Finalization of the BIORIMA database and some complementary material measurement and testing is ongoing and will be combined with these validation studies in the final year to further refine and improve the RMF, to ensure that the current DSS prototype will be fit-for-purpose, most efficient, reliable, and user-friendly. Ultimately, it will enable end-users to successfully analyse and provide all the relevant information required by current regulation, such as REACH or the new EU MDR 2021.

On behalf of the BIORIMA team, we wish you a safe and pleasant summer and hope to hear back from you!

For a more complete view of the R&D activities that have been performed so far in BIORIMA and to get in touch with our experts, please feel free to:

- visit our website (www.biorima.eu),
- follow us on Twitter: @biorimaproject
- Join us on LinkedIn
- visit our stakeholder forum www.biorima.eu/forum

More information about BIORIMA can be found at the end of this newsletter.

Best regards
Rudolf Reuther (Editor)
Lesley Tobin (Production)
Lisa Bregoli and Stefania Melandri (Review)

The project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 760928.

## NanoTox 2021—A virtual success showcasing the latest research and development in nanosafety research

The nanosafety community met virtually for their 10th International Conference on Nanotoxicology - Nanotox between 20th to 22nd April 2021. This year's conference was jointly organised by three leading EU Horizon 2020 Projects: BIORIMA, GRACIOUS, and PATROLS - focusing on the development of novel tools for evaluating human and environmental hazard, and strategies for nanomaterial characterization, grouping, and read-across for risk analysis.

The conference not only showed the outputs and results from three years of research from these three projects, but also showcased the latest trends and developments in the field of nanosafety. Topics included hazard characterisation and assessment, risk assessment and governance, release and exposure, alternative hazard testing methods as well as Safe(r) by design (SbD) of nanomaterials and advanced materials.

*"NanoTox2021 has been an opportunity to showcase three key interacting projects to the nanosafety community. Right from the start of these three projects we planned to facilitate this meeting and we are so pleased that it has been a huge success,"* remarked Vicki Stone, Project Coordinator of the GRACIOUS Project, Heriot-Watt University.

Overall, the conference welcomed 361 participants from 33 countries, who attended 82 oral presentations, 117 poster presentations and seven keynote presentations. Participants included representatives from academia, research institutions, industry, governmental institutions and NGOs.

Shareen Doak, PATROLS Project Coordinator, Swansea University, added: *"It has been fantastic to see so many participants, including early career researchers, actively engaged during the conference. We are very pleased as organisers that we could provide a virtual platform that still enabled scientific exchange not only within academia, but also with industry and governmental institutions."*

Among the many highlights of the event was the awards ceremony, in which prizes were presented for six categories. These included:

- Best Oral: Prof Em. Dr Harold Krug (Nanocase GmbH, Switzerland) - Hazard assessment in nanotoxicology - the CoCoN database science approach
- Best Student Oral: Battuja Batbajar Dugershaw (St Gallen Empa, Switzerland) - Indirect embryo-foetal risk of nanoparticles: Impact on human placental function, the release of placental signalling factors and subsequent alterations on angiogenic and neurodevelopment processes.
- Best Poster: Dr Tobias Lammel (University of Gothenburg, Sweden) - Toxicity assessment of nanoparticulate TiO2 UV filter alone and in binary mixtures with organic UV filters using fish gill cells (RTgill-W1)
- Best Student Poster: Gerrit Bredeck (Leibniz Research Institute for Environmental Medicine, Germany) - Possible impact of foodborne engineered nanoparticles on the murine gut microbiome.

*Cntd →*

The project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 760928.

BIORIMA partners fully participated in the event's proceedings, with INIA reporting on three communications, including:

- David Hernández-Moreno, José María Navas, María Luisa Fernández Cruz, Lipid and iron nanobiomaterials only produce toxic effects in fish cell lines after a long-term exposure. Oral communication
- Kerstin Hund Rinke, Karsten Schlich, Cecilia Diaz Navarrete, Anne Jurack, Burkhard Knopf, María Luisa Fernández Cruz, David Hernández Moreno, Nicolas Manier, Pascal Pandard, Susana I.L. Gomes, Bruno Guimarães, Janeck J. Scott Fordsmand, Mónica J.B. Amorim;Experiences with a higher tier test design simulating environmental fate and effect of medical products after the use phase. Poster
- Mónica J.B. Amorim, María Luisa Fernández-Cruz, Kerstin Hund-Rinke and Janeck J. Scott-Fordsmand; Environmental hazard testing of nanobiomaterials. Poster

Additionally, under Theme 1 of the event: Hazard Characterisation of Nanomaterials and Advanced Materials, Subtheme: Environmental hazard characterization and mechanisms, the following research was presented:

## Lipid and iron nanobiomaterials only produce toxic effects in fish cell lines after a long-term exposure

David Hernández-Moreno, José María Navas, María Luisa Fernández Cruz

Department of Environment and Agronomy, National Institute of Agriculture and Food Research and Technology (INIA), Madrid, Spain, fcruz@inia.es

### Introduction

The short and long-term toxicity of different nanobiomaterials (NBMs) were evaluated *in vitro* in different rainbow trout cell lines. The RTgill-W1, RTL-W1 and RTS-11 were exposed for 24h to a range of concentrations (0.78 – 100 µg/mL) of lipid (SLN-nutra-Dis, SLN-nutra-Sol and LP-eye) and $Fe_3O_4$PEG-PLGA NBMs. The RTgill-W1 was used for the long-term exposure to 20 and 100 µg/mL NBMs during 28d (weekly cell renewal). Recovery was also tested after a 14d exposure and 14d recovery periods.

### Results

None of the NBMs studied provoked cytotoxicity after 24h exposure at the used concentrations ($IC_{50}$>100 µg/mL). After 28 d exposure, none of the SLN-nutra NBMs exerted a toxic effect. However, LP-eye and $Fe_3O_4$PEG-PLGA at the highest concentration caused a 50% decrease in cell viability. For these NBMs a concentration-related effect was observed. Cells previously exposed to $Fe_3O_4$PEG-PLGA for 14 d showed an almost complete recovery after 14 days in clean medium. However, cells exposed to 20 µg/mL of LP-eye recovered completely whereas no recovery was observed for cells pre-exposed to 100 µg/mL.

### Conclusions

These results evidence the need to test the long-term toxicity of NBMs and show differences in cytotoxicity for different NBMs probably associated to different mechanisms of toxic action. Rtgill-W1 cells are appropriate to screen short and long-term toxicity of NBMs providing valuable information about NBMs toxicity in fish.

### Summary

The NBMs assayed are not toxic after a short-term exposure for fish cell lines but the LP-eye and $Fe_3O_4$PEG-PLGA produce concentration-dependent long-term toxicities which can only be reversed in the case of the $Fe_3O_4$PEG-PLGA NBMs.

Acknowledgements: This work was funded from the European Union's Horizon 2020 Programme under Grant Agreement No 760928 (BIORIMA - BIOmaterial RIsk MAnagement). Colorobbia Consulting SRL Italy) and Nanovector SRL (Italy) supplied the iron and lipid NBMs, respectively.

In the closing remarks, Lang Tran, Project Coordinator BIORIMA, IOM stated: *"Our three projects are coming to an end but we are looking forward to showcase final results at the next conference"*

The next conference NanoTox 2024 will take place in Singapore. More details will follow soon. Meanwhile, if you would like to access the conference content, it will be available until near the end of July. Visit and download the materials from the exhibitors – Yordas and BlueFrog are exhibiting as well as EBRC.

The project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 760928.

# BIORIMA at EuroNanoForum 21

Earlier in May, BIORIMA presented its activities at Europe's largest networking conference focusing on nanotechnologies and advanced materials science, innovation and business: EuroNanoForum21, organised by the INL – International Iberian Nanotechnology Laboratory under the Portuguese Presidency of the Council of the European Union in the first half of 2021

ENF addresses the role of nano-enabled technologies and industries to the scientific community, representatives from industry, research and innovation, and policymakers.

The two-day event this year provided an opportunity for experts across different sectors to identify policy options and priorities on the role of Nanotechnology and Advanced Materials, and to share views on technical, industrial and social challenges and define the extent to which nanotechnology and advanced materials will play a part in the solutions Europe needs.

Addressing current issues, the conference addressed Nanotechnology and Advanced Materials as the key elements to guarantee the functioning, long term durability, safety, and environmental compatibility of many devices, machinery, and services.

Advanced materials will be fundamental for the transition to greener technologies, and a more sustainable future, making a significant contribution to the ambitious goals set by the European Green Deal, thus the focus was on the role of nanoindustry on the road to a greener, more resilient Europe.

Fore more information:
https://euronanoforum2021.eu/
https://www.youtube.com/watch?v=-xtkIYzMfZg


BIO RIMA
BIOmaterial RIsk MAnagement

In light of increasing regulatory demands on the use of medical devices (MD) and advanced therapeutic medicinal products (ATMP), the EU-funded BIORIMA project is taking a lead in developing an integrated risk management framework for the safe handling of nanobiomaterials (NBM) used in medical applications.

Here we highlight project outcomes in BIORIMA'S final year.

## BIORIMA Project Overview

BIORIMA is developing:

- New tools and methods to assess human and environmental risks that may be associated with nano-structured biomaterials along their life cycle and for particular product value chains, including their production and use in different medical applications, possible release routes to the environment up to their final disposal.
- A web-based integrated risk management (IRM) framework to guide potential end-users (industries and regulators) to select and use the most appropriate tool or method to estimate the hazard of and exposure to NBM, and resulting risks associated with their production and use in medical applications, to meet new regulatory requirements and customer needs.

## Integrated Risk Management Framework and DSS

The BIORIMA Integrated Risk Management Framework (IRMF) and web-based Decision Support System (DSS) have been further refined.

These major project outcomes offer various strategies for end-users, including regulators, manufacturers and users of NBM in medical devices (MD) and advanced medicinal therapeutic products (AMTP), to assess human health and environmental risks along their life cycle, in addition to clinical trials on their efficiency and side effects[1].

[1]Giubilato et al. 2020, Risk Management Framework for Nano-Biomaterials Used in Medical Devices and Advanced Therapy Medicinal Products, DOI:10.3390/ma13204532).

## NBM Characterisation and Testing Data

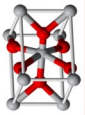
BIORIMA's multidisciplinary research team continues to update and improve the collection and curation of data and SOPs generated on the characterization and testing of NBMs.

Meanwhile, the ongoing comprehensive characterization campaign includes a large set of industrial and lab-scale NBMs to support exposure, fate and risk assessment, and the development of Safer by Design (SbD) tools: two major goals of BIORIMA. For this, we have followed up the properties and biotransformation of NBMs in relevant media, including different cell culture media, artificial gastrointestinal fluids, osteoarthritic synovial fluids, synthetic sweat, and artificial fresh and marine waters.

## Safer by Design

The BIORIMA SbD approach was tested in three different case studies, including:

(1) Ag doped fibres for wound dressings;
(2) TiO2 based nanomaterials for sunscreen creams; and
(3) Fe-based NPs for theranostic applications, as representative test materials.



A specific case carried out by our Hong Kong University partner developed protective layers designed and synthesized for NBM to reduce their toxicities.

These material devices included porous silica dioxide and biocompatible amorphous carbon to coat AgNPs. In addition, an alternative green support was prepared for drug delivery from the inter-crosslinking of two biocompatible polymers.

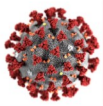
## Human and Environmental Exposure

Studies on the development of human and environmental exposure assessment tools, devices and probabilistic models have been finalised, as has a simulation of a massive release of NBM. Leeds University succeeded in developing novel methods to assess the release of NBMs from the fracture/fatigue/tear of medical implants into the body. Based on these methods ISO and CEN standards for implants have been developed.

New results have been published on the assessment of human health (WU) and environmental effects (UAVR) of NBMs using *in vitro* (cell culture) and *in vivo* (animal) studies. As part of this research, the role of the bio-corona formation on NBM toxicity has been further investigated and suitable methods developed to study the composition of the protein corona and its interaction with NBMs.

## The COVID-19 Task Force

In response to the EU call to participate in the global effort to combat the COVID-19 pandemic, BIORIMA has formed a COVID-19 task force and has already published a peer-reviewed paper on the use of nanomedicine against the SARS-COV-2 virus, showing the great potential of results produced to contribute to the control of the pandemic.



To access the publications related to these contents and to find out more, read our latest newsletter, visit the publication page on our website, and pay a visit to our forum.

**Useful links:**
Join us on LinkedIn: https://www.linkedin.com/company/biorima | Visit our website: www.biorima.eu
Visit our Stakeholder forum: www.biorima.eu/forum | Follow us on Twitter: @biorimaproject

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# Nanosafety Training School: From Basic Science To Risk Governance:

20th - 25th June 2021

## Interprofessional Education Training School [Virtual]

Coming to you live from Venice, Italy

The next NanoSafety Training School, organised within the EU funded Horizon 2020 projects BIORIMA, GRACIOUS, NanoInformaTIX, PATROLS, NANORIGO, RiskGone and Go4Nano, will take place virtually 20th - 25th June 2021. BIORIMA is a major initiator of this year's edition of the school and the goal is to transfer the knowledge generated in BIORIMA to the early stage researchers and practitioners from the new projects.

Become part of an interactive, exciting week and enrich your knowledge by developing multidisciplinary expertise!

## Register here before 16th June: https://www.greendecision.eu/wp/nanosafetytrainingschoolvirtual/

**Who should attend?**

- Early-stage researchers
- PhD's students and Post-Docs
- Senior researchers
- Industry
- Governmental Agencies
- Medical Personnel
- Anyone interested in Safe Nanotechnology, Risk Assessment and Nano-Medicine

**School Topics**

- Hazard to Human Health & Environment
- Fate & Exposure Assessment
- Nanomedicine: from the lab to the market
- Modelling
- Grouping & Read Across Approaches
- Risk Governance

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***Logistics and Administration:***

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Attendance is free of charge. The maximum number of newly accepted registrations is 200 people and will be on a first come-first served basis. Recordings will be made publicly available on the school website after the event.

The project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 760928.

# Estimating nanobiomaterial releases into the environment and identifying local hotspots

*By Marina Hauser and Bernd Nowack, Empa*

Nanobiomaterials (NBMs) are nano-sized materials which are designed to interact with the human body for a medical purpose. Not many nano-applications are currently on the market, but scientists all around the world are studying possible NBM applications. Two of the most investigated NBMs are nano-silver (nano-Ag) and poly(lactic-co-glycolic acid) (PLGA). Nano-Ag is used due to its antibacterial, antifungal, and antiviral properties in applications such as catheters, would dressings, bone cement, or bone tissue engineering. The polymer PLGA has great potential for application as drug delivery agent to reduce side effects during cancer treatment. Pharmaceuticals have been found worldwide in soil and manure, as well as surface, ground, tap and drinking water. Since NBMs have very similar applications to pharmaceuticals, their flows along the life cycle and into the environment are likely similar as well.

As part of the BIORIMA project, we evaluated the flows of nano-Ag and PLGA as well as the three BIORIMA case study materials $Fe_3O_4$PEG-PLGA, MgHA-collagen and PLLA-Ag into technical and environmental compartments in Europe. We applied an explorative full market-penetration scenario meaning we considered all applications that were either already on the market or likely to reach the market soon and assumed 100% market penetration for each application. The material flow model used in the analysis is shown in Figure 1.

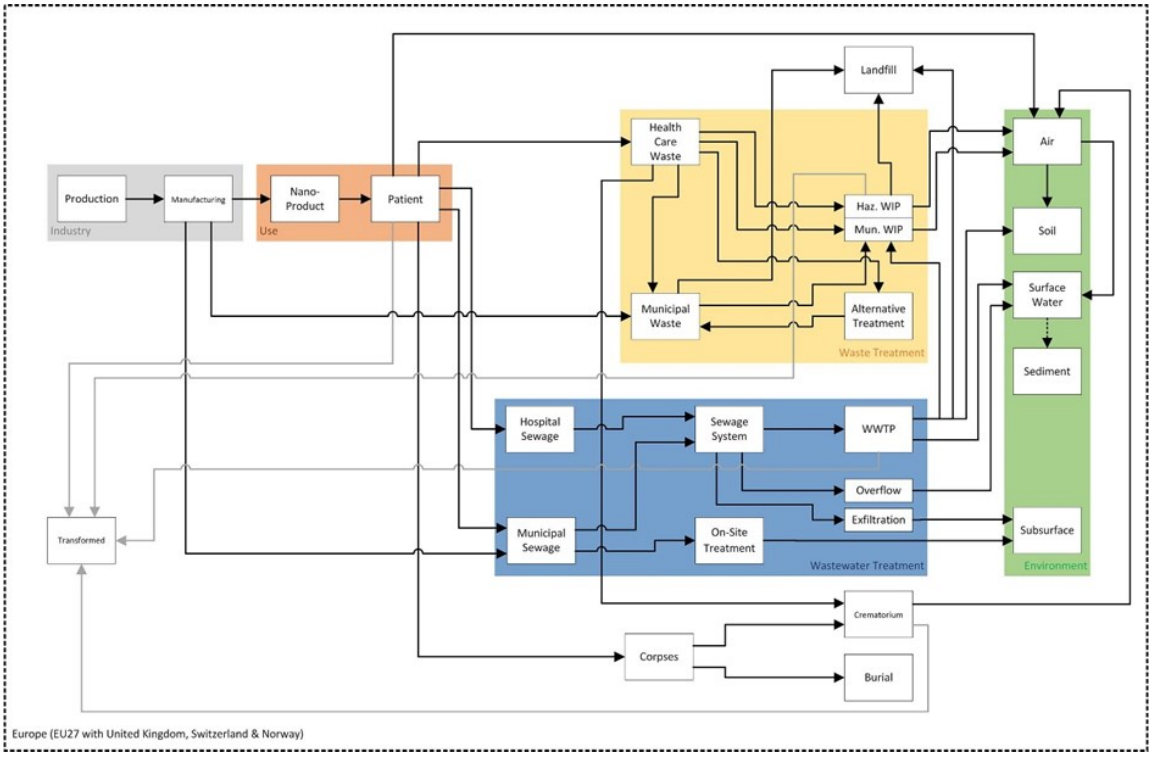


*Figure 1: Structure of the material flow model used to track the NBMs through their lifecycle from production and manufacturing to their incorporation into medical products and then through to their elimination via waste and wastewater treatment until they finish in the environment. Figure taken from Ref. 1.*

*Cntd→*

The project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 760928.

We predict that the majority of nano-Ag (as NBM) ends up in health care waste and from there flows to the incinerator and eventually landfills. PLGA on the other hand is predicted to mainly be metabolized in the body during its application. A small amount is excreted and enters the sewage system. In general, we found that the NBM's application plays an important role in its further distribution. Using the flows into different environmental and technical compartments, we could calculate European worst-case predicted environmental concentrations (wc-PECs, worst-case because fate is excluded). PLGA had the highest predicted concentration of the evaluated materials in all compartments. The highest concentrations can be expected in sewage sludge with up to several 400 µg/kg for PLGA. In surface water, we calculated European averages of up to 400 pg/l for PLGA.

European average PECs can be a good starting point, however, NBMs have very specific applications and are applied in very specific settings (meaning hospitals). This means that average PECs are not very representative. Therefore, we developed a spatially explicit model for NBM releases. We connected all hospitals to their respective wastewater treatment plant and distributed the release of PLGA based on the size of the hospitals. This allowed us to calculate a map with release hotspots. Parameterizing the model for Switzerland, we predict that the highest releases are going to occur in large cities with big hospitals. In a next step, we took the river discharge into account to calculate local PECs in rivers. Now, the highest concentrations are predicted to occur at medium sized hospitals with low discharge rivers (see Figure 2). The concentrations here were up to 13 times higher than the average Swiss wc-PEC. We expect the same local hotspots for other pharmaceuticals or materials used in in medical settings.

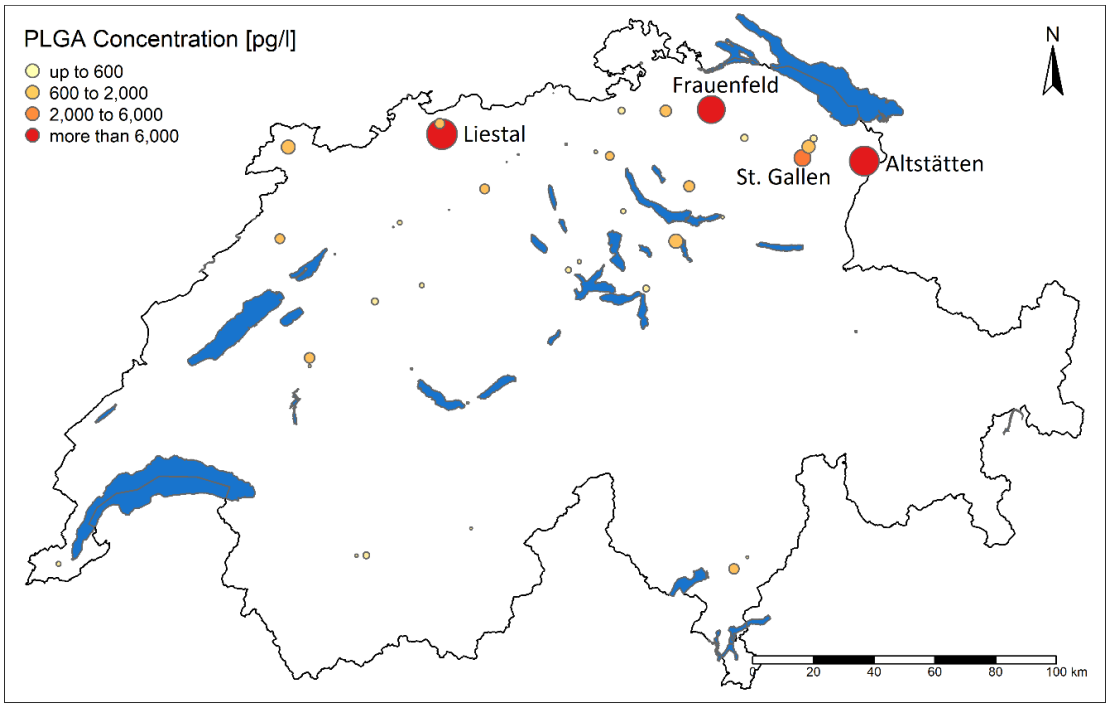


*Figure 2: Worst-case predicted environmental concentration of PLGA in Switzerland in 46 river segments with releases >0.1 kg PLGA/year. Figure taken from Ref. 2.*

References:

Hauser, M., Nowack, B., 2021. Probabilistic modelling of the release of nanobiomaterials from medical applications into the environment. Environ. Int. 146 (106184), 1–13. https://doi.org/10.1016/j.envint.2020.106184

Hauser, M., Nowack, B., in press. Modelling local nanobiomaterial release and concentration hotspots in the environment. Environmental Pollution. In press. https://doi.org/10.1016/j.envpol.2021.117399

The project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 760928.

## Joanneum Research Using Open Flow Microperfusion

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JOANNEUM RESEARCH used Open Flow Microperfusion (OFM) to investigate dermal uptake of nanobiomaterials (NBM) into the body (www.openflowmicroperfusion.com).

OFM probes were inserted into the dermal tissue and dermal interstitial fluid was continuously sampled. This enabled time-resolved monitoring of the dermal NBM uptake.

Further, together with the BIORIMA partners CONSIGLIO NAZIONALE DELLE RICERCIIE, KAROLINSKA INSTITUTET and UIÌIVERSITA CA' FOSCARI VENEZIA we investigated the effect of silver and titanium NBM-coatings on the unspecific immune response in the skin in a novel approach. Using OFM probes we delivered NBMs directly into the dermal tissue. Dermal interstitial fluid was sampled with the same OFM probe and subsequently analyzed for unspecific immune responses. The experimental phase is finished and final results will be available in summer 2021.

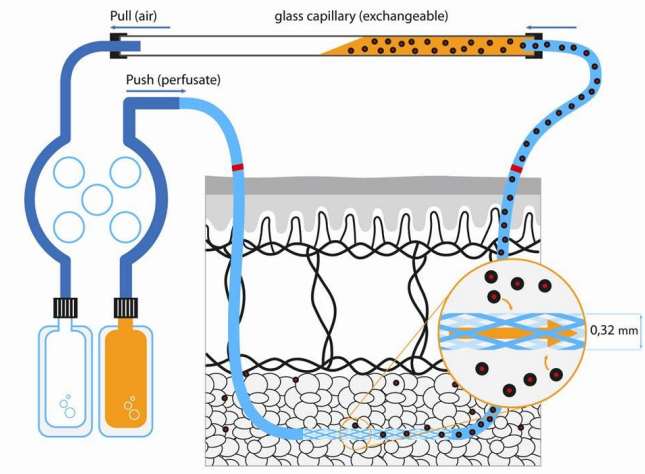


Image credit: https://www.joanneum.at/en/health/infrastructure/open-flow-microperfusion-ofm
More information and images

## CEA Grenoble Reports

BIORIMA WP 3 Fate and Exposure, Task 3.4 Strategies and methods for exposure monitoring and bio-monitoring

In the framework of WP3, CEA Grenoble together with the UNITO have completed a series of measures including both exposure assessment and biomonitoring in workers from a French dental company. Significant levels of nano-sized dusts have been measured on the workplace following field measurement performed by the CEA Grenoble Thereafter, Biomarkers of exposure and biomarkers of early effects reflecting subtle changes of lung biopathology have been selected in order to investigate potential absorption during the work shift or potential early biological alterations following exposure. The main goal of such an approach is to assess the exposure at the individual level, taking into account all the routes of exposure and all the individual characteristics of volunteers. Even in absence of validated biomarkers of exposure specific to nanomaterials, the objective of this study is to explore any shift of candidate biomarkers of exposure and effects in relevant biological matrices during a working shift as compared to non-exposed people.

Following approval of the protocol by the French Ethical Committee, six workers from the dental company, in charge of manufacturing dental prosthesis volunteered to the study. They were taken blood, urine and exhaled breath condensate samples both at the beginning and at the end of a working week. Ten workers from the CEA were also included as unexposed controls. Biological analysis including the measure of trace metals specific of the dental activity, oxidative stress biomarkers and the measurement of inflammatory cytokines are ongoing in both the CEA and the UNITO. The outcome of this study is expected by September.

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The project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 760928.

## Ethics in Nanotechnology—Publication

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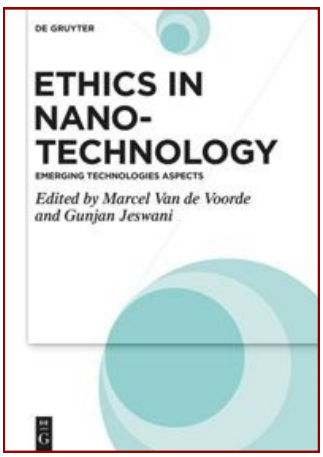
BIORIMA partner Prof. Bengt Fadeel together with BIORIMA Advisory Board member Dr Phil Sayre has co-written a key chapter for a soon-to-be-published book titled "Ethics in Nanotechnology." The chapter is titled: "Toward a revitalized vision of ethics and safety for the revolutionary nanotechnologies".

Commenting on this work, Prof Fadeel stated: "In our view, safety assessment of nanomaterials should fulfill the following three criteria, which we refer to as the R.I.P. guidelines for nanotoxicity testing:

(1) R = relevant (meaning realistic and relevant *in vitro* or *in vivo* models, that generate results relevant for risk assessment);
(2) I = integrated (or: intelligent, as in integrated or tiered approaches to safety assessment, starting with acellular or *in vitro* tests);
(3) P = predictive (as in: *in vitro* results that are predictive of *in vivo* outcomes, but also results that allow for grouping of nanomaterials on the basis of predictive screening; cf. *in silico* modelling, e.g., structure-activity relationships or SARs)."

Prof Fadeel added that this represents the authors' personal views on safety assessment, amongst other things.

For more details of the book, visit: https://www.degruyter.com/document/isbn/9783110701883/html




## An Update from the University of Paris

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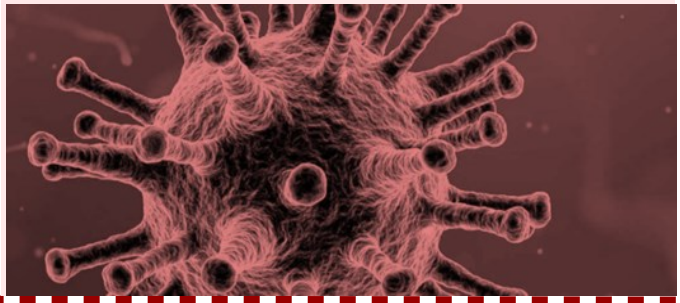
As previously reported, researchers of University of Paris succeeded in establishing a 3D preclinical model of the human bronchial epithelium using the Calu-3 cell line as an alternative to primary cells to evaluate the long-term toxicity of drugs or particles. They now published this research (Sanchez-Guzman et al. *Sci Rep* **11,** 6621 (2021) doi.org/10.1038/s41598-021-86037-0) demonstrating the viability and functionality of the model for 21 days without subculturing.

The epithelial cell secretome was fully characterized and compared to primary cells, highlighting the role in the immune response of the bronchial epithelium. This cell model also expresses the ACE-2 angiotensin-converting enzyme 2) receptor and the neuropilin-1 receptor, which are involved in SARS-CoV-2 infection of the lung epithelial cells which supports the use of this preclinical model for testing novel therapeutic strategies against Covid-19.

The researchers now use this model to evaluate the long-term effects of chronic exposure to low doses of NBM by performing repeated treatments at the air-liquid interface mimicking the in vivo situation, also evaluating the composition of the protein corona formed after interaction of NBM with the epithelial secretome.

The development and validation of this 3D model as an alternative to animal-based inhalation studies sets up the floor for screening the hazardous potentials of NBM.



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# Project News

**Newsletter 4— June 2021**

**Developing an Integrated Risk Management Framework for Nano-BioMaterials used in medical devices and advanced therapeutic medicinal products**

## Publications

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A paper concerning a joint study of University of Torino, Karolinska Institutet, RCSI (+ Polytechnic of Torino, INRIM and EC-Joint Research Centre) has recently been published online.

Titled: Efficacy, biocompatibility and degradability of carbon nanoparticles for photothermal therapy of lung cancer, the paper can be found in Nanomedicine, Future Medicine, 2021, https://doi.org/10.2217/nnm-2021-0009

The authors are: Ida Kokalari, Sandeep Keshavan, Mizanur Rahman, Elena Gazzano, Giulia Barzan, Luisa Mandrile, Andrea Giovannozzi, Jessica Ponti, Giulia Antonello, Marco Monopoli, Guido Perrone, Enrico Bergamaschi, Chiara Riganti, Bengt Fadeel, Ivana Fenoglio

NanoMedicine International Conference and Exhibition 2021

**20 - 22 Oct. 2021 I Milan, Italy (Hybrid mode event)**

Don't miss the 3rd edition of the NanoMedicine International Conference - NanoMed 2021, to be held in Milan from 20-22nd October 2021. **NanoMedicine 2021** will cover the most recent international developments in the field of Nanobiotechnology and Nanomedicine. Participants will get a complete overview on the state of the art in these fields and on the research carried out and the latest results. Recent advances, difficulties and breakthroughs as well as emerging and future trends of the converging fields of Nanotechnology, Biotechnology and Medicine will be discussed. The event offers to the participants from both science and industry the opportunity to discuss new cooperation projects.

More information here

## Poster Presentation

Dr Sonja Boland (HDR)
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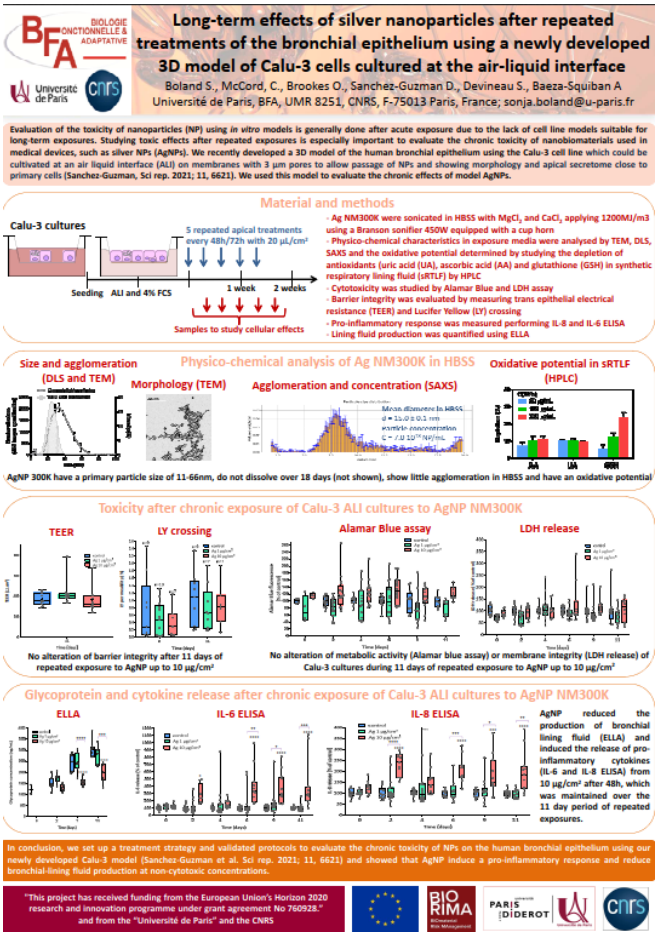
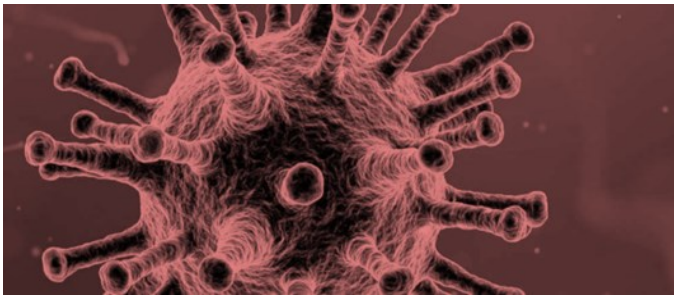
Université de Paris submitted the poster below to the LIVe 2021 Lung in vitro event organized virtually by Epithelix and Altertox on 15th of June.



The project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 760928.

# Project News

**Newsletter 4— June 2021**

**Developing an Integrated Risk Management Framework for Nano-BioMaterials used in medical devices and advanced therapeutic medicinal products**

## ABOUT BIORIMA

BIORIMA stands for 'Biomaterial Risk Management' The project aims to develop an integrated risk management (IRM) framework for nano-biomaterials (NBM) used in Advanced Therapeutic Medicinal Products (ATMP) and Medical Devices (MD).

## COVID-19

In the current COVID-19 climate, the project is identifying science and technology solutions across BIORIMA which could be rapidly developed and deployed to reduce exposure and hazards posed by COVID-19. We are now identifying partners outside BIORIMA (including other EU-funded projects) to further promote these initiatives. Overall, we aim to bring the BIORIMA risk management framework for safe NBMs to bear on the present and future pandemics.

## The BIORIMA RISK MANAGEMENT FRAMEWORK

The BIORIMA RM framework is a structure upon which the validated tools and methods for materials, exposure, hazard and risk identification/assessment and management are allocated plus a rationale for selecting and using them to manage and reduce the risk for specific NBM used in ATMP and MD.

Specifically, the IRM framework will consist of:

- Risk Management strategies and systems, based on validated methodologies, tools, and guidance, for monitoring and reducing the risks together with methods for evaluating them
- Validated methodologies and tools to identify the potential Exposure and Hazard posed by NBM to humans and the environment
- A strategy for Intelligent Testing (ITS) and Tiered Risk Assessment for NBM used in ATMP and MD.

The BIORIMA workplan covers these major themes:

- Materials
- Exposure
- Hazard
- Risk.

BIORIMA will generate methods and tools for these themes for use in risk evaluation and reduction.

## THE BIORIMA TOOLBOX

The BIORIMA toolbox will consist of:

- Validated methods/tools for materials synthesis
- Reference materials bank
- Methods for human/environment exposure assessment and monitoring
- (Eco)-toxicology testing protocols
- Methods for prevention of accidental risks – massive release or explosion
- A tiered risk assessment method for humans/environment
- An intelligent testing strategy for NBM
- Risk reduction measures, including a safer-by-design approach.

BIORIMA will deliver a web-based Decision Support System to help users, especially SMEs, evaluate the risk/benefit profile of their NBM products and help to shorten the time to market for NBM products. These products include implants, devices, sensors, tissue regeneration, targeted drug delivery equipment; in vivo imaging/biosensing and coating of implants or wounds; knee and hip joints; and dental repairs, among many others. The project's outcomes will be of benefit to patients and workers such as medical / healthcare staff, workers dealing with production as well as end-of-life treatment/disposal/incineration (occupational exposure) of these products.

**Notes to Editors**

The BIORIMA project has 43 partners from 14 different countries and is planned for four years (2017-2021). The project has received funding of almost 8 million EUR from the European Union's Horizon 2020 research and innovation programme under grant agreement No 760928.

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The project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 760928.