Feb 2021

Project News

Newsletter 3 — February 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 third BIORIMA newsletter and the first one for 2021, giving you a short overview about the project's achievements since the last edition and the plans for its final year.

While a tiny, roughly 100 nm virus still determines our life on a global level, BIORIMA has succeeded in proceeding as planned and sustaining momentum from the outset to establish for the first time a risk management framework for the safe handling of nano-engineered biomaterials (NBM) used in medical applications. None of us could imagine a year ago that we would find ourselves in a situation that would change our way of working and meeting so emphatically. Luckily, however, and due to the nature of the methods and materials we are developing in BIORIMA, the results we produce can significantly support the combat of the ongoing pandemic, not only in the use of the NBM we developed as carriers for vaccines, but also in future treatments against Covid-19.

During the past month, our multidisciplinary research team has progressed in further building-up the BIORIMA database, for example by continuing to update and improve the Excel templates for the collection and curation of data and SOPs generated on the characterisation and testing of NBMs. This will allow all partners to easily access and share all the forthcoming generated new experimental data in a harmonised and interoperable way.[1]

The still ongoing comprehensive characterisation 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.

Cntd p2

BIORIMA is an interdisciplinary European research initiative, and the only one of this kind to develop robust and validated methodologies to assess and manage any risks of NBMs when used in medical devices (MD) and advanced medicinal therapy products (AMTP), beyond clinical tests, including safe-by-design strategies to minimize or eliminate these risks.

A comprehensive testing and method validation program has been set up to improve the applicability of existing tools and approaches for human and environmental hazard and exposure assessment to NBM. The developed methodologies are integrated into a risk management framework (RMF) and a web-based Decision Support System that guides end-users to comply with existing regulations by finding the best practical solutions for testing and handling of NBMs.

This 3rd Newsletter will update you on the most recent progress and achievements obtained within BIORIMA in this field.

We will highlight some of the latest research activities and outcomes that have been recently generated within the project and hope they may attract your interest and serve you in your daily business and research.

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

Our forum is where you can get in direct contact with BIORIMA experts, post a question or any topic you want to discuss, or just give us your feedback. 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.

These efforts will also help to further harmonise developed methods with international standards and guidelines, as well as align with the requirements of the BIORIMA project database.

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.[2] A specific case carried out by our Chinese partner, Hong Kong University, 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.[3]

Studies on the development of human[4] and environmental exposure[5] assessment tools, devices and probabilistic models have been finalised, as has a simulation of a massive release of NBM.[6] As previously reported, 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.[7, 8]

Moreover, new results have been produced and published on the assessment of human health (WU) and environmental effects (UAVR) of NBMs by using *in vitro* (cell culture) and *in vivo* (animal) studies.[9] 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. [10]

In the final year, some selected test methods/assays will be subjected to "round robin" interlaboratory comparison studies to test their robustness and validate their performance to ensure the reliability of generated data. [11]

Finally, 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.[12]

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

These two 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. [13, 14]

In addition, a first round of surveys and on-site visits to industries has been conducted to assess the suitability and applicability of established characterisation, test methods and tools to real world situations. These case studies have demonstrated that the IRMF and DSS support the implementation of exposure, hazard, risk assessment and risk mitigation strategies, and, importantly, safety measures, to comply with innovation and regulatory requirements.[15]

To evaluate the readiness and applicability of the results achieved, and specifically, to effectively manage any risks associated with the handling or disposal of NBMs when used in MDs or AMTPs, Key Exploitable Results (KER) have been identified that show a great innovative and market potential for the developed materials, techniques, and tools, and for new future research activities.[16]

References:

1. Institute of Occupational Medicine (IOM) (Contact: lang.tran@iom-world.org)
2. CNR (Contact: anna.costa@istec.cnr.it)
3. Hong Kong University of Science and Technology (Contact: zwmao@zju.edu.cn; ocjcheng@ust.hk)
4. RCSI (Contact: marcomonopoli@rcsi.ie)
5. EMPA (Contact: bernd.nowack@empa.ch)
6. RCSI and EMPA (Contact: marcomonopoli@rcsi.ie; bernd.nowack@empa.ch)
7. Leeds University (Contact: t.a.wilkins@leeds.ac.uk)
8. T A Wilkins (Rapporteur), L Boehm, M Falzetti, G Klotz, D Mooney, E Simakova, K Wild, T Zadrozny, H Berg, D Bernard, C Dupas, M Leonowicz, J Mieres: "Policy & Processes for Accelerating Nano-, Bio-, Materials & Production Technologies Innovation in Horizon 2020"; EC NMBP Advisory Group on Innovation EC Strategy white paper, Luxembourg, 2014
9. WU – UAVR (Contact: hans.bouwmeester@wur.nl; mjamorim@ua.pt)
10. RCSI (Contact: marcomonopoli@rcsi.ie)
11. KI (Contact: bengt.fadeel@ki.se)
12. KI (See article on COVID-19 Task Force. Contact: bengt.fadeel@ki.se)
13. ITENE (See IRMF Validation Webinars article francisco.huertas@itene.com; cfito@itene.com)
14. T A Wilkins (Rapporteur), L Boehm, M Falzetti, G Klotz, D Mooney, E Simakova, K Wild, T Zadrozny, H Berg, D Bernard, C Dupas, M Leonowicz, J Mieres: "Policy & Processes for Accelerating Nano-, Bio-, Materials & Production Technologies Innovation in Horizon 2020"; EC NMBP Advisory Group on Innovation EC Strategy white paper, Luxembourg, 2014.
15. ITENE (francisco.huertas@itene.com; cfito@itene.com))
16. ENAS (Contact: rudolf.reuther@enas-online.com)

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

Invitation—Register Now: Integrated Risk Management Framework and Decision Support System Demonstration Webinars: 25th-26th February 2021

Following months of development, we are delighted to announce that the BIORIMA Integrated Risk Management (IRM) Framework and Decision Support System (DSS) are ready for demonstration with real case examples.

You are invited to take part in one of two free, interactive sessions where you will have the opportunity to find out about the BIORIMA project and the purpose, principles and potential applications of the IRM and the DSS we are developing. You will then be able to validate the systems and provide feedback using a questionnaire.

Session 1: Thursday 25th February 15:30-17:00 CET
Session 2: Friday 26th February 9:30-11:00 CET

These sessions will also provide an opportunity for you to find out how you, developers, manufacturers, and users of Nano-Biomaterials (NBM) and associated Medical Devices (MD) and Advanced Therapeutic Medicinal Products (ATMP) can benefit from these main BIORIMA output and results.

Please register here. The link to join will be sent to you in the week of the webinar
For more information, email Francisco Huertas López

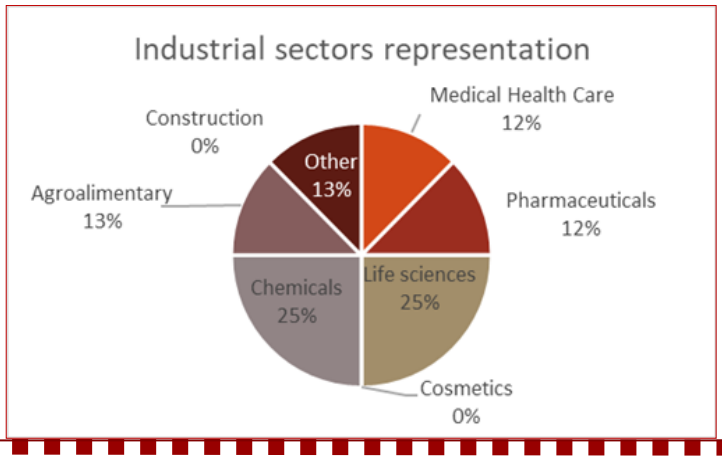
Report on Validation Webinars—October 2020

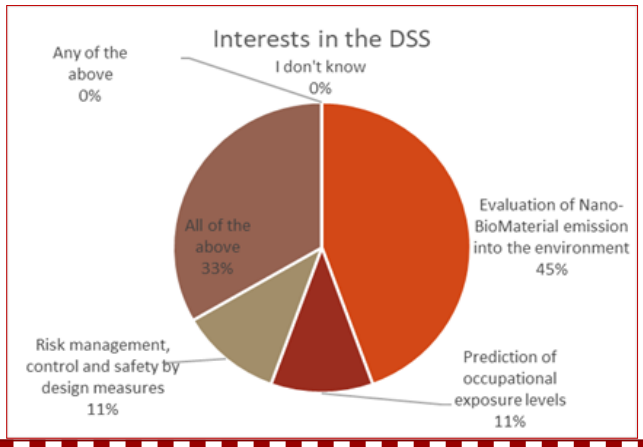
IRMF Local Validation Webinar: 14th October 2020

The main objective of this webinar was to check whether the IRMF and the DSS are filling the necessities of the industrial partners inside the BIORIMA consortium (Colorrobia, IRES, Finceramica, Nanovector and ElectroSpinnning). Proposed Key Performance Indicators (KPIs) were evaluated as personalized questionnaires for each company. Questions addressed different categories, such as risk assessment, risk mitigation, risk awareness, regulatory issues, and economic impact (see figure below). In general, there was a good acceptance of the need of the tools and framework developed, although the biggest conclusion was that there is a need to better explain and train companies on how to use these major BIORIMA results.

IRMF Remote Validation Webinar: 15th October 2020

This webinar was designed to explain the IRMF to stakeholders that could potentially use this risk management framework. There was a total of 26 representatives from different nanotechnology sectors (such as medical and health care, pharmaceuticals, life sciences, chemicals, agro-alimentary sector, and others). Close to a 100% of the answers were positive regarding the interest in the IRMF, DSS and other results from the BIORIMA project, for example in the evaluation of the potential NBM release into the environment . All the participants wanted to know more and would like to attend in a future training event on the IRMF and DSS.





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The COVID-19 Task Force (TF)

BIORIMA has recently formed a COVID-19 Task Force (TF) with representatives from all the technical WPs in BIORIMA (see website update).

The mission statement of the TF is to identify science & technology solutions across BIORIMA which could be rapidly developed and deployed to reduce exposure and hazard posed by COVID-19 and identify partners outside BIORIMA (including other EU-funded projects) to further promote these initiatives. Overall, the aim is to bring the BIORIMA risk management framework for safe NBMs to bear on the present and future pandemics.

Members of the Task Force at present are: Anna Costa (WP2) (vice chair), Bernd Nowak (WP3), Bengt Fadeel (WP4) (chair of TF), Danail Hristozov (WP5), Rudolf Reuther (WP6), Terry Wilkins (WP4-5) (S&T officer of TF).

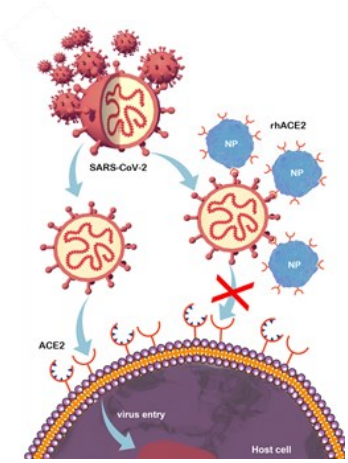

Image: Potential nanotechnology-enabled solution.
From: Wilson Jones G, et al. Nanomedicine (2020).

This schematic figure shows SARS-CoV-2, the coronavirus that causes COVID-19, and its host receptor, ACE2. We and others have postulated that synthetic nanoparticles decorated with recombinant human ACE2 could potentially act as decoys, intercepting the virus and thereby preventing the entry of the virus into susceptible host cells.

Further reading:

Wilson Jones G, Monopoli M, Campagnolo L, Pietroiusti A, Tran L, Fadeel B. No small matter: a perspective on nanotechnology-enabled solutions to fight COVID-19. Nanomedicine (Lond). 2020 Oct;15(24):2411-27].

Leeds University – Example of BIORIMA's Accelerated Innovation Concept applied to Rapid Point of Care Testing for Covid-19 Infection

Professor Wilkins's extensive experience in accelerated innovation, demonstrated in Leeds's BIORIMA safe-by-design replacement hip joint technology, together with his commercial immuno- and DNA PCR- test developments, has proved valuable for the Oxford University (UK)/ Suzhou (CN) research collaboration and its spinout SME Oxsed.

He joined the Board of Directors in June, to guide setting up the Oxsed as social enterprise to commercialise its rapid low-cost Point-of-Care Covid-19 DNA PCR test. It won the Royal Academy of Engineering President's prestigious Covid-19 Special Pandemic Award on 24 August 2020, following successful completion of clinical trials testing passengers flying out of London Heathrow airport in the summer. In September, it secured EU CE and US FDA medical device approvals. The business was bought by the Hong Kong based company Prenetics Ltd on 28 October 2020, to scale up manufacturing and roll out rapid testing at airports to screen all passengers flying between the UK, China and Singapore.

This is an example of Accelerated Radical Innovation described in his EC H2020 NMBP AG Task Force report[1]. From business incorporation to successful trade sale in 5 months!

[1] T A Wilkins (Rapporteur), L Boehm, M Falzetti, G Klotz, D Mooney, E Simakova, K Wild, T Zadrozny, H Berg, D Bernard, C Dupas, M Leonowicz, J Mieres: "Policy & Processes for Accelerating Nano-, Bio-, Materials & Production Technologies Innovation in Horizon 2020"; EC NMBP Advisory Group on Innovation EC Strategy white paper, Luxembourg, 2014.

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Recent Output from BIORIMA

The BIORIMA Partners have produced a large body of work including publications, which are accessible from the BIORIMA website and the BIORIMA Forum.

Moreover, a number of abstracts have been submitted to NanoTOX2021 and are waiting for confirmation. The abstracts and contact details are on the BIORIMA Forum, to enable you to initiate or participate in ongoing discussions with the experts about their work and results.

These include:

"*Exploring the biocompatibility, efficacy and biodegradability of carbohydrates-derived carbon nanoparticles for photo-thermal therapy of lung cancer*"
Contact: Ida Kokalari i
da.kokalari@unito.it

Long-term evolution of the epithelial cell secretome in preclinical 3D models of the human bronchial epithelium
Contact: Stephanie Devineau
stephanie.devineau@u-paris.fr

Pulmonary effect of exposure to Fe3O4-PEG-PLGA nanoparticles via pharyngeal aspiration in wild type and Nrf2 knockout mice
Contact: Gaku Ichihara
gak@rs.tus.ac.jp

"Toward a revitalized vision of ethics and safety for the revolutionary nanotechnologies".
Contact: Bengt Fadeel
bengt.fadeel@ki.se

Unmasking the Surface Effect: A superficial view of nanotoxicology
Contact: Bengt Fadeel
bengt.fadeel@ki.se

A battery of tests for nanobiomaterial high throughput cyto- and genotoxicity testing
Contact: Marie Carriere:
marie.carriere@cea.fr

Decision Support System for risk assessment and management of nano(bio)materials used in medical devices and advanced therapy medicinal products
Contact: Alex Zabeo alex.zabeo@greendecision.eu;
Virginia Cazzagon virginia.cazzagon@unive.it

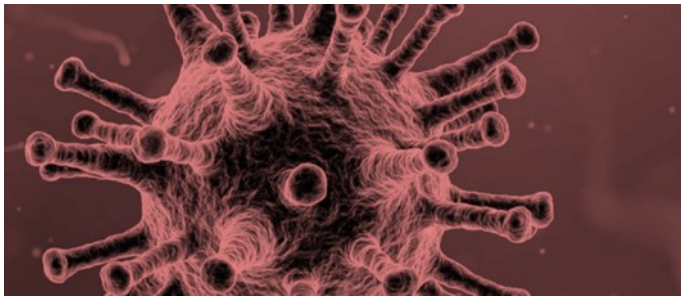
In vitro Alternatives to Acute Inhalation Toxicity Studies in Animal Models Dania Movia, Adriele Prina-Mello
Contact: Dania Movia
dmovia@tcd.ie

New descriptors in toxicology prediction of nanomaterials: Using quasi-ab initio MD simulations for the estimation of aqueous ZnO and TiO2 surface structure parameters
Contact: Benjamí Martorell Masip
benjami.martorell@urv.cat

Converting grouping Integrated Approaches to Testing and Assessment (IATAs) to for the effective risk assessment of nanobiomaterials with medical applications
Contact: Suzanne Gillies
S.L.J.Gillies@hw.ac.uk

Developing Integrated Approaches for Testing and Assessment of nanobiomaterial safety following intravenous exposure
Contact: Suzanne Gillies
S.L.J.Gillies@hw.ac.uk

Experiences with a higher tier test design simulating environmental fate and effect of medical products after the use phase.
Contact: Kerstin Hund-Rinke
Kerstin.Hund-Rinke@ime.fraunhofer.de



Introducing 'Open Research Europe' - open access publishing platform

The European Commission is preparing the launch of Open Research Europe, the European Commission scientific publishing service .

The Director-General of the Commission Research Department, Mr. Jean-Eric Paquet, has communicated a introduction to the service, which can be found in the Participant Portal's dedicated section under this link.

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INNO4COV-19 Open Call

Apply now to the Open Call April 2021 Round

The call aims to provide financial support to companies with the goal of accelerating the development and commercialization of innovative solutions that tackle COVID-19 and that have already been validated in lab environments (TRL6 or higher).

Deadline 30th April

Companies or small consortia of companies established in one of the EU Member States or H2020 associated countries.
The sectors of focus may include healthcare / medicine / biotech / biopharma, and IT-related topics (e.g. robotics, automation, electronics, nanotech, etc).

For more information or to apply, use this link.

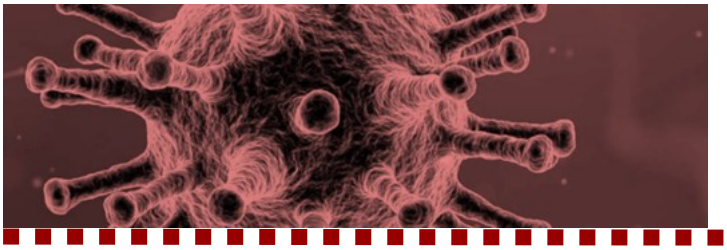
Nanosafety Training School

From Basic Science to Risk Governance

Event Date: 20th June 2021 - 25th June 2021

The Interprofessional Education Training School & Young Scientist Forum that was due to take place in March this year in Venice, Italy, was unfortunately postponed due to the COVID-19 pandemic. Plans are now underway to host it in June 2021, organised within the EU-funded Horizon 2020 projects BIORIMA, GRACIOUS, NanoInformaTIX, PATROLS, Gov4Nano, NanoRIGO, and RiskGone.

Keep an eye on the Biorima project website for updates.



NANOTOX 2021

Tuesday 20th April – Thursday 22nd April

This year, due to the current COVID pandemic and the restrictions imposed by the UK and Scottish Governments on face-to-face meetings, the NanoTox 2021 Organising Committee has taken the difficult decision to move the conference to a Virtual Conference to ensure the safety of our attendees and invited speakers.

The Virtual Conference remains aimed at personnel from research and academic institutions as well as from industry, government agencies, and other relevant organisations interested in:

- Nanotechnology
- Hazard and risk assessment of nanomaterials and advanced materials, and their governance
- Alternative methods for nanomaterial hazard testing, release and exposure.
- Safe(r) by design (SbD) of nanomaterials and advanced materials.

The 2021 Virtual Conference is jointly organised by three leading EU Horizon 2020 Projects, BIORIMA, PATROLS and GRACIOUS, focusing on development of novel tools for evaluating human and environmental hazard, and strategies for nonmaterial characterisation, classification, grouping and read-across for risk analysis.
BIORIMA has submitted a significant number of abstracts, some of which are highlighted in the previous article.

Registration is now open here

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

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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

Contact details

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