Suggested table of contents for a concept note:

Title of the suggested Action:

**Resistance and biodegradation of macrolide in the environment (RBIOMAC)**

Subtitle (or short description in one sentence):

RBIOMAC is aiming at characterizing microbes resistant to macrolide antibiotics in the environement and microbes able to successfully degrade those compounds to avoid their dispersal in the environment.

**Description of the Action (approx. 1 page):**

The use, overuse and sometimes misuse of antibiotics in human and veterinary medicine are major promoters for the development and spread of multiresistant bacteria world-wide. The problem is amplified by release of antibiotics into environment including soils, surface and ground waters. Environmental bacteria have therefore been shown to be a reservoir of antibiotic resistance genes and a potential source of novel resistance genes in clinical pathogens. One of the dominant point pollution sources for antibiotics are effluents from antibiotic manufacturing plants and wastewater treatment facilities collecting wastewater from sewage, hospitals and veterinary clinics. Many studies have shown that the elimination of antibiotics in conventional wastewater tratment plants is poor and consequently, these effluents or sludges could be a possible route for the spread of both persistent antibiotic residues and antibiotic resistance bacteria from wastewater treatment plants.

An overall goal of this project is to characterize mixed microbial culture, selected from municipal wastewater treatment plant which was shown to efficiently degrade azithromycin, one of the most widely used macrolide antibiotic in human medicine in the world. This will be done by investigating macrolide-resistance determinants from activated sludge in order to determine whether it is a source of clinically relevant antibiotic resistance. Macrolide-resistance genes will be isolated from metagenomic libraries built from a pool of cultured bacteria. Resistant clones will be identified, sequenced and characterized. The second goal is to estimate the role of individual culture members in azithromycin degradation by isolation of bacterial strains and evaluation of its azytromicyn catabolic activity by ultra-high-performance liquid chromatography coupled to quadrupole time-of-flight mass spectrometry (UHPLC-QTOF).

Obtained results will warant new knowledge that will allow better understanding of potential persistent environmental reservoirs and novel alleles of macrolide-resistance genes as well as biodegradation processes and their possible application.

The proposed action will be executed by the consortium of two partners: INRA/Université de Bourgogne, UMR Agroécologie in Dijon, France and Ruđer Bošković Institute, the Division for Marine and Environmental Research in Zagreb

References to running activities, lessons learnt from other regions, etc. (one paragraph)

N Udikovic-Kolic is already studying antibiotics fate in the environment. F Martin-Laurent directing the research group working on microbial degradation of pollutants at the INRA of Dijon is currently working at the Agriculture and AgriFood Canada under the supervision of Ed Topp in the framework of a program funded by OECD entitled ‘Genetic characterization of environmental bacterial isolate able to degrade veterinary antibiotics’. North-American researchers are working on antibiotics fate in the environment because of the contamination of farmyard manure with veterinary antibiotics used to promote the growth of livestock. Even if the situation is slightly different in Europe since the use of antibiotics as growth promoter is forbidden, animals are treated with antibiotics to get rid of diseases, and consequently farmyard manure is contaminated with antibiotics but with concentrations much lower than those encountered in North America. Keeping in mind that antibiotics are showing accumulation kinetics it is most likely that in the next decade the nasty situation currently ongoing in North American countries will be occurring in Europe. Therefore in this context, RBIOMAC is anticipating this probable situation by taking into account the lessons learnt from North American countries.

**Actors to be involved in the implementation and their roles (max. half a page):**

At this stage RBIOMAC involves two laboratories already collaborating notably in the framework of SEE-ERA-NET-PLUS program (FP7 project) entitled ECOFUN-MICRBIODIV coordinated by F Martin-Laurent. Based on this initial bilateral collaboration, actors will be invited to join this action of research. Possible actors to be involved are already working in the field of pesticide biodegradation in collaboration with F Martin-Laurent: Dirk Springael (University of Leuven, Belgium), Sebastien Sorensen (GEUS, Kopenhagen, Denmark) and Ed Topp (Agriculture and AgriFood Canada).

**Expected impact (one paragraph):**

RBIOMAC is aiming at estimating the dispersal of antibiotic resistance genes in the environment by using a combination of microbial and molecular approaches. To do so microbes resistant to antibiotics will be isolated and enumerated on specific medium. The abundance of resistance genes will be estimated by quantitative PCR performed on DNA extracted directly from soils. These results will help us to define a scenario of the evolution of the dispersal of microbe resistant to antibtiotics in the environment. In addition, RBIOMAC is aiming at characterizing microbes able to degrade antibiotics in the environment to estimate the purifying capability of the soil and its resilience. These results will be of prime interest in order to estimate the extent of this environmental problem with consequences on human health. It will also offer or not possible cleaning strategies to eliminate antibiotics from the environment.

**Relevance to the WBC region (one paragraph):**

RBIOMAC will be based on the expertise of N Udikovic-Kolic working on antibiotics degradation. This theme of research is relying on an environmental issue shared by numerous countries of the European continent where organic matter contaminated with veterinary antibiotics are applied to agricultural field to enrich soil with carbon in order to promote crop production and keep soil quality.

Author: name, affiliation, contact details (but you may also submit contributions anonymous)

Nikolina Udikovic-Kolic

Division for Marine and Environmental Research

Rudjer Boskovic Institute

Zagreb, Croatia

nikolina.udikovic.kolic@irb.hr

And

F Martin-Laurent

INRA

UMR Agroécologie

17 rue Sully

BP 86510

21065 France

Fabrice.martin@dijon.inra.fr

N Udikovic-Kolic