NACIONALNI INŠTITUT ZA BIOLOGIJO

Kako smo napisali uspešen projekt

Fate and effects of cytostatic pharmaceuticals in the environment and identification of biomarkers for an improved risk assessment on environmental exposure

CytoThreat

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NACIONALNI INŠTITUT ZA BIOLOGIJO

Razpis

Environment (including Climate Change) Calls: FP7-ENV-2010

- **Publication Date:** 30 July 2009
- **Budget:** € 175 000 000
- **Deadline:** 05 January 2010 at 17:00:00 (Brussels local time)
- **Specific Programme(s):** Cooperation

Activity 6.1 Climate Change, pollution and risks

Sub-Activity 6.1.2 Environment and health

Area 6.1.2.2 Health effects of environmental stressors other than climate change

ENV.2010.1.2.2-2 Human health and environmental effects of exposure to pharmaceuticals released into the environment

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WORK PROGRAMME 2010

Sub-Activity 6.1.2 Environment and health

Area 6.1.2.2 Health effects of environmental stressors other than climate change

ENV.2010.1.2.2-2 Human health and environmental effects of exposure to pharmaceuticals released into the environment

The aims:

1. to improve the knowledge on risks related to human health and ecosystems, due to the exposure to pharmaceuticals and their derivates, which are released into the environment.
2. To investigate the potential short- and long-term human health and environmental impacts
3. To integrate the more advanced ecological health risk assessment models and methods into human risk assessment.
4. Can include innovative measurement strategies, sampling techniques, modelling and database building.
5. To consider effects of mixtures
6. To consider different kinds of relevant biological effects.

Expected impact:

Improved risk assessment for human health and ecosystems for pharmaceuticals. The results should contribute to relevant EU policies.

Kaj pa zdaj?

- Najti in pridružiti se projektni skupini – nismo uspeli.
- Prijaviti svoj projekt!

Izhodišča

- **Osredotočimo se na citostatike v okolju**
  - O njihov učinkih vemo veliko, so biološko zelo aktivne učinkovine in potencialno zelo nevarne, njihova prisotnost in učinki na okolje so v primerjavi z drugimi farmacevtiki malo raziskani, ker so t.i. predvidene koncentracije v okolju (PEC) prenizke, da bi bila potrebni ekotoksikološki testi, malo verjetno je, da se bodo druge projektne skupine specifično osredotočile na to skupino farmacevtikov v okolju.
- **Povzetek predloga projekta:**
  - Cilji, metodologije in pristopi…(1 stran zelo splošno)
- **Izbira potencialnih partnerjev:**
  - Specifična ekspertiza, oprema, medsebojno dopolnjevanje, multidisciplinarnost, prenos znanja
- **Povabilo in podpis pisem o nameri:**
  - Zelo pomembno

Osnovni zahtevi, da bo projekt uspešen

I. Predlog projekta vključevati **vse** v razpisu navedene cilje

II. Prepričati mora ocenjevalce

1. Scientific and/or technological excellence (*relevant to the topics addressed by the call*)

- Soundness of concept, and quality of objectives
- Progress beyond the state-of-the-art
- Quality and effectiveness of the S/T methodology and associated work plan

2. Quality and efficiency of the implementation and the management

- Appropriateness of the management structure and procedures
- Quality and relevant experience of the individual participants
- Quality of the consortium as a whole (including complementarity, balance)
- Appropriateness of the allocation and justification of the resources to be committed (staff, equipment,…)

3. The potential impact through the development, dissemination and use of project results

- *Contribution, at the European [and/or international] level, to the expected impacts listed in the work programme under relevant topic/activity*
- Appropriateness of measures for the dissemination and/or exploitation of project results, and management of intellectual property.

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1. Scientific and/or technological excellence (*relevant to the topics addressed by the call*)

The main objectives of CytoThreat and progress beyond the state-of the-art:

- **To assess the occurrence and fate of cytostatic pharmaceuticals, their metabolites and transformation products in treatment systems and in the environment.**
  - The obtained data will present the basis for toxicological part of proposed project.
- **To explore potential delayed and irreversible effects of cytostatic pharmaceuticals at environmentally relevant concentrations in aquatic experimental models, and compare the data to those obtained in human experimental models.**
  - The parameters LD or EC50, NOEL, will be derived that are currently missing.
  - Toxicogenomic studyes will allow extrapolation to the low dose range, and should facilitate identification of threshold concentrations.
  - Development of *in vitro* models will allow the evaluation of the potential long term effects cytostatics and comparison of the responses in aquatic and human experimental models.
- **To explore combined effects of mixtures of cytostatic pharmaceuticals, their excreted metabolites and transformation products formed in the environment or waste water treatment.**
  - The data will enable linking the presence of cytostatics in environmental samples and discharges to assess their relative contribution to observed toxicity.
- **To develop, based on the obtained results, guidance on how to improve the environmental and human risk assessment of cytostatics released into the environment.**
  - Provide information on the occurrence of cytostatic drugs in the environment and missing basic ecotoxicological data that will enable risk assessment based on experimental data.
  - From the transcriptomic biomarkers of the tested cytostatics it will be possible to determine the so called No Observed Transcriptional Effect Level (NOTEL) value. This parameter can be used to prioritize potency of cytostatic in the environment.

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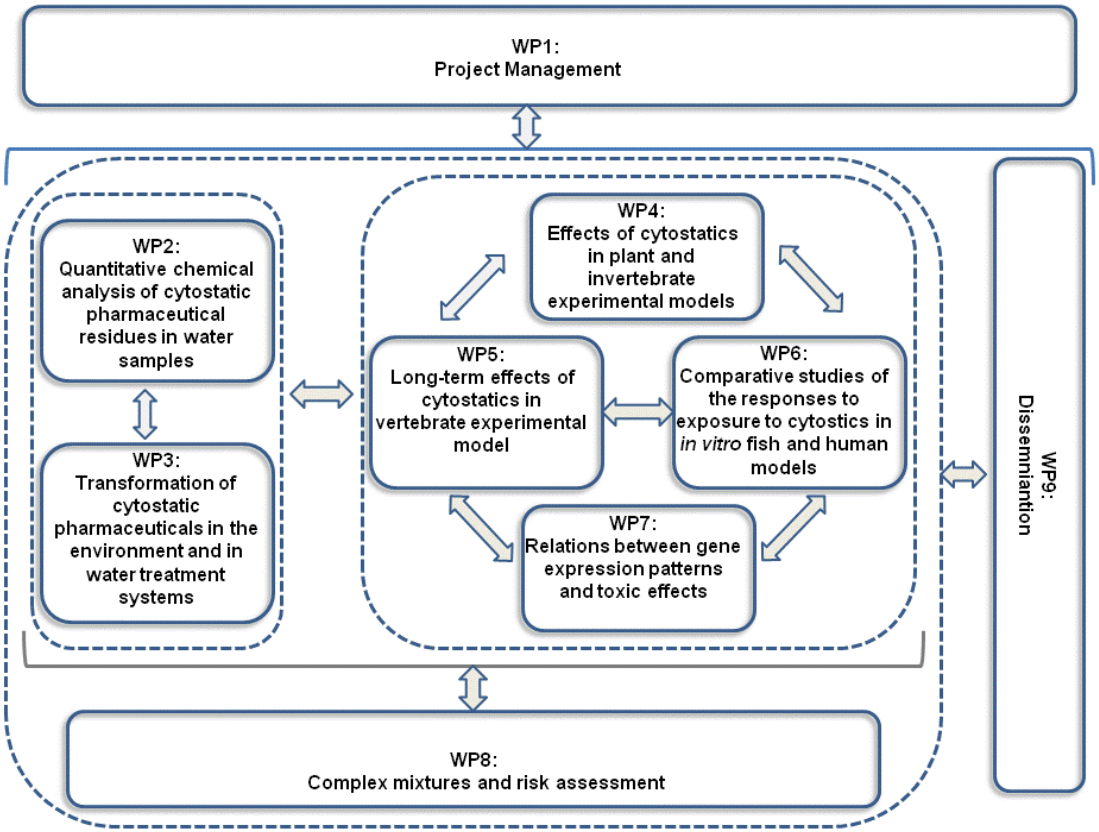
1. Scientific and/or technological excellence (*relevant to the topics addressed by the call*)

S/T methodology and associated work plan plan



Prikazati povezanost in soodvisnost delovnih sklopov;

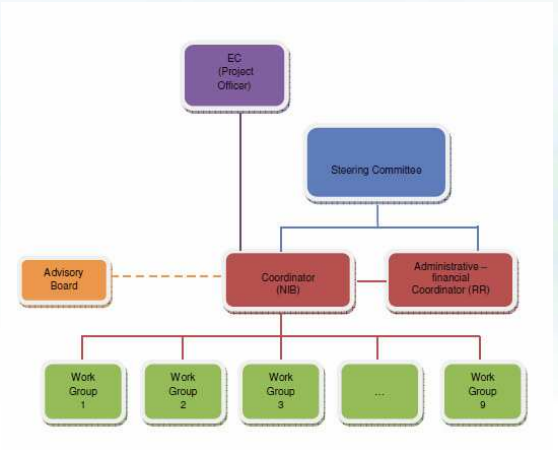
Vsak delovni sklop ima zelo jasno vsebinsko in časovno opredeljene:

- Cilje
- Mejnike (milestones) in
- Dosežke (deliverables)

2. Quality and efficiency of the implementation and the management

Sodelovanje z izkušenimi svetovalci za projektno upravljanje in administrativno -finančno koordinacijo (RR&CO))!!

- Jasna organiziranost upravljanja projekta
- Definirane naloge, odgovornosti in pravice posameznih teles
- Jasno opisane za projekt relevantne kompetence partnerjev ter njihova vloga v okviru projekta
- Zelo natančno in transparentno opredeljeni viri (osebje, oprema…) ter razdelitev stroškov



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CytoThreat konzorcij

CytoThreat consortium is composed of **9 partners** from **5 EU member states** (Austria, Italy, Slovenia, Spain and Hungary) and **2 associated countries** (Croatia and Serbia):

1.National Institute of Biology (NIB): *coordination, in vitro studies in cell lines and zebrafish embryos, toxicogenomic analysis of in vivo and in vitro experiments*

2.Jožef Stefan Institute (JSI): *new analytical methods, chemical analysis of degradadion products, interlaboratory validation of analitical methods…*

3.Medical University Vienna (MUW): *higher plant systems, risk assessment*

4.Szent István University (SZIE): *in vivo acute and chronic studies in zebrafish*

5.Dipartimento Scienze della Vita, Seconda Universita di Napoli (SUN): *acute and chronic studies in Daphnia*

6.Spanish Council of Scientific Research (CSIC): *chemical analysis of traces of cytostaics in water samples, determination of occurence…*

7.Institute for Medical Research and Occupational Health (IMI) *in vitro and in vivo genotoxicity determination (comet assay, MN assay)*

8.Institute for Multidisciplinary Research, University of Belgrade (IMSI): *genotoxic effects in mussel*

9.RR & CO. Knowledge Centre Ltd. (RR&CO) *administrative and financial coordination*

3. The potential impact through the development, dissemination and use of project results

Contribution, at the European [and/or international] level, to the expected impacts listed in the work programme under relevant topic/activity

A. Contribution of project results to improved risk assessment for human health and ecosystems for pharmaceuticals:

– CytoThreat will contribute to an improved risk assessment for human health and ecosystems for cytostatic pharmaceuticals by providing accurate data on their environmental concentrations and toxicological data on key parameters (LC50, NOEC) required in risk assessment procedures.

B. Contribution of project results to the relevant EU policies/strategies

1. Environment and Health Action Plan 2004-2010 the 2nd main theme: Filling the knowledge gaps by strengthening research on environment and health and identifying emerging issues (Action 7: Develop methodological systems to analyse interactions between environment and health; Action 8: Ensure that potential hazards on environment and health are identified and addressed)
2. Together for Health: A Strategic Approach for the EU 2008-2013 (White Paper): CytoThreat project results will contribute to Strategic Objective 2: Protecting citizens from health threats, to the following action within this strategic objective: Strengthen mechanisms for surveillance and response to health threats, including review of the remit of the European Centre for Disease Prevention and Control
3. Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH): "*development of alternative methods for the assessment of hazards of different (chemical) substances" through the evaluation and* confirmation of predicitive potential of zebrafish embryo test and *in vitro cell based test systems for long* term *in vivo effects based on early biological and molecular markers.*

3. The potential impact through the development, dissemination and use of project results

Appropriateness of measures for the dissemination and/or exploitation of project results, and management of intellectual property.

The overall objectives of the dissemination are oriented in the following directions:

- To create the critical mass of interest and to raise awareness among the relevant stakeholders and policy makers necessary for the deployment of the results of the present project related to the effect of cytostatic drugs released into environment and threat that they present to aquatic biota and human health;

–Web materials, press conferences, press releases and publication of articles, promotional materials, education materials

- To share the results of the project with the academic and research community interested to the topics addressed by the project and to stimulate further research in the filed covered by the present project;

–Scientific publications, scientific reports, workshops and lab meetings, international conference

Exploitation of the results:

- Transfer of knowledge
- Preparation of subsequent proposals.
- Policy recommendations

Ocena: 13.5/15

- **Scientific and/or technological excellence (*relevant to the topics addressed by the call*): 4.5/5**
- The proposal addresses all aims of the call text. The proposal has a clear rationale for the choices made and is well focused, targeting a highly important topic. The methodology to be implemented is very well described and appropriate for the aims of the study. The proposal clearly describes the current approaches and guidelines for risk assessment and chooses to study the effects of doses that usually do not go for phase II testing due to the low predicted environmental concentration (PEC). The progress beyond the-state-of-the-art is very well described and gives a clear indication on how this will be achieved. *However, the genotoxicity testing proposed does not represent the very latest state of the art.* The selection of one class of compounds is a strong point of this proposal as it will provide focus.
- **Quality and efficiency of the implementation and the management: 4.5/5**
- The management plan is very well described. The presented decision-making mechanisms and structures involved and the indicated flow of information should enable a smooth and successful progress of the project. While the list of deliverables is detailed and shows a continuous flow of work and development, *this is not reflected in the simple GANTT-chart.* All members of the consortium are well qualified and have the necessary experience in their respective field of science. The consortium includes a complementary body of institutes and partners. The resources are well justified and adequate. The resources are reasonably distributed between partners and WPs.
- **The potential impact through the development, dissemination and use of project results: 4.5/5**
- The proposal presents a very well written impact section and the consortium is well aware of relevant policy and scientific issues in the area of concern. It explains well how the proposal will contribute to and support EU policies and risk assessment. The dissemination plan is very well described. The final outcome of the project will be available to stakeholders, policy makers, academic and research communities and to the general public .*The targeted stakeholders could have been better identified.*

Pomembno!

Pri pisanju FP7 projektov je te treba razumeti kot POSLOVNE PROJEKTE z raziskovalno vsebino in

NE kot raziskovalne projekte.

Zahvala

- Dr. Ester Heath in sod. (IJS)
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