Cod. ATECO C 10, M 72

AGRIFOOD/ LIFE SCIENCES

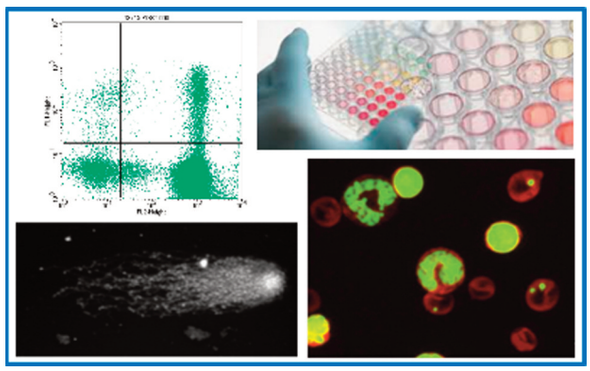
INTEGRATED, HIGH PERFORMANCE APPROACH FOR TOXICOLOGICAL AND FUNCTIONAL ASSESSMENT OF ACTIVE INGREDIENTS AND COMPLEX MIXTURES IN FOOD

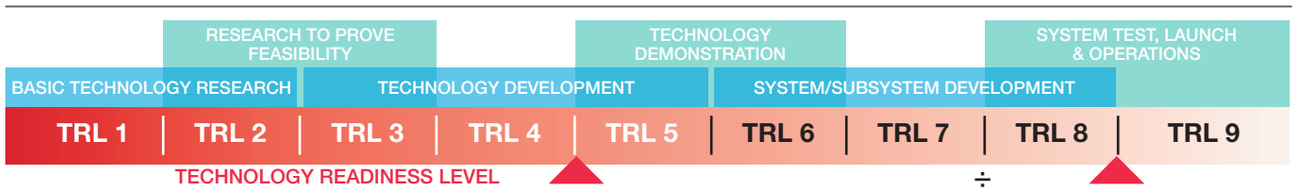
Innovative aspects and related benefits I development and integration of genotoxicity tests and multiparametric analyses of cellular functionality in state-of-the-art in vitro cell systems for a high performance toxicological screening of active ingredients and complex mixtures. Development and implementation of an innovative approach to exploit mouse models for hazard characterization and risk assessment associated with oral exposure to potentially harmful substances: assessment of genotoxic damage at multiple complexity levels, DNA, gene, chromosome; integration of organ-specific toxicity/genotoxicity analyses in validated sub-chronic toxicity testing to improve cost-effectiveness ratio of animal experiments.

Use I consultancy services to companies producing dietary supplements and fitoextracts in order to:

- contribute to safety assessment of plant extracts and vegetal waste derived biomolecules employed as phytotherapeutic medicinal products or nutraceuticals;
- contribute to determine the functional properties (antioxidizing and antimutagenic activities) of vegetable extracts used as dietary supplements.

Activities undertaken and in progress I The ENEA Laboratory of Biosafety and Risk Assessment provides consultancy services to companies for the toxicological assessment of plant extracts. Currently, the Laboratory is taking part in a Project funded by the European Food Safety Authority (EFSA) aiming at the toxicological characterization of food mycotoxins. Within a EU Seventh Framework Programme Project, the Laboratory participates in a study aiming at the toxicological evaluation of nanoparticles used as food additive.





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Cod. ATECO M 72

DEVELOPMENT AND ASSESSMENT OF THE IMMUNO-MODULATING ACTIVITY OF BIOTECH PRODUCTS, SMALL MOLECULES AND OTHER IMMUNO-THERAPEUTICS

Innovative aspects and related benefits | In recent years, the open innovation model, characterized by cooperative interactions between research institutes and pharmaceutical industries, strengthened the development of innovative pharmaceuticals. The immunology area represents one of the most interesting areas for biotech companies. The ENEA has skills, knowledge and experimental models that can foster pharmaceutical companies and other stakeholders in the development of immuno-modulating drugs by using and/or developing innovative assays with procedures shifted from the basic research. ENEA also supports technology transfer to companies where, assays developed by ENEA, can be implemented to adhere to GLP and/or GMP procedures.

Use | Pharmaceutical and biotech companies, including SME, and other stakeholders to:

- assess the immunological effects of biopharmaceuticals and small molecules;
- assess the immuno-modulating properties of natural products;
- assess therapeutic effects in experimental models for immuno-mediated diseases;
- develop innovative assays with procedures translated from basic research.

Activities undertaken and in progress | ENEA provides support to enterprises to evaluate products for immunoregulation and for immunotherapy. Collaborations with pharmaceutical companies and CRO are currently active and/or have been carried out to evaluate biological and biotech products as well as small molecules to modulate immune functions, using *in vitro* and *in vivo* systems and preclinical models for immune-mediated diseases.

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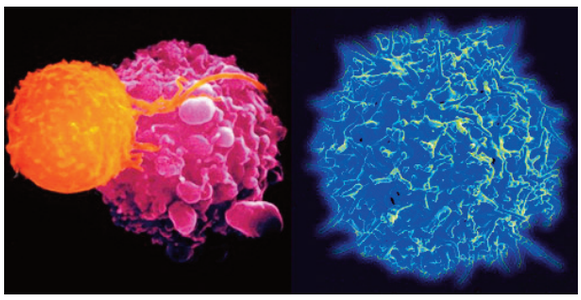

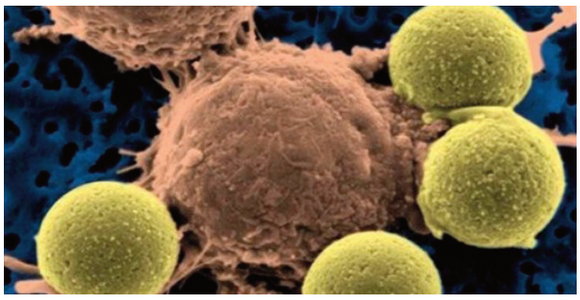

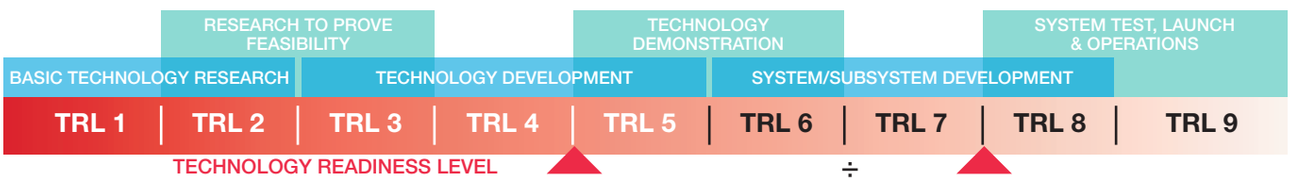

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Cod. ATECO M 72

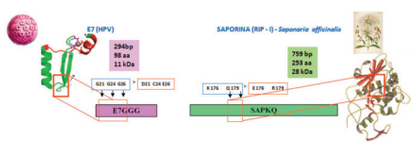
LIFE SCIENCES

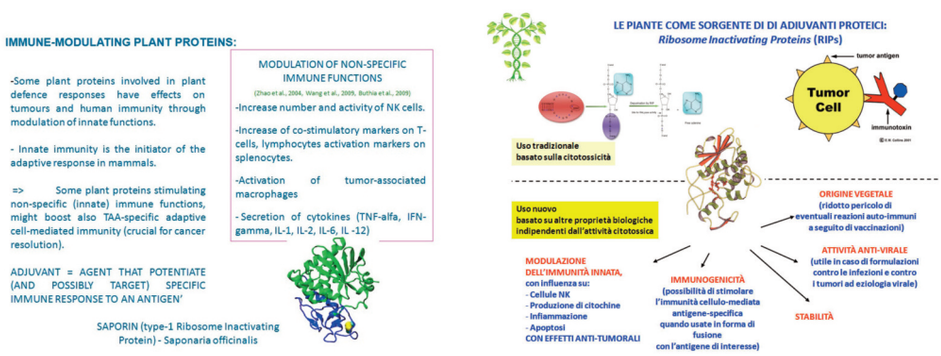
GENETIC CHIMERAS BETWEEN PLANT SEQUENCES AND VIRAL AND/OR TUMOR ANTIGENS: IMMUNOTHERAPY OF CANCERS ASSOCIATED WITH HUMAN PAPILLOMAVIRUS (HPV) INFECTIONS

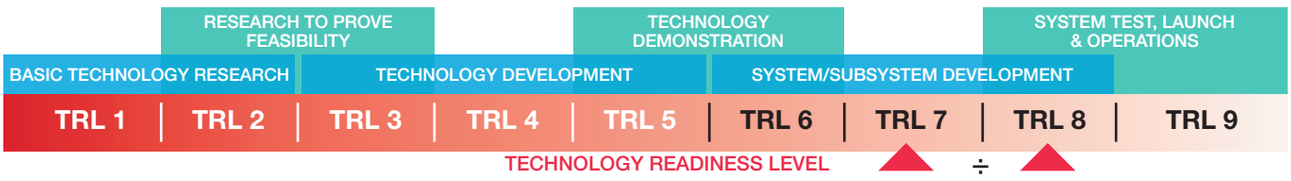
Innovative aspects and related benefits | The Human Papilomavirus (HPV) is the aetiological cause of many different tumours among which cervical, ano-genital and head/neck cancers. No specific therapies exist for the therapy of these tumours able to avoid recurrence of lesions. Targeting the HPV-associated antigens (i.e. the E7 and E6 onco-proteins) offer the possibility to tailor intervention and produce specific anti-HPV tumour therapies.
The technology* is based on a genetic vaccine where the E7 gene is fused to a sequence encoding a variant of the plant protein 'saporin' from *Saponaria officinalis*. The fusion induces an effective presentation of the tumour-associated antigen E7 to the immune system which is responsible for the tumour regression that is observed in two distinct mouse models (one model is an orthotopic model for heah/neck tumours), in particular upon intra-tumoural injection.

Use | Anti-tumour immunotherapy is being exploited for clinical use with surprising results. Being HPV responsible of all the tumours affecting mankind by 5%, and due to the availability of two vaccines with only proven efficacy to prevent infection, it is envisable that the reference market for pharmaceutical companies producing cancer immunotherapeutics might be of hundreds of millions of people. Immunotherapy might be of great importance in reducing the burden of the disease in particular in Developing Countries, where screening and surveillance programs are lacking.
The concept of the technology, that refers to the immunotherapy of HPV-related tumours, is applicable to all cancers which pathogenesis is due to specific tumour-associated antigens.

Activities undertaken and in progress | Combinations with immuno-, radio-, chemo-therapy. Studies aiming to elucidate the cellular and molecular mechanisms of action of the vaccine. Evaluation of the activity of the vaccine in a protein-based version produced in plant expression systems.
*European Patent ENEA, IFO/IRE, Università dell'Aquila, Franconi R., Massa S., Venuti A., Spanò L. 'Vaccines based on genetic chimera of viral and/or tumoral antigens and plant proteins'. EP n. 2456785 Notified in Italy, France, Germany.







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Cod. ATECO M72

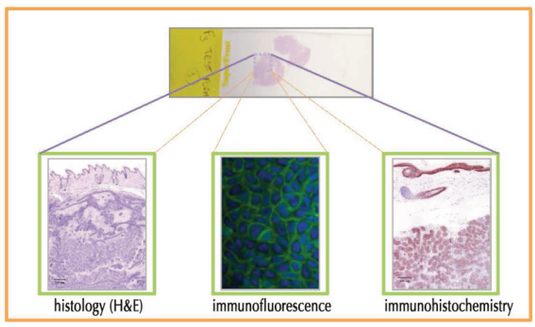
LIFE SCIENCES

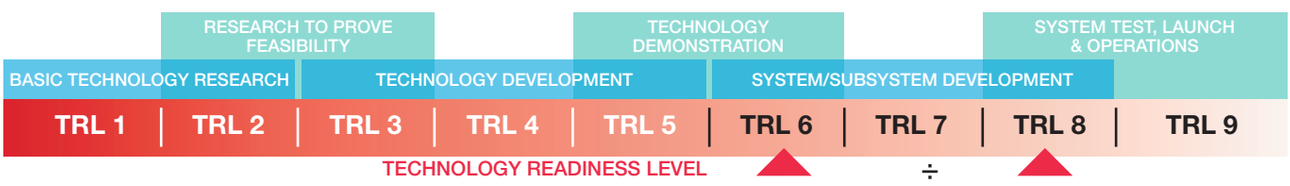
NEW APPROACHES TO OBTAIN EFFECTIVE DRUGS IN TREATMENT OF CANCER AND DIAGNOSIS OF PATHOLOGIES WITH HIGH SOCIAL IMPACT

Innovative aspects and related benefits | Antitumor activity of small synthetic molecules through creation and study of mouse models (*e.g.*, immunosuppressed mice transplanted with engineered and/or tumor cells) for identification of molecular targets for "smart" drugs, suitable to improve the therapeutic index of the disease under study. Assessment of potential risks to humans: acute and subacute toxicity, determination of the maximum tolerated dose.

Use | *In vivo* reproduction of molecular changes (new and/or already known) identified in human cancer by creation and study of mouse models.
Development of new drugs to inhibit or modulate the biological activity induced by genetic alterations detected.
Development of basic knowledge, procedures and technologies for transfer of products, drugs and cutting-edge systems for therapy of pathologies with high social impact to the National Health Service and the industry.

Activities undertaken and in progress | Identifying new therapeutic strategies targeting the stem cells in order to prevent/limit the growth & dissemination of cancer cells. Design and execution of tests aimed at assessing the biological potential of natural molecules and pharmaceutical products in the prevention of side effects of tumor radiotherapy in skin. Development of innovative radiation therapies in combination with other drugs. Established collaborations with the pharmaceutical industry and preclinical testing of cancer drugs in *in vivo* model systems.





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Cod. ATECO M 72

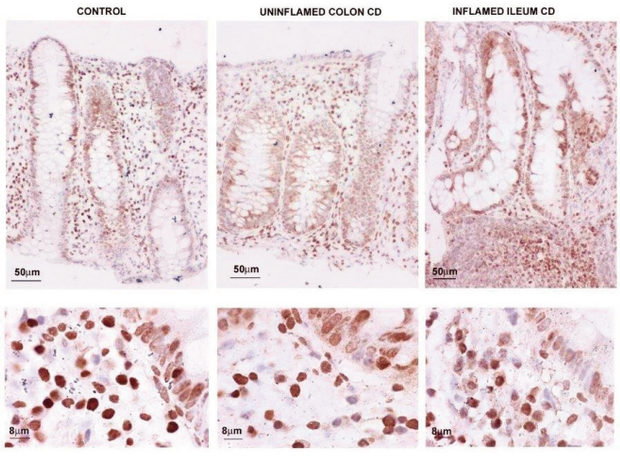
INFLAMMATORY DISEASES OF THE GASTROINTESTINAL TRACT: DEVELOPMENT OF NEW BIOMARKERS AND MEDICAL DEVICES IN A PUBLIC-PRIVATE NETWORK

Innovative aspects and related benefits I Identification and characterization of novel biomarkers of chronic inflammatory disorders of gastrointestinal tract in substitution of highly invasive and expensive diagnostic methods. Identification and characterization of medical devices (molecules having no pharmacological nature) to be used for the treatment of inflammatory intestinal and extra-intestinal diseases in order to reduce the use of highly toxic drugs.

Use I

- development of diagnostic and prognostic kit to commercialize;
- development of medical devices to commercialize in place of or alongside the pharmacological therapies;

Activities undertaken and in progress I Many chronic inflammatory diseases, in particular those involving the gastrointestinal tract, are in great increase in recent years, especially in children. They involve the use of drugs with important side effects. Studies are in progress, in collaboration with the Department of Pediatrics and Neuropsychiatry and the Department of Cellular Biotechnology and Hematology of the University of Rome Sapienza and with national Companies (Italchimici SPA, DMG Srl, Italdevice Srl) aimed at identifying and characterizing molecules with strong anti-inflammatory properties, but without side effects on health of the patient, which may be used in addition to and replacement to conventional therapies. Another field of study concerns the identification of faecal biomarkers of inflammation, to be used for diagnosis and monitoring chronic inflammatory bowel disease, replacing the current highly invasive diagnostic methods. In the past, proteins considered good biomarkers of intestinal inflammation (HMGB1) and molecules with marked anti-inflammatory activity (glycyrrhetinic acid, krill oil) have been identified.



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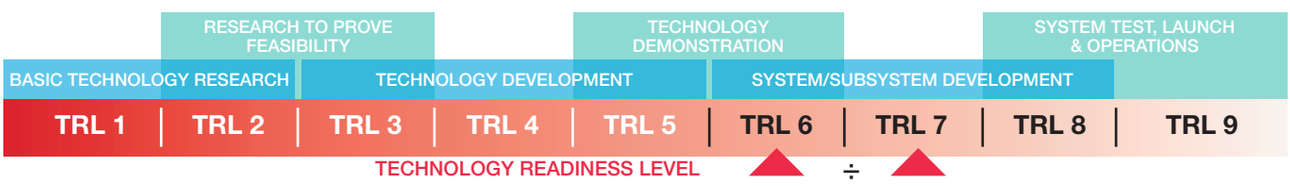

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Cod. ATECO M 72

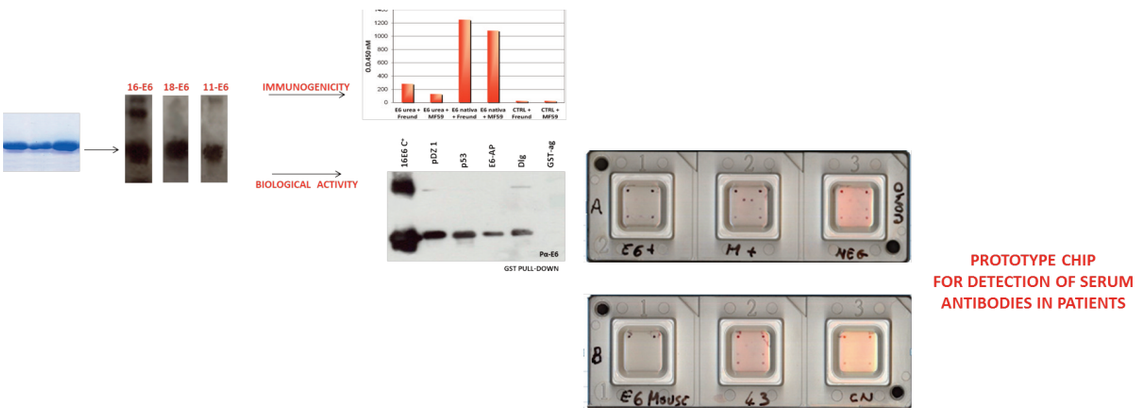
LIFE SCIENCES

RECOMBINANT VIRAL PROTEINS/ONCOPROTEINS FOR THE DEVELOPMENT OF NEW DIAGNOSTIC KITS FOR HUMAN PAPILLOMAVIRUS (HPV)- RELATED CANCERS

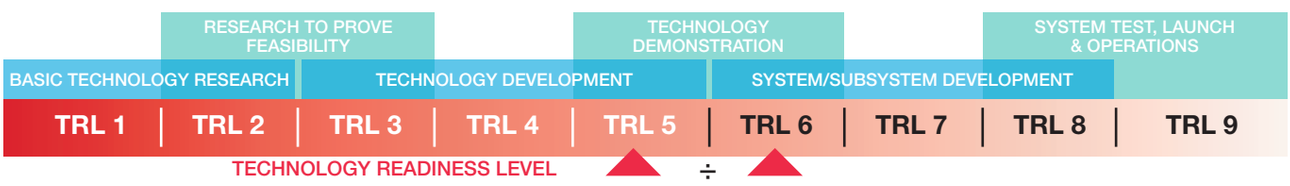
Innovative aspects and related benefits | The high-risk human papillomaviruses (hR-HPVs) are the etiologic agents of cervical cancer and are associated to anal and oropharyngeal cancers. The over-expression of E6 and E7 oncoproteins is a necessary step toward HPV disease progression and cancer: their direct/indirect detection offers new opportunities to develop tests to distinguish self-resolving HPV infections from infections that are progressing to cancer.
Recently, the HPV16 E6 protein has been identified as an early biomarker for HPV-driven cancers, since E6 seropositivity was found to be present more than 10 years before the diagnosis of oropharyngeal cancers.
Our goal is the development of simple/rapid/reliable/portable/low-cost diagnostic kits for early detection of HPV-associated cancer.

Use | The HPV E6 protein is extremely difficult to obtain as soluble when expressed in a recombinant form. A new procedure* was set up to obtain a stable, unmutated E6 protein (from HPV-16, -18, -11) in native conditions. The E6 and E7 oncoproteins, together with other recombinant HPV proteins produced in our lab, can be used for the development of new diagnostic kits as well as to get highly specific antibodies that are still lacking in the market.

Activities undertaken and in progress | We have immobilized the HPV E6 and E7 proteins on a prototype chip for detection of serum antibodies in patients ('Biotecnoform' project, 'Sviluppo di metodi diagnostici per l'identificazione di malattie infettive virali ed emergenti'). In 2012, with a collaborative industrial research project 'CHP-Chip proteomico per HPV: … realizzazione di prototipi di diagnostica avanzata' we won a financial support from FILAS (Finanziaria Laziale di Sviluppo, Prot. N. 1067- CUP F57I12000120009). However, this project was not performed due the withdrawn of one industrial partner bought from an Indian company.
*Italian patent n° 1379103 (30/08/2010): Franconi R., & Illiano E. (2007). 'Proteina E6 di HPV ricombinante, solubile e in forma biologicamente attiva, procedimento per la sua preparazione, usi e vaccini terapeutici che la comprendono.'



PROTOTYPE CHIP FOR DETECTION OF SERUM ANTIBODIES IN PATIENTS



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Cod. ATECO C 26

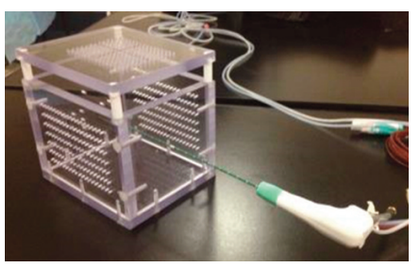
ELECTROMAGNETIC TECHNOLOGIES FOR HEALTH

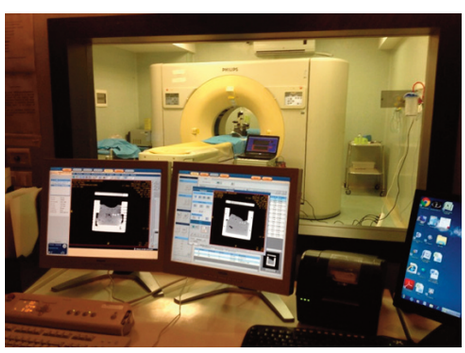
Innovative aspects and related benefits I The increasing development and spread of technologies based on electromagnetic fields leads to interesting perspectives for biomedical applications in the areas of clinical diagnostics and therapies (also known as theranostic). ENEA has multi-skill and high specialisation expertise necessary for the development, optimisation and quality control of new products and protocols: from *in silico* modelling to pre-clinical experimentation. Specifically, ENEA has realised an integrated platform (*in silico* tools and experimental systems) for technological development, predictive analysis and testing of electromagnetic devices for biomedical and theranostic applications.

Use I

- Development and testing of electromagnetic devices for biomedical and theranostic applications;
- Support to definition of clinical protocols and treatment planning;
- *In silico* modelling and predictive analysis;
- Pre-clinical experimentation;
- Non-destructive measurements and testing;
- Quality control.

Activities undertaken and in progress I Support to the development and experimental characterization of a novel interstitial antenna for microwave thermal ablation – currently used in several hospitals all around world – in the framework of an industrial research project funded by FILAS-Regione Lazio.
Collaborations with Italian hospitals and biomedical factories for the development of theranostic devices and protocols for treatment planning.





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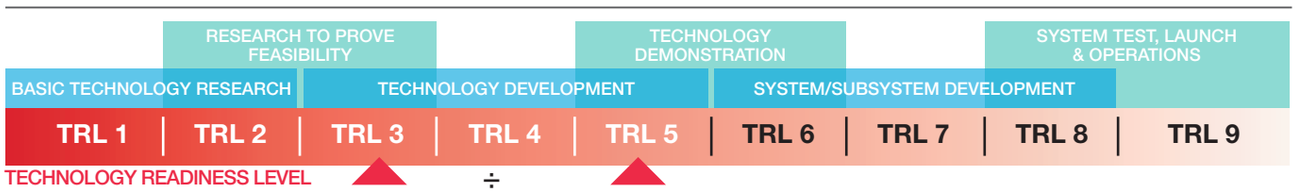

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Cod. ATECO M 71

EXPOSURE ASSESSMENT TO ELECTROMAGNETIC FIELDS BY RADIOMETRIC AND DOSIMETRIC TECHNIQUES

Innovative aspects and related benefits | The increasing development and spread of technologies based on electromagnetic fields (EMFs) leads to some concerns on the impact on occupational and general public exposure to such fields. In this framework, occupational exposure assessment represents an interesting issue of strong industrial impact, as the employer is obliged to perform a risk assessment (D.lgs 81/2008), taking into account the EMF exposure also. Occupational exposure limits were fixed in the Directive 2013/35/EU of the European Parliament and of the Council, which has to be transposed by 1 July 2016 by member states. Risk assessment should provide not only EMFs exposure assessment, but even the definition of correct usage procedures of devices to avoid a negative effect on professional applications of high technological impact. ENEA developed methodologies for the exposure assessment to EMFs in the frequency range 0 Hz – 8 GHz. To this aim, radiometric measurements techniques and, if needed, dosimetric evaluations by means experimental measurements and numerical tools can be employed.

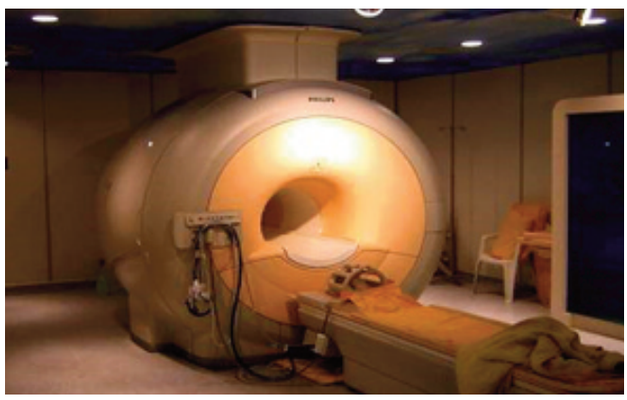
Use |

- Support to companies and public administration for the occupational and/or public exposure assessment to EMFs;
- Non-destructive measurements and testing;
- Quality control.

Activities undertaken and in progress | Set up of procedures for the occupational and/or environmental exposure assessment to EMFs.
Collaborations with Italian hospitals for the occupational exposure assessment in sanitary environments with a particular attention to magnetic resonance imaging.
Advice to public administrations.

(a) (b)

(a) Example of a multiple frequency occupational exposure scenario
(b) simulation model



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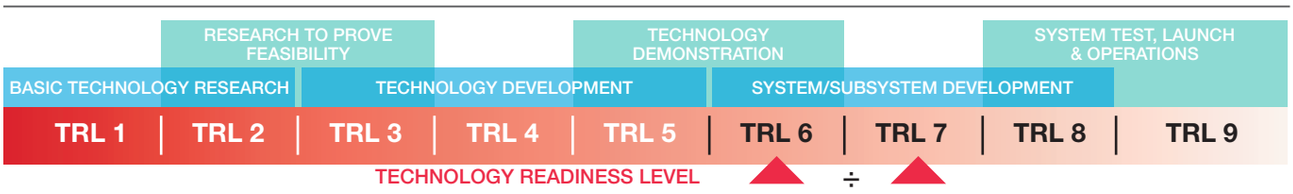

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