European Metrology
Research Programme

EURAMET

Health impact report

A summary of the outputs and impact of the EMRP collaborative research projects in the Health Theme.

The aim of the Health Theme is to develop the measurement methods and techniques to support diagnosis and treatment of serious health conditions. The research is focused on improving disease diagnosis by increasing the accuracy of disease identification and ensuring safe, accurate and effective therapies.

EURAMET e.V. - the European Association of National Metrology Institutes

Measurement matters

Measurement underpins virtually every aspect of our daily lives, helping to ensure quality and safety, supporting technological innovation and keeping our economy competitive.

Supported by the European Commission, EURAMET's **European Metrology Research Programme (EMRP)** brings together National Measurement Institutes in 23 countries to pool scientific and financial resources to address key measurement challenges at a European level.

The programme is designed to ensure that measurement science meets the future needs of industry and wider society. Research is structured around six themes – Energy, Environment, Health and Industry – as well as the measurement needs of emerging technologies and the fundamentals of the SI measurement units that form the basis of Europe's measurement infrastructure.

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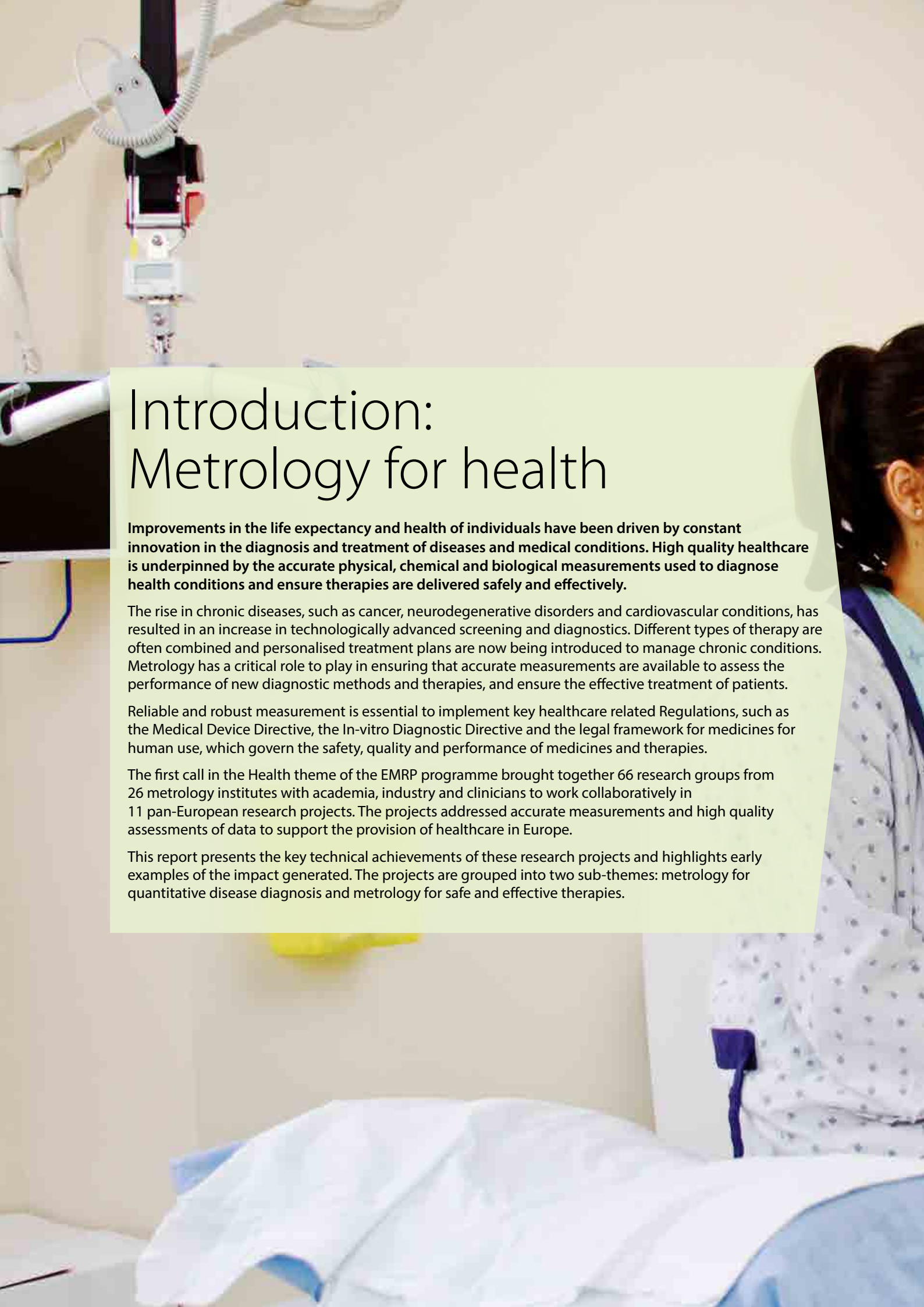


Introduction: Metrology for health

Improvements in the life expectancy and health of individuals have been driven by constant innovation in the diagnosis and treatment of diseases and medical conditions. High quality healthcare is underpinned by the accurate physical, chemical and biological measurements used to diagnose health conditions and ensure therapies are delivered safely and effectively.

The rise in chronic diseases, such as cancer, neurodegenerative disorders and cardiovascular conditions, has resulted in an increase in technologically advanced screening and diagnostics. Different types of therapy are often combined and personalised treatment plans are now being introduced to manage chronic conditions. Metrology has a critical role to play in ensuring that accurate measurements are available to assess the performance of new diagnostic methods and therapies, and ensure the effective treatment of patients.

Reliable and robust measurement is essential to implement key healthcare related Regulations, such as the Medical Device Directive, the In-vitro Diagnostic Directive and the legal framework for medicines for human use, which govern the safety, quality and performance of medicines and therapies.

The first call in the Health theme of the EMRP programme brought together 66 research groups from 26 metrology institutes with academia, industry and clinicians to work collaboratively in 11 pan-European research projects. The projects addressed accurate measurements and high quality assessments of data to support the provision of healthcare in Europe.

This report presents the key technical achievements of these research projects and highlights early examples of the impact generated. The projects are grouped into two sub-themes: metrology for quantitative disease diagnosis and metrology for safe and effective therapies.

Highlights

Multidisciplinary measurement solutions for healthcare

For the first time, the European metrology community is working collectively to conduct the healthcare research needed to improve measurements and analysis. EURAMET established a multidisciplinary **Health Task Group** and a **Health research theme** under EMRP to bring together metrology expertise in physics, chemistry and biology to support improved diagnosis and treatment of medical conditions.

The European Commission and national governments invested €74M in health focused collaborative research, involving research groups in 28 European NMIs and Designated Institutes (DIs), 46 academic groups and 40 businesses and healthcare providers.

Map of participating NMI and DI

Accurate measurements for better health outcomes

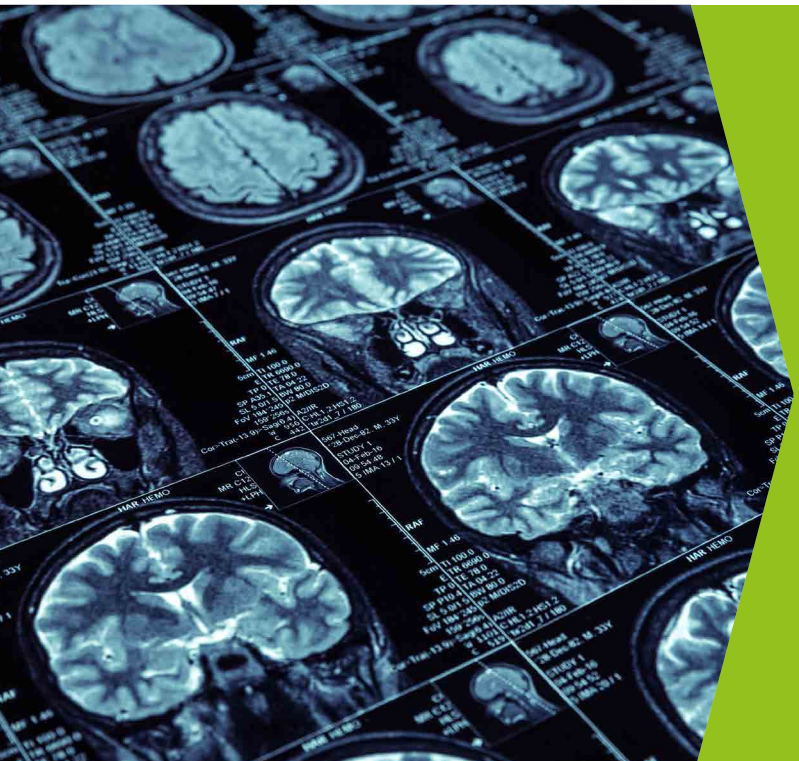
Improved diagnosis of tuberculosis

For the first time, digital PCR (Polymerase Chain Reaction) methods, which amplify bacterial DNA for disease diagnosis are available to traceably quantify infectious agents to the SI. EMRP research validated the method for three systems of infectious agents: tuberculosis (bacterial system), cytomegalovirus (viral DNA system) and influenza (viral RNA system). The results have already been used to validate commercially produced reference materials for tuberculosis, and are supporting improved diagnosis and surveillance of this disease.

Ultrasound treatment for cancer, stroke and bone repair

Over the last decade there has been a dramatic increase in the use of High Intensity Focused Ultrasound (HIFU) for treating cancer, stroke and bone repair.

EMRP research established traceable dosimetry for HIFU via validated measurement techniques, reference standards and modelling methods that quantify exposure and the dose to human tissue. This dosimetry infrastructure will support robust clinical trials and effective HIFU treatment.



Improved MRI imaging, improved patient safety

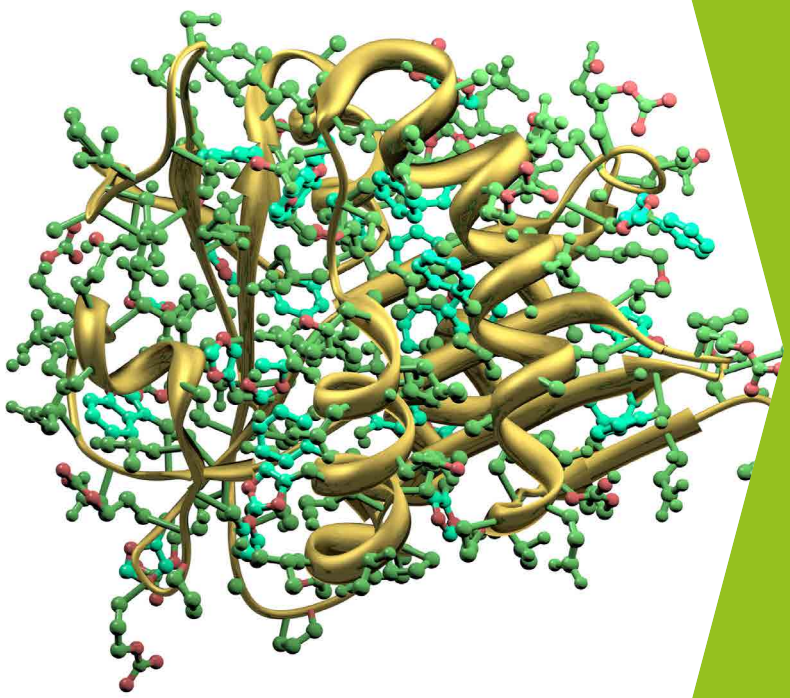
New MRI scanners, using high strength 7 Tesla magnetic fields, provide more detailed images and improve diagnoses. But before these can be used routinely they must comply with international safety standards. EMRP research developed numerical procedures to compute radio-frequency fields throughout the patient's body, and measurement tools to check and validate these simulations. As a result, novel protocols can more accurately calculate safe exposure levels and demonstrate that these scanners are safe to use. Together with contributions to a new international IEC standard for safety verification and certification of new MRI scanners, the research has helped to establish guidelines for safe scanner design, paving the way for their adoption in clinical practice.

Innovation in diagnosis

Extracellular vesicles are cell fragments present in body fluids, such as blood and urine. They have a role in inter-cell communication and also in the spread of diseases such as cancer. This unique role gives them the potential to be used for new non-invasive methods of early diagnosis, drug efficacy studies and drug delivery. EMRP research identified the optimal procedures for collection, preparation and storage of extracellular vesicles, and standardised ways of measuring their size and population. Many international research groups have adopted these procedures and have improved the comparability of results. A simple extracellular vesicle extraction methods for preparing blood samples for disease study is now commercially available helping to promote the use of these important inter-cellular disease communicators in diagnosis.

Simpler, faster diagnosis

In-vitro diagnostics devices (IVDs) have the potential to reduce healthcare costs through rapid diagnosis of diseases at the point of care by detecting and measuring biomarkers. The biochemical interface contains 'probe' molecules which capture specific 'target' biomarkers from the patient sample. EMRP research developed the first reference biomolecular interfaces for IVDs, as well as techniques to accurately characterise the properties of probe and target molecules. These developments enabled IVD manufacturers to develop increasingly accurate and reliable devices for a broad range of health conditions. Chalmers University of Technology in Sweden has demonstrated that a new cell developed for detecting biomarkers can be used to detect the proteins associated with Alzheimer's disease. The technique is being patented and has the potential to be developed into a simple diagnostic tool for a range of diseases including cancer, HIV and hepatitis.



Designing new antibiotics

Diseases are becoming increasingly resistant to antibiotics, limiting treatment options. Developing new antibiotics is costly and time consuming with no guarantee of success or commercial return on the investment. EMRP research established a new design tool that can cost-effectively link the molecular structure of a potential antibiotic to the desired therapeutic effect. This enables the prediction and monitoring of biological processes at the molecular and cellular level for a range of medical applications. The research has, in collaboration with the academic community, already generated a new antibiotic which can be delivered through the skin and has the potential for creating the next-generation of antibiotics.

First EMRP Health projects at a glance

Total investment €74M

Pooling expertise of
26 NMIs and DIs from
17 European countries
plus the NMIs from USA, China, and Russia

22 hospitals

46 academic research groups

40 businesses and healthcare providers

12 published newsletters and press releases

124 presentations at workshops and seminars, reaching an audience of 3,100 people

194
articles in peer-reviewed journals

86
training courses delivered to over
1,000
people

531
presentations at conferences

113
contributions to
52
technical committees and working groups of standards organisations

Supported the development of improved instrumentation with projected sales of
€210M

4
contributions to draft standards and published standards

Advancing quantitative diagnosis

Measurement challenges

Quantitative diagnosis of healthcare conditions using robust scientific techniques and requiring less individual judgement are needed to improve health outcomes. Reliable quantification requires measurement techniques that are traceable to the SI system to ensure accuracy from the lab to the patient.

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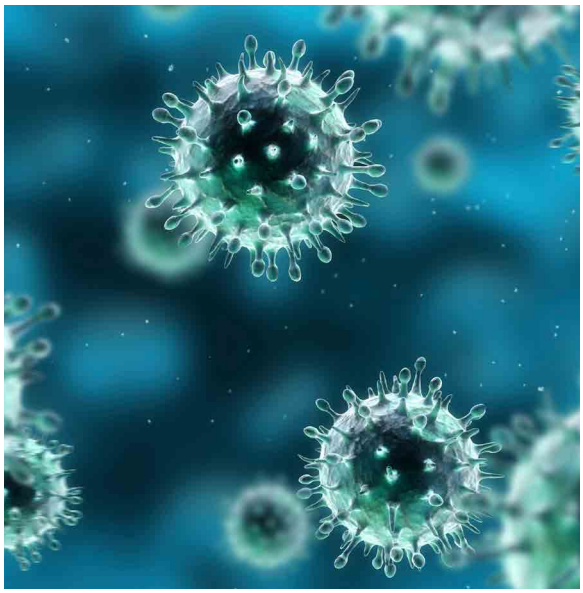
A particular challenge in healthcare is the accuracy of chemical and biological measurement methods. In physical measurements (length, mass, electrical field signals etc.) there is a well-established system of metrology providing traceability to the SI system of units and measurement accuracy, but for chemical and biological measurements this system is less well developed. Such a system will support the accurate diagnosis and monitoring of healthcare conditions. Importantly, measurement traceability to the SI system ensures that results are robust, reliable and the same wherever and whenever they are made. Accurate measurement also has an important part to play in controlling the costs of diagnosing and managing health, and in the assessment and validation of new diagnosis techniques.

EMRP research addresses traceability of chemical and biological measurements across a range of diagnosis methods through improving:

- **Traceability of biological measurements of pathogens**
- **Measurements to identify and quantify key biomarkers for disease**
- **Methods to assess the quality and performance of materials used in diagnostic devices**
- **Measurements and simulations for the safer use of MRI scanners**
- **Measurements to support and protect hearing**

Key technical achievements:

Infectious disease diagnosis



Respiratory tract infections such as pneumonia, influenza and tuberculosis account for almost 50 % of all deaths from infections. Accurate and rapid disease diagnosis is important for public health protection, monitoring transmission in the community and checking for increasing antibiotic resistance.
The infectious disease testing market is growing rapidly, with the in-vitro diagnostics predicted to be worth $75.1 billion by 2020. Molecular diagnostic technologies will be a major driving force behind this growth, but there are issues concerning quality, comparability and traceability of measurements.

Bacteria and viruses present in clinical samples at very low levels make accurate disease detection and measurement challenging. A lack of measurement consistency can lead to over- or under-diagnosis, resulting in costly and inappropriate treatment.
The EMRP project HLT08 Metrology for monitoring infectious diseases, antimicrobial resistance, and harmful micro-organisms successfully developed highly accurate SI traceable methods to support the quantification of bacteria in clinical samples and generated reference materials for use in External Quality Assessment schemes.

The project:

- **Developed quantitative, validated methods for the measurement of viruses and bacteria** with known uncertainties for digital polymerase chain reaction (PCR) methods used for extracting and rapidly amplifying DNA.
- **Developed a reference material and measurement framework using traceable digital PCR approaches** in collaboration with end-user communities. The calibration and quality assurance of current clinical PCR for diagnostic kits and 'in-house' clinical tests for detecting bacterial diseases was improved.
- **Evaluated new and emerging molecular approaches** (next generation sequencing and epidemiology) for the surveillance and monitoring of bacterial infectious disease load and detection of antimicrobial resistant mutations.
- **Evaluated new and emerging diagnostic technologies for the rapid detection of infectious agents** including the measurement challenges associated with rapid, near-patient testing.

The project team worked with the standards, quality assurance and clinical communities to ensure the widest adoption of improved measurement methods and traceability. The project's PCR reference material has enabled a number of clinical labs to confirm their PCR instruments' response and gain SI traceability, and the digital PCR technique is now being included in relevant ISO standards. The provision of a metrology framework helps healthcare providers and the biotechnology/diagnostic industry to demonstrate the reliability and robustness of their assays and ultimately supports improved traceability for disease diagnosis and treatment. The research outputs are particularly important for supporting the proposed new network of Reference Laboratories for Class D (infectious pathogens) In Vitro Diagnostic devices (IVDs) and meeting the requirements for metrological traceability in the new EU IVD regulation.

More information is available at	HLT08 Metrology for monitoring infectious diseases, antimicrobial resistance, and harmful micro-organisms (INFECT-MET) www.euramet.org/project-HLT08
Contact	Carole Foy (LGC) carole.foy@lgcgroup.com

New diagnostic biomarkers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Extracellular vesicles, or EV, are cell fragments present in body fluids, such as blood and urine. They are different in patients and healthy people so can be used as biomarkers for diseases such as cancer, diabetes and cardiovascular disease. Using extracellular vesicles as biomarkers would be less invasive than current techniques and could aid early detection of common diseases and reduce the cost of healthcare. However, detecting EV is difficult because of their small size. Current techniques can only detect around 1–2 % of the total amount present, which is insufficient for disease diagnosis.

The EMRP project HLT02 Metrological characterisation of microvesicles from body fluids as non-invasive diagnostic biomarkers developed reliable sample preparation procedures, a method for isolating EV and comparable and standardised ways of measuring their size and population. These techniques have been disseminated internationally as a route for introducing harmonised clinical practices prior to the creation of documentary standards – a precursor to the introduction of the use of EV as a diagnostic tool.

The project:

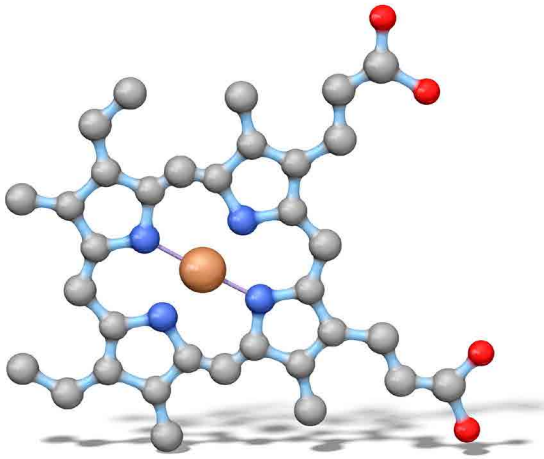
- **Developed a light scattering method capable of measuring the refractive index of small particles** in biological samples, making it possible to derive the true diameter of EV in suspension for the first time.
- **Developed an EV reference standard** suitable for use in the calibration of flow cytometry instruments, routinely used for analysing the EV in biological research samples.
- **Developed reliable, standardised procedures and best practice** for the collection, handling and storage of samples; and pioneered the use of an existing size exclusion chromatography technique (SEC) for the concentration of EV in samples prior to analysis.
- **Demonstrated the feasibility of using atomic-force microscopy** to identify the specific protein present in a single type of EV.
- **Enabled the comparison of EV measurement results** between different instruments and institutions, which will facilitate multi-centre EV trials.

Flow cytometry, a frequently used technique for EV analysis, now benefits from a metrological infrastructure that ensures the analysis results are sufficiently accurate and robust to be used for disease diagnosis. Widespread adoption of the technique in clinical practice requires formal documentary standards to support quality assurance systems in hospitals. Three key international organisations (ISAC, ISEV and ISTH) for EV research have come together to draft a standardised procedure that will incorporate the methods developed in the project for sample preparation and measurement. This is an important first step towards the introduction of an ISO / IEC documentary standard.

More information is available at	HLT02 Metrological characterisation of microvesicles from body fluids as non-invasive diagnostic biomarkers (MetVes) www.euramet.org/project-HLT02
Contact	Rienk Nieuwland (VSL) rnieuwland@vsl.nl

Biomarkers for diagnosis and treatment

A metalloprotein is a protein with a metal ion within its structure, such as haemoglobin (Hb), which contains iron. Metalloproteins are important biomarkers for conditions ranging from anaemia to Down's syndrome. They are also used in cancer treatment but their wider adoption in clinical practice is limited as there are no traceable measurement methods for many metalloproteins.



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The EMRP project HLT05 Metrology for metalloproteins developed methods for quantifying the many different types of metalloprotein using isotope dilution mass spectrometry (IDMS) and isotope dilution Raman spectrometry (IDRS). New methods for separating, identifying and quantifying proteins in patient samples helped to reduce the effects of other interfering molecules during diagnosis of medical conditions. The project developed reference measurement procedures and traceability for methods, which will enable better quantification of metalloproteins in biological samples.

The project:

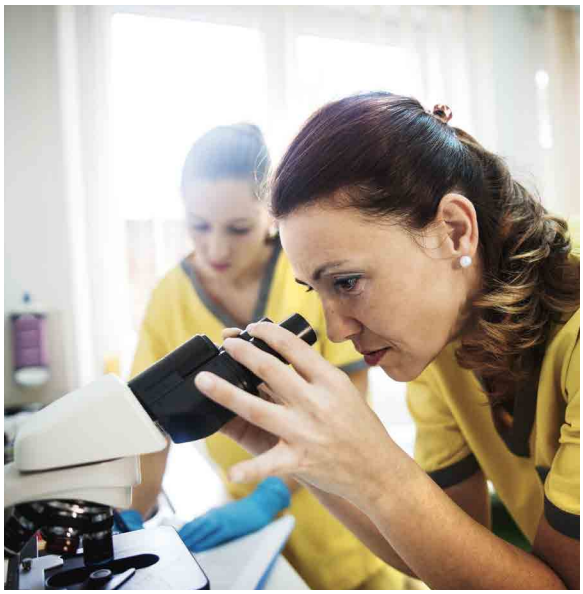
- **Investigated and confirmed the suitability of various chromatography separation methods** for separating metalloproteins from blood samples or serum, prior to analysis by IDMS or IDRS.
- **Prepared and characterised isotopically labelled materials** for purity, metal content and isotopical enrichment for use with IDMS.
- **Developed validated measurement procedures** for an IDMS technique that minimises the effects of any potential species changes and/or losses of metal, important for diagnosing diseases and for cancer treatments.
- **Developed an isotope dilution Raman method for the quantification of total haemoglobin (Hb)** and used this with other candidate reference methods to confirm the performance of existing routine methods (HiCN and AHD) used in accredited clinical laboratories.

The primary reference methods developed in the project provide traceability to measurement standards and establish compliance with EU regulations, including the In-Vitro Diagnostics (IVD) Directive. The AHD method for determining total Hb in blood samples will soon become an internationally established reference technique important in anaemia testing. This will reduce reliance on the HiCN method which uses toxic potassium cyanide. The IDMS procedures developed in the project allow complexes of vanadium in human blood serum to be quantified at the relevant clinical levels needed for the treatment of diabetes. The characterised, isotopically-labelled materials can be used in mass spectrometry to determine the levels of total Hb and haemoglobin A2 in samples of blood, offering the potential to test for blood diseases, such as β-thalassaemia and Sickle cell anaemia.

More information is available at	HLT05 Metrology for metalloproteins (Metallomics) www.euramet.org/project-HLT05
Contact	Claudia Swart (PTB) claudia.swart@ptb.de

Analysising biomolecular surfaces

Diagnosing and managing disease is increasingly reliant upon the detection and measurement of biomarkers on a materials surface. In-vitro diagnostic devices have the potential to reduce healthcare costs through rapid diagnosis at the point of care (at home or in the clinic), by replacing expensive laboratory techniques and equipment. They use 'probe' molecules attached to a surface which capture specific 'target' biomarkers for analysis. Currently only a few materials satisfy the European IVD Directive performance requirements.



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The EMRP project HLT04 Metrology for the characterisation of biomolecular interfaces for diagnostic devices developed new reference materials and biomarker analysis techniques to aid instrument manufacturers and researchers in the development of better IVDs for a broad range of medical conditions.

The project investigated methods important for developing new diagnostic methods and:

- **Developed the first reference nanoparticle interfaces and the first flat reference interface**, based on biotin molecules attached to a gold surface.
- **Developed a method for measuring the number of target molecules** attached to each nanoparticle by combining optical spectroscopy with particle size measurement.
- **Demonstrated the importance of reference surfaces** in establishing the response of target molecules binding to IVD probe molecules.
- **Demonstrated the feasibility of soft X-ray spectroscopy to measure interface properties** and developed a novel measurement device to analyse probe molecule distribution, orientation and structure.
- **Demonstrated the feasibility of using Secondary Ion Mass Spectrometry** (SIMS) to measure both the distribution and structure of probe molecules on flat interfaces, and developed the techniques to detect multiple target molecules using unique labels.
- **Developed an optical waveguide device** capable of ultra-sensitive detection of molecules on surfaces without using labels.

The project delivered the first successful inter-laboratory study of nanoparticle interface chemistry using the reference materials developed. The standardised sample preparation and data analysis procedures developed within the project gave consistent results and will lead to harmonised interface measurements, facilitating the acceptance of interface IVD and encouraging new device development. Two patent applications are being drafted based on the project's research. The first is a cell for soft X-ray fluid interface analysis that enables a 'wet' interface to be analysed by ultra-high vacuum spectroscopy techniques, reducing the need for expensive and time consuming synchrotron hard x-ray experiments and with potential application in infra-red spectroscopy. The second is a novel optical waveguide device incorporated on to a silicon chip, which enables the visualisation of bonds forming and breaking between antibodies / proteins, which is of interest to a major pharmaceutical company.

More information is available at	HLT04 Metrology for the characterisation of biomolecular interfaces for diagnostic devices (BioSurf) www.euramet.org/project-HLT04
Contact	Alice Harling (NPL) alice.harling@npl.co.uk

Next-generation MRI safety

Magnetic Resonance Imaging (MRI) is an indispensable tool in modern medicine with around 23 million patient examinations in the EU each year and an excellent safety record. However, some new advances in MRI scanning have not yet made it into hospitals because of unresolved safety issues for both patients and medical staff.

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The EMRP project HLT06 Metrology for next-generation safety standards and equipment in MRI improved risk assessments for next generation of MRI scanners, which are using 7 Tesla magnetic fields, providing more complete and robust safety data for both patients and medical staff. The project has enabled better image quality, improved diagnoses and shorter scan times; and evaluated safety margins for patients with metal implants.

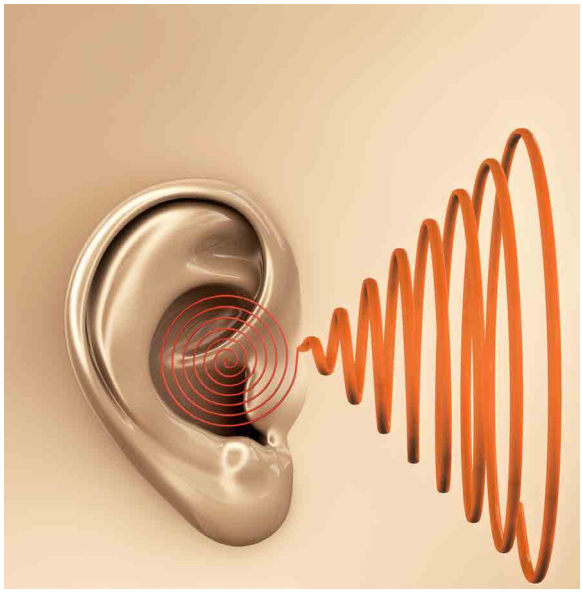
The project:

- **Developed traceable measurement methods for RF electromagnetic fields for determining absorbed RF power generated by 7 Tesla MRI scanners** and used these to validate patient body simulations.
- **Calculated the Specific Absorption Rates (SAR) and temperature increases for different examples**, demonstrating that the temperature increase in the tissue was less than expected due to internal cooling mechanisms and much safer for the patient than expected.
- **Confirmed that there no violations of regulatory limits under normal clinical working conditions** for staff working near an MRI scanner either in the low frequency or radio-frequency (RF) ranges.
- **Established that the photons for targeted radiation therapy are not affected by the magnetic field of an MRI scanner** which allows the two techniques to be used simultaneously.
- **Used simulations and sensors to measure the tissue temperature close to different shaped metal implants** and found that this can pose a risk to patients. Careful risk assessment is required for safe MRI scanning of patients with metal implants.

The project demonstrated that the levels of both low frequency and RF fields near MRI scanners are safe, which will facilitate the routine clinical use of high magnetic field 7 Tesla MRI scanners. Philips, a key European MRI manufacturer is already using the research findings, tools and techniques to assess the performance of a novel measurement method being incorporated into its new scanners. This will help clinicians make more accurate risk assessments for patients with implants, who are not currently able to benefit from MRI scans. Philips, working in partnership with Elektra, has used the projects portable calibration device in an MRI-targeted external radiotherapy machine to enable traceability to the SI.

More information is available at	HLT06 Metrology for next-generation safety standards and equipment in MRI (MRI Safety) www.euramet.org/project-HLT06
Contact	Bernd Ittermann (PTB) bernd.Ittermann@ptb.de

Hearing perception and assessment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Accurate understanding and assessment of human hearing is essential to both diagnosing hearing problems and protecting human health. The EMRP project HLT01 Metrology for a universal ear simulator and the perception of non-audible sound addressed two separate aspects of human hearing. Firstly, improving the accuracy of the hearing assessments of new born babies and young children through the development of new ear simulators specifically matched to their smaller ear sizes. This will enable earlier identification and resolution of hearing problems. Secondly, developing a better understanding of the physiological responses to the potentially hazardous infrasound (low frequency) or ultrasound (high frequency) which lie outside audible limits.

The project:

- **Developed a family of prototype ear simulators** for new born babies and small children including validation of the complete design process and calibration procedures for their use.
- **Demonstrated that Magnetoencephalogphy (MEG) and functional magnetic resonance imaging (fMRI)** can identify the deep areas of the brain that respond to infrasound and airborne ultrasound stimuli and are therefore suitable tools to develop an understanding of these potential hazards.
- **Established the world's first primary airborne sound pressure measurement standards** for up to 160 kHz, enabling ultrasound fields to be reliably quantified for the first time.
- **Developed a laboratory protocol for measuring airborne ultrasound sources** which can potentially be used to evaluate the ultrasonic fields generated by equipment, and ensure its safe operation.
- **Led to the formation of a UK action group** on the Health Effects of Ultrasound in Air (HEFUA) to raise awareness of the health hazard posed by airborne ultrasound.

The prototype ear simulators, specifically designed for calibrating hearing assessments of new born babies and young children, were trialled by instrument testing labs operating in this field and shown to be suitable for practical use. An ISO standard is being developed to define the calibration procedure based on these new simulators. This will ensure the adoption of the procedure by hospitals and support improved hearing assessments.

Industrial processes or technologies can emit infrasound or airborne ultrasound and concerns exist about whether this non-audible sound presents a hazard to hearing or health. The project demonstrated that the brain does respond to stimuli from both infra- and ultra-sound, and that measurements of ultra-sound fields in the vicinity of emission sources are possible. Determining ultra-sound field strengths with greater accuracy forms the basis for further investigations into safe worker exposure limits.

More information is available at	HLT01 Metrology for a universal ear simulator and the perception of non-audible sound (EARS) www.euramet.org/project-HLT01 Details of the follow-on project: Metrology for modern hearing assessment and protecting public health from emerging noise sources (15HLT03 EARS II) www.euramet.org/project-15HLT03
Contact	Christian Koch (PTB) christian.koch@ptb.de

Supporting safe and effective therapies

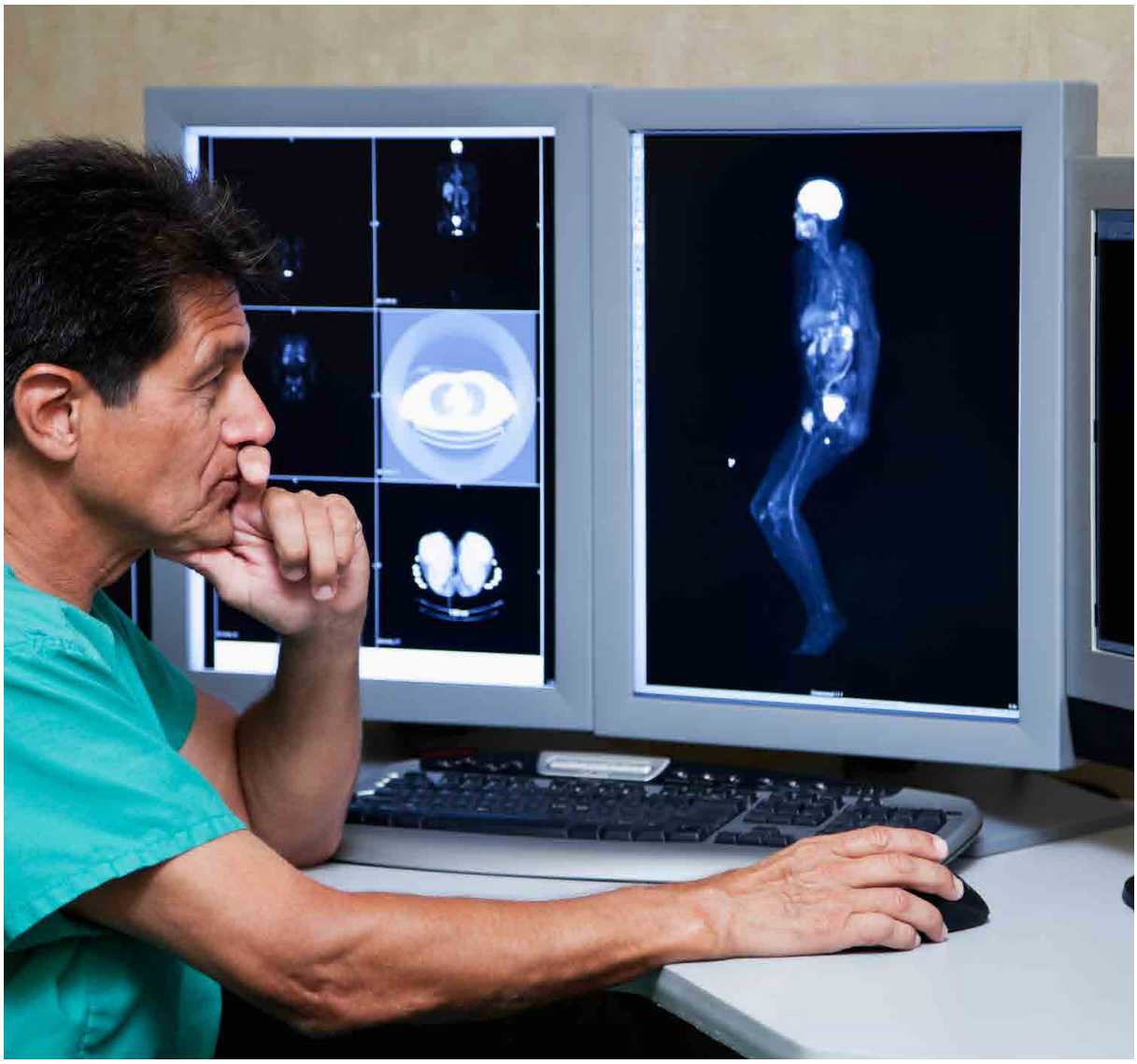
Measurement challenges

A wide range of physical, chemical and biological approaches are used to treat diseases and other health conditions, including drugs or physical therapies such as radiotherapy and ultrasound. All of these have risks as well as benefits, and accurate measurement is essential to ensure that the treatment delivered will cure or manage the condition while minimising any harmful side-effects.

All therapies require practical, accurate measurement methods and tools for use in healthcare environments.

EMRP research has supported research that addresses:

- **Accurate measurements for ultrasound therapy, radiotherapy and molecular radiotherapy**
- **Accurate measurements for drug delivery via intravenous infusion**
- **New measurements for determining the biological origin of disease in order to develop new pharmaceuticals**



Key technical achievements:

Dosimetry for ultrasound therapy

Ultrasound is a long established treatment for kidney stones, soft tissue injuries and also surgical applications including cataract surgery. The last decade has seen a dramatic increase in new uses of ultrasound as a surgical and therapeutic tool, some using very high power levels. An inability to deliver the required ultrasound dose for clinical treatment accurately is leading to potential over, or under, exposure to the patient. This can cause harm or fail to provide the anticipated benefit, and is hampering the introduction of new ultrasound curative or restorative treatments.

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The EMRP project HLT03 Dosimetry for Ultrasound Therapy developed the basis for High Intensity Focused Ultrasound (HIFU) dose determination and the heating effects induced using validated modelling methods and phantoms to replicate the body during treatment.

The project:

- **Developed ultrasound calibration sources and improved test methods** for tissue-mimicking materials used in HIFU body test models.
- **Produced validated body test models and measurement devices** suitable for transferring traceability from the laboratory to the clinical HIFU machine based on an infrared camera that enables monitoring of the temperature distribution on the phantom surface.
- **Developed a complex heat propagation model for HIFU** that calculates HIFU scattering off rib cage surfaces and enables the optimisation of treatment to the targeted organs while minimising heating to the ribs.
- **Investigated the effect of heating rate on tissue over time** and identified that slow heating offered a better treatment than rapid heating.

The enhanced European measurement infrastructure for therapeutic ultrasound resulting from the project is already being used by equipment manufacturers to assess and validate ultrasound instrumentation. The project team has made contributions to draft documentary standards and a published regulation. One standard (IEC60601-2-62) is part of a series of standards within the European Medical Devices Directive and it is also referenced by the US Food and Drugs Administration (FDA) amongst others, meaning that all manufacturers of HIFU equipment must comply with it. Improved equipment assessment and validation against IEC standards is helping manufacturers bring HIFU equipment to market and establishing a more homogenous global regulatory and purchasing environment. This will give healthcare providers a greater range of reliable therapies and the ability to tailor treatment plans.

More information is available at	HLT03 Dosimetry for Ultrasound Therapy (DUTy) www.euramet.org/project-HLT03	
Contact	MSU	msu@npl.co.uk

Dosimetry for complex radiation field therapy

Modern radiotherapy treatments aim to deliver the highest possible dose to the smallest possible area, to limit the damage to healthy tissues. This is achieved using complex radiation fields that deliver intense radioactive doses to areas of only a few millimetres across. However, the methods to measure these doses are not accurate enough, and improvements are needed to bridge the gap between the reference standard and clinical conditions. Lack of standardisation of dose measurements means treatments may not meet the requirements set out by the International Commission on Radiation Units and Measurements (ICRU).

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The EMRP project HLT09 Metrology for radiotherapy using complex radiation fields developed primary standards and good practice guidelines to improve the accuracy of dose measurements in clinical settings. This enables clinicians to demonstrate that the delivered dose matches the planned treatment.

The project:

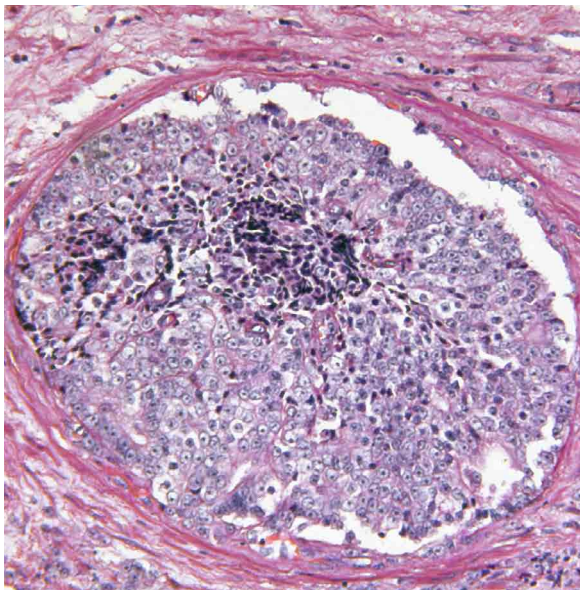
- **Developed and validated new references for 'absorbed dose to water' for medium x-ray energies**, which are important in the delivery of radiotherapy.
- **Determined and validated correction factors for water and graphite calorimeters and ion chambers** used to realise the absorbed dose to water - a surrogate for the body - for new forms of scanning clinical proton and ion beam therapy.
- **Developed a traceable measurement system for the verification of dose and its distribution in complex radiation fields** used in treatment plans.
- **Developed and validated measurement methods using body models to enable the accurate verification of treatment plans** and generated guidelines for use by the European radiotherapy community.

The project team worked with radiotherapy equipment manufacturers, hospitals and regulators to ensure the improved measurement traceability developed in this project is relevant and suitable for adoption by the user community. To address calibration requirements for highly focused complex field x-ray therapy beams, the project developed a new calorimeter to measure the absorbed dose to water needed to meet ICRU requirements. An improved calibration chain has been implemented linking absorbed dose to water standards to clinical instruments and patient treatment for the small radiation therapy fields used during cancer surgery and therapy. The project also demonstrated that commercial diamond detectors (developed in a precursor project) used to validate dose in traditional radiotherapy are suitable for generating a direct traceability chain for the new types of small therapy beams being introduced in to cancer therapy.

More information is available at	HLT09 Metrology for radiotherapy using complex radiation fields (MetroEXT) www.euramet.org/project-HLT09
Contact	Jean Marc Bordy (CEA) jean-marc.bordy@cea.fr

Measurements for molecular radiotherapy

Molecular radiotherapy (MRT) specifically targets cancerous cells through the use of radioactive treatments that attach themselves to tumours in specific parts of the body, such as the liver. Currently, molecular radiotherapy is used in palliative care but it has the potential to become a first line treatment for cancer. Tailoring MRT for individual patients relies on accurately measuring the radioactivity of the drug and determining the therapeutic dose delivered to the tumour.



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The EMRP project HLT11 Metrology for molecular radiotherapy successfully divided the radiation treatment process into a series of steps that could be related to primary standards, and developed methods for verifying the accuracy of each step. The project investigated the use of imaging techniques, to determine the dose delivered to the target tumour site.

The project:

- **Developed the world's first primary standard for molecular radiotherapy** that enables measurement of the absorbed radiation dose to water from a radioactive solution.
- **Developed measurement methods to accurately determine the activity of the radioactive drugs used in MRT**, and extended an existing activity measurement method to highly radioactive MRT radiotherapy levels.
- **Developed methods for calibrating and validating quantitative imaging techniques** using body models with traceability to the SI.
- **Established best practice measurement procedures and traceability to existing absorbed dose standards for a range of radionuclides used in MRT**.
- **Constructed mathematical models that link the radioactivity of the drug, the fraction of it that accumulates in the organ and its biological half-life**. This enabled an accurate determination of the amount of radiation absorbed by the tumour and the therapeutic dose delivered to the tumour.

The project team worked closely with the nuclear medicine community, including academics, clinicians and manufacturers of MRT instrumentation and materials. Project outcomes will be incorporated into a chapter of the MRT dosimetry handbook and protocols within the IAEA Human Health Series, providing a single highly regarded reference document for nuclear medicine physicists and clinicians. Commercial imaging software developers are interested in using the project's step-wise approach for determining the absorbed radiation dose, and offering it as a commercial product for the nuclear medicine community. For example, highly accurate radioactivity measurement of Yttirum-90 microspheres has been achieved as a result of this project. This is the first step towards individualised patient treatment plans.

More information is available at	HLT11 Metrology for molecular radiotherapy(MetroMRT) www.euramet.org/project-HLT11
Contact	Vere Smyth (NPL) vere.smyth@npl.co.uk

Measurements for drug delivery

Infusion is an important way of supplying critical drugs to vulnerable patients, but it is essential to know the amount of the drug delivered. Knowing the flow rate of the drugs, or how fast a quantity of drug is delivered, is vital for safe health care. Currently, drug delivery at low flow rates cannot be set up with sufficient accuracy to meet prescribed treatments. Very low flow delivery rates are difficult to validate and inaccuracy in delivery can be dangerous to vulnerable patients.

The EMRP project HLT07 Metrology for drug delivery developed measurement capabilities for low flow rates, between 1 nanolitre per minute and 100 millilitres per minute, and assessed the performance of commercial flow meters and drug delivery systems. It also made drug delivery more reliable by improving calibration services and producing best practice guides.

The project:

- **Developed primary standards and compared facilities at European NMIs to demonstrate equivalence for low liquid flow rates** suitable for drug delivery for palliative care and anaesthesia.
- **Assessed the accuracy of commercially available flow meters** and found that environmental factors such as temperature, back pressure and viscosity did not significantly affect performance.
- **Assessed and characterised complete infusion drug delivery systems** including the pump, and disposable syringes, tubes and needles; and demonstrated that the flow rates can be seriously affected by using non-compatible components.

Drug delivery by infusion is used to deliver anaesthetics, insulin and vasoactive drugs to millions of patients every year, but dosing errors can occur. This project examined infusion technology in clinical settings to develop a better understanding of the causes of errors and ways to minimise and avoid them.

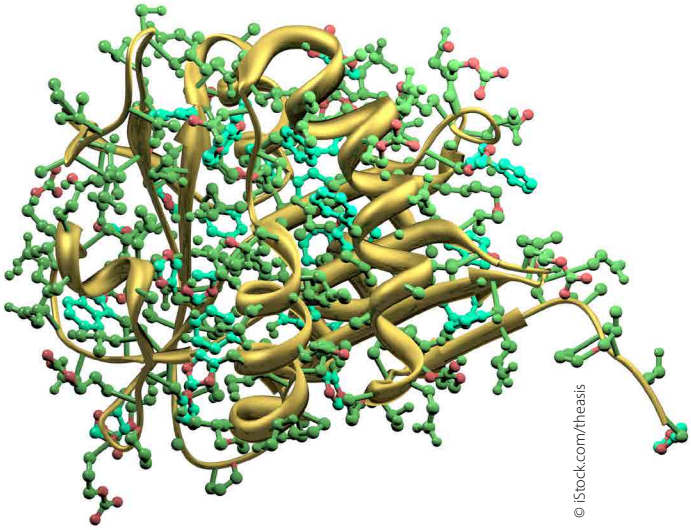
Low and ultra-low flow infusion devices are particularly difficult to accurately calibrate and improved knowledge of calibrating infusion equipment in clinical environments will reduce errors in precision drug delivery. The knowledge and experience developed in the project have been shared with infusion equipment suppliers and the healthcare community, as well as collated into a best practice guide available in an e-learning format. A flow instrumentation manufacturer has achieved accreditation for low flow calibrations so ensuring the robustness of the measurements made by its products, and two hospitals in Europe have also been able to validate the performance of their in-house reference flow meters used to calibrate clinical infusion pumps.

More information is available at	HLT07 Metrology for drug delivery (MeDD) www.euramet.org/project-HLT07	
Contact	Peter Lucas	plucas@vsl.nl

Methods for drug development

Diseases are becoming increasingly resistant to antibiotics, limiting our ability to treat certain patients. Developing new antibiotics is costly and time consuming with no guarantee of success. So despite their significant importance for public health, antibiotics are not seen as a profitable business by many pharmaceutical companies.

The EMRP project HLT10 Metrology for biomolecular origin of disease established new design tool that can cost-effectively link the molecular structure of a potential antibiotic to the desired therapeutic effect. A major computer company supplied main frame computer time to enable the project to perform numerous software iterations, ultimately leading to the generation of a template that can be used to design new drug molecules to a pre-set specification.



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The project:

- **Provided a set of validated chemical structures that indicate a molecule's desired biological effects** enabling purely artificial designs and re-designs of novel, efficient antibiotics using a template.
- **Established methods and materials for the evaluation and screening of biomolecules with potential for use as antibiotics** such as small proteins.
- **Developed experimental and computational methods to validate how antibiotics engage with their targets on a molecular scale**.
- **Developed innovative imaging methods for the visual monitoring and imaging of antibiotic behaviour in real time**.

The project has laid the basis for direct and real-time measurements of biomolecular processes of therapeutic relevance. It is now possible to predict and monitor biological processes at the molecular and cellular level, and therefore develop novel diagnostics, antibiotics and biofilm-resistant materials. The research team worked closely with industry and clinicians to ensure widespread applicability and adoption of the new capabilities. As a result, researchers at the University of Oxford have generated a new antibiotic with potential for delivery through the skin, and financial support for a clinical trial is being sought. A European leader in industrial biotechnology is also investigating potential commercialisation of the molecular design methods developed in the project to efficiently develop new drugs.

More information is available at	HLT10 Metrology for biomolecular origin of disease (BiOrigin) www.euramet.org/project-HLT10	
Contact	André Henrion	andre.henrion@ptb.de

Focus on impact

All EMRP projects engage widely with user communities who can benefit from the research. For the Health theme, this includes a wide range of medical clinicians and researchers and also instrument and therapy machine manufacturers who require effective measurements and innovative methods for improved disease diagnosis and treatments.

The new metrology capabilities and skills developed in the projects will support better disease diagnosis, treatment and therapy delivery over many years. There are already examples of the adoption of the research outputs. An important early adopter is the therapy and imaging sector that makes use of improved metrology capabilities to develop new products for clinical use in the diagnosis and treatment of degenerative diseases and cancer.

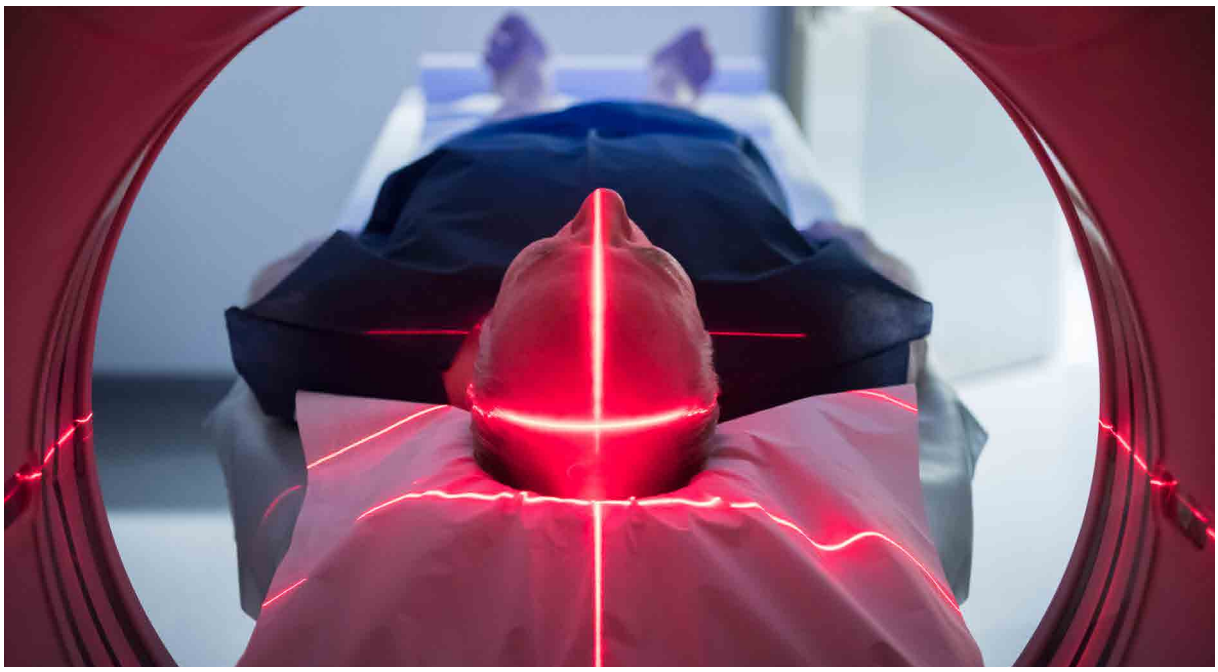
A survey of companies that engaged with the EMRP Health theme projects demonstrated early impacts in the form of innovative products and services with projected sales of €210M.

Extensive engagement

Improving radiotherapy success

Elekta and Philips, two leading companies in radiotherapy and MRI imaging, are jointly developing an innovative combined MRI-linac for use in cancer treatment. A new calibration method developed by the EMRP project Metrology for next-generation safety standards and equipment in MRI is an essential part of the calibration of the new MRI-linac combination. Elekta and Philips are now working towards the introduction of the MRI-linac combination in to clinical practice in 2017. This will support improved treatment of tumour cells, while minimising exposure of surrounding healthy tissue.

MRI-guided radiotherapy, delivered by MRI-linacs, is set to further improve the success of radiotherapy by providing more detailed images of patients during treatment, enabling clinicians to better target tumours. The robust and easy-to-perform calibration method developed by the project provides essential support to the safe, effective introduction of this innovative, high-value medical technology and the benefits it brings to Europe's economy and quality of life for citizens.



MRI standards spur innovation

The magnetic fields of powerful MRI machines can cause medical staff to suffer "motion-induced" effects such as sensations of nausea, vertigo and disturbed vision. This may have serious patient safety implications as new MRI-guided surgical procedures are introduced.

National health authorities and regulators rely on reference documents from International safety standardization organizations when setting legal limits for medical clinician and patient safety. One such reference is the International Commission on Non-Ionizing Radiation Protection (ICNIRP) 2014 publication on specific exposure levels for staff performing tasks near operating MRI machines. These are used in the EU Directive 2013/35/EU which governs medical clinician safety near magnetic fields.

The EMRP project Metrology for next-generation safety standards and equipment in MRI's assessment procedure provides hospitals with a strategy for evaluating the safety of staff actions when planning new surgical procedures. This enables hospitals and staff to have greater confidence when identifying critical situations which may exceed safety limits and permits the early introduction of strategies to reduce debilitating "motion-induced" sensations an important step towards the safe performance of new MRI guided surgical procedures.

High resolution brain scans

Before high resolution 7 Teslar (T) MRI scanners are introduced into clinics for diagnosing diseases like Alzheimer's, Parkinson's and Multiple Sclerosis, they need to demonstrate that they do not generate potentially harmful temperature rises in the body. Research performed in the EMRP project Metrology for next-generation safety standards and equipment in MRI has helped to establish a safe design for this high-end technology, paving the way for its adoption into routine clinical use.

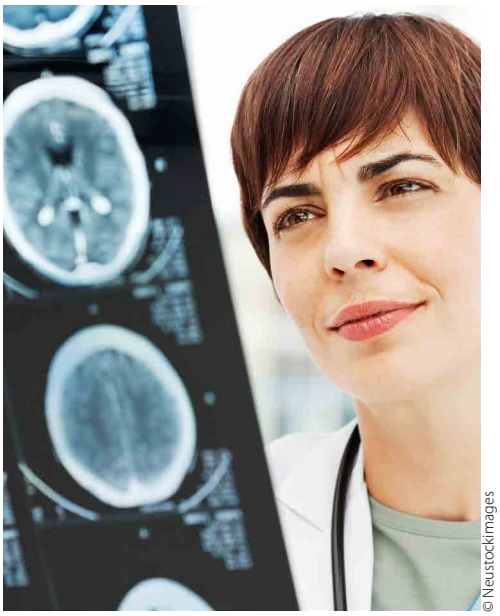
The project developed numerical procedures to compute radio-frequency fields and hence temperature rises throughout the patient's body, and measurement tools to check and validate these simulations. Novel measurement tools and protocols are now available to more accurately calculate exposure levels and to demonstrate 7T MRI scanners are safe to use. Project findings will be adopted in a new international IEC standard, enabling safety verification and certification of 7T MRI scanners.

Demonstrating the safety of these new machines clears the path to clinical adoption, opening up markets for manufacturers of these machines. This will provide hospitals with access to technology allowing the earlier diagnosis, and consequently earlier intervention in degenerative brain diseases such as Alzheimer's, Parkinson's and Multiple Sclerosis.

Safer MRI for metal implant wearers

Philips, a global electronics and medical technology company, has upgraded its MRI scanners so that they can be used safely for imaging patients with metal implants such as hip replacements or wires in pace makers. Using measurement methods and simulations developed by the EMRP Project, Metrology for next-generation safety standards and equipment in MRI, Philips validated a new innovative feature that uses the measurement of the MRI's radiofrequency fields and dynamic magnetic field strength to determine potential tissue heating. Operators can then make adjustments to MRI settings to ensure patient safety. Philips believe that this new innovative method for determining tissue heating caused by MRI scanning in real-time will give the company a market leading capability.

An improved understanding of the heating effects of MRI magnetic fields on metal implants will open up safer MRI scanning to an increased number of patients.



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Targeting tumours accurately

PTW, a market leader in dosimetry equipment for radiation therapy, has commercialised the prototype diamond detector developed during a previous Euramet project. The PTW microDiamond detector has now been tested in photon, electron, proton and carbon ion therapy beams during the EMRP project Metrology for radiotherapy using complex radiation fields. This demonstrated its capability to be used with all types of radiotherapy and not degrade in the radiation as other detectors do.

A set of new correction factors for the microDiamond were established in this EMRP project that opens up the potential for this novel radiation proof instrument to be used to make the highest quality calibration for radiotherapy machines.

Greater accuracy in measuring multi-beam radiotherapy delivery will give clinicians increased confidence in being able to match planned dose to that delivered, opening up further the potential for individually designed patient therapies.

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Accurate ultrasound cancer therapies

High Intensity Focused Ultrasound, HIFU, a promising new cancer treatment which uses multiple extremely focused ultrasound beams to destroy tumours, has taken a major step towards widespread clinical use. The EMRP Project, Dosimetry for Ultrasound Therapy, has provided traceable calibration routes for HIFU beams by validating a new ultrasound calibration instrument, which is being commercialised by ultrasound measurement specialist GAMPT mbH.

GAMPT and PTB developed a hydrophone – an underwater microphone – which was tested using a new calibration and testing facility for HIFU. By calibrating the new hydrophone a traceability chain is created for clinical HIFU instruments, ensuring confidence in measurements of beam strength, and so allowing clinics to accurately calculate individual treatment regime's for patients.

GAMPT has now commercialised the world's first Hydrophone capable of measuring HIFU beams at clinical power providing a vital calibration tool for manufacturers and users of HIFU instruments. Whilst still in its early days, HIFU is already being used to treat prostate cancer and neural brain conditions, and is undergoing trials in many other areas. The HIFU calibration capability, the GAMPT hydrophone and best practice have contributed to IEC standards – providing the infrastructure to make HIFU a reality for cancer treatment.

Accurate dose means effective therapy

MRT can target cancer cells while minimising harm to healthy tissue, however there are no standardised methods to measure the actual dose delivered at the cancer tumour site or to critical normal tissues such as the kidneys or bone marrow. This European project was the first to develop standardised methods for the measurement of absorbed dose in individual patients undergoing MRT. Using the project's methods clinicians will be able to plan the treatments of individual patients and demonstrate that the MRT doses have been delivered safely.

The International Atomic Energy Agency (IAEA) is producing a new Health Series publication on Dosimetry for Radiopharmaceutical Therapy to assist so clinicians can accurately deliver Molecular radiotherapy (MRT). New processes and methodologies developed during the EMRP project Metrology for molecular radiotherapy will be incorporated into this publication which forms a best practice and reference document for the MRT community. This will help to increase the effective use of this cancer treatment.

Targeting cancer

Sirtex, an international company producing novel palliative cancer treatments, was one of the first to benefit from greater calibration accuracy for their yittrium-90 microspheres.

The project Metrology for molecular radiotherapy examined the radioactivity of the microspheres before use and at the tumour site. The project determined all the factors that contribute to calibration of the drug's activity before it is given to a patient, from the importance of a uniform container to understanding the hospital activity meter's response to the yittrium-90.

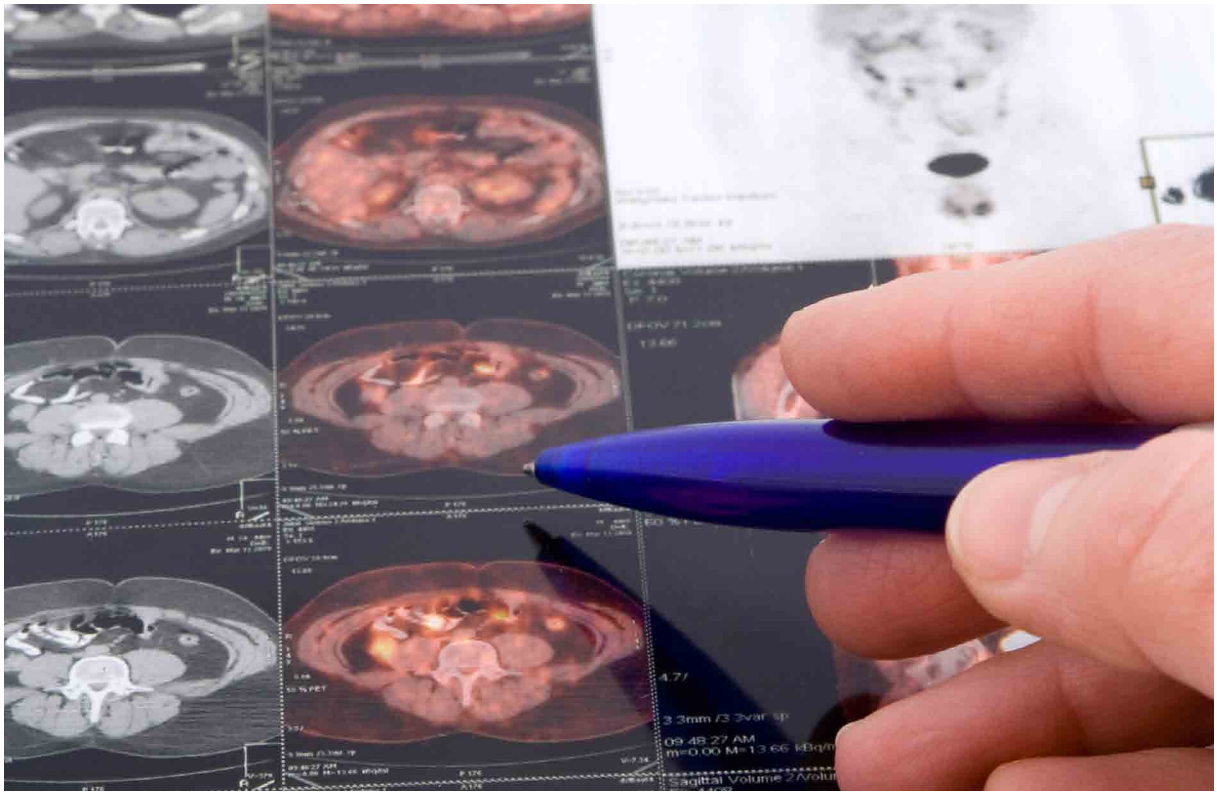
As a result of the project, Sirtex now have a better understanding of what can affect activity measurements and are implementing changes to improve traceability and accuracy of measurement. This, coupled with research linking microsphere activity to quantitative imaging will support the wider adoption of yittrium-90 microspheres as a safe and effective palliative cancer treatment. These novel MRT treatments have future potential for use as front line cancer treatments once a robust link between activity and therapeutic dose, and thus treatment response, is established.

Traceability boost for cancer therapy

A portable counting system based on counting flashes of light generated as radioactive decay occurs in a scintillant, has now been tested for use with the high-activity, high-energy, radioactive drugs used in nuclear medicine clinics, such as yittrium-90. The instrument is self-calibrating, and can be used to directly calibrate activity meters in nuclear medicine clinics.

Test calibrations were performed at the Italian cancer centres based at the Regina Elena National Cancer Institute and Ospedale Pediatrico Bambino Gesù, as part of the EMRP project Metrology for molecular radiotherapy. Sirtex, a company that markets yittrium-90 microsphere technology for molecular radiotherapy (MRT) is keen to have institutions use this direct radioactivity calibration system to ensure traceability and confirm the activity of therapy given to patients.

Use of the new system will lead to greater accuracy in the radioactive measurements which are used in calculations of radiation dose to both cancer tissue and to the surrounding healthy tissue. This enables the generation of very accurate therapy delivery data for specific patients and enables better treatment adjustments to individual patient's needs.



Better infant hearing tests

Acoustic Metrology Ltd (AML) a UKAS accredited calibration laboratory, evaluated a new prototype ear simulator for babies and small children. The prototype was developed specifically for calibrating the small head phones used in infant hearing assessments by the EMRP project Metrology for a universal ear simulator and the perception of non-audible sound. AML demonstrated that current equipment and methods could be easily adapted to make use of the new calibration ear simulator - an important consideration in the ease of adoption of any new calibration device in hospitals.

A new IEC working group has been set up to review the current standard and will be incorporating the use of infant sized ear simulators developed in this project, as well as other improvements to child hearing assessment testing.

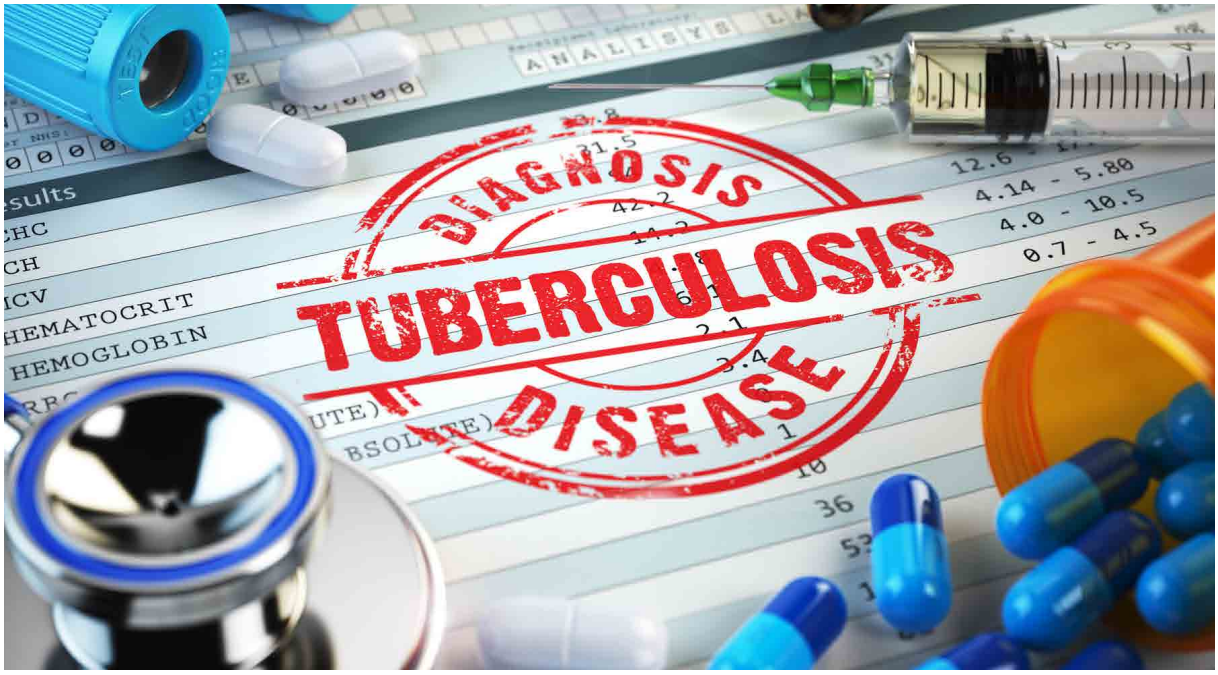
Access to these infant ear simulators, backed by international standards, will lead to greater accuracy in national hearing assessment tests, and new improved instruments for measuring child hearing. This in turn will lead to more accurate diagnoses and early intervention strategies, helping to promote language development in affected infants.

Faster TB diagnosis

Modern pathological laboratories increasingly use a technique called polymerase chain reaction (PCR) to specifically detect bacterial DNA, if present in patient samples, in a matter of hours for analysis and disease diagnosis.

Great Ormond Street Hospital, an important TB pathology laboratory in the UK, participated in a recent performance exercise that confirmed their in-house PCR techniques were very accurate in correctly detecting TB bacteria types. The exercise used a high accuracy digital PCR (dPCR) method, which rapidly amplifies and counts individual bacterial DNA targets, to assign copy number values to reference materials to enable greater measurement traceability than previously possible. Traceabilty, via the dPCR technique was established in the EMRP project Metrology for monitoring infectious diseases, antimicrobial resistance, and harmful micro-organisms. To take the calibration to pathology laboratories the project developed a well characterised TB reference material based on bacterial samples supplied by the UCL centre for Clinical Microbiology based at the Royal Free Hospital.

Pathology laboratories using PCR methods to rapidly amplify TB bacterial DNA can now have confidence in the accurate diagnosis of the type and severity of TB infection in days rather than weeks. This is important as it enables a more rapid and rigorous TB diagnosis and will reduce initial standard TB treatment with long established antibiotic regimens to which TB is becoming increasingly resistant.



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Better flow measurement, safer patients

The Hospital Garcia de Orta in Portugal was one of the first to use a new low flow calibration service for its drug infusion systems. As a result of validated facilities developed in the EMRP project Metrology for Drug Delivery, calibrations can now be performed in Europe at the very low flow rates important for infusion drug delivery. The project also investigated how varying the supplier of disposable infusion line components affects the rate of drug delivery. The team discovered that for reliable infusion line operation it is best to use only consumables from the infusion pump manufacturer. Performing calibrations using the system as it will be assembled for use is essential to ensure effective and safe infusion drug delivery.

The Hospital Garcia de Orta now has greater confidence in its QA system and ensures that only infusion line consumables from a single manufacturer are used in the hospital as a result of using the new calibration system. By calibrating its infusion lines from the pump to the patient using its precisely calibrated 'master' meter it can confirm flow rates in its clinical units. This ensures that vulnerable patients will receive vital drugs at the prescribed infusion.

Higher Precision for Insulin Infusions

CeQur, an international medical technology company, is developing a three-day personal insulin pump for diabetics and used the new low flow calibration facilities developed to test the performance of their insulin pump. The project, Metrology for drug delivery commissioned and validated new European calibration facilities capable of delivering the very slow flow rates used in infusion drug delivery.

With an accurate low flow calibration for the CeQur system's vital insulin pump and knowledge gained from the project's investigations into the effects of system components on drug delivery rates, CeQur have improved their quality system. This ensures that every CeQur insulin system will operate at the very slow flow rates required for a continuous insulin delivery over long term system use.

This is an example of how improved quality control of components in a medical systems are critical to the precise delivery of essential and life-saving medication. This has been made possible by the provision of new European calibration facilities matched to user needs.

Increasing access to anaemia testing

A new diagnostic test for anaemia, which is less toxic and cheaper than the current test, has taken its first steps towards international recognition as a reference method.

Timely treatment of anaemia effectively restores health and can raise national productivity levels by as much as 20 % in developing countries. However, the current standard diagnostic test measures blood haemoglobin levels using potassium cyanide, a toxic compound which is difficult to procure and discard. The EMRP project Metrology for metalloproteins developed a standardised test method and reference materials, which link haemoglobin measurements to the SI units for the first time.

The German standards organisation DIN is incorporating this method into its existing standard on blood sample analysis and has proposed that CEN undertake a new work item on reference methods for determining blood haemoglobin levels. This is an important first step towards the new method's inclusion in an international standard and eventual replacement of the current method, which will reduce the cost of anaemia diagnosis and management.

Counting bio-particles to spot cancer

Extracellular vesicles (microvesicles) are small particles shed into the bloodstream which have potential for use in point-of-care diagnostic devices to detect cancers, diabetes and heart disease.

The International Society on Thrombosis and Haemostasis (ISTH) has demonstrated to the extracellular vesicles research community the importance of harmonised measurement results using a new reference material developed in the EMRP project Metrological characterisation of microvesicles from body fluids as non-invasive diagnostic biomarkers. Samples containing this reference material, were used in an ISTH funded comparison to 33 research labs. Differences in results across the labs highlighted the need for greater standardisation in the flow cytometry measurements commonly used to count extracellular vesicles.

ISTH, with two other influential organisations – the International for Extracellular Vesicles, and the International Society for Advancement of Cytometry – have now formed a new working group to develop guidance on extracellular vesicles measurement practice as a first step towards an IEC standard. This guidance will promote the use of the projects reference materials and changes to instrument operating methods to enable flow cytometers to be better tuned for measuring the small small extracellular vesicle particles present in blood samples.

Spotting inter-cell communications

Izon Science, a manufacturer of bio-particle analysis instruments, has developed and commercialised a simple kit for preparing blood samples for an exciting new area of disease study – extracellular vesicles (EV). The method and kit rely on optimised procedures for collection, preparation using size exclusion chromatography (SEC) and storage of EV developed in the EMRP project Metrological characterisation of microvesicles from body fluids as non-invasive diagnostic biomarkers.

Two hundred and fifty labs worldwide are now using the iZon kits to filter tiny extracellular vesicles (EV) particles or microvesicles from blood using the project's SEC technique. EV are key in inter-cell communications, and play an important role in the spread of cancer and other diseases. They are generating considerable excitement amongst medical researchers who believe they hold promise for new methods of early diagnosis, drug efficacy studies, and drug delivery mechanisms.

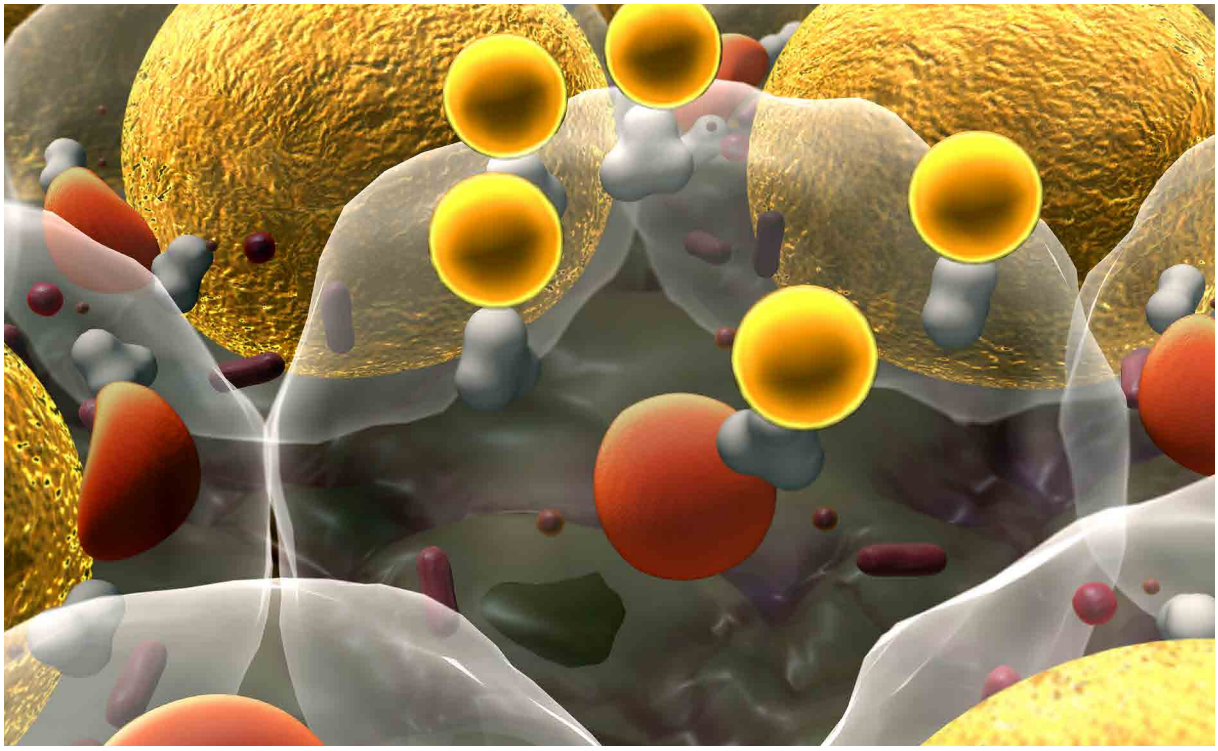
This standardised preparation method will encourage the widespread uptake of EV measurements, which it is hoped will lead to major advances in diagnosis and treatment of a wide range of serious diseases.

Simpler disease diagnostics

Chalmers University of Technology in Sweden, has perfected and demonstrated a new cell for detecting biomarkers – molecules in body fluid samples that are indicators of cancers and other diseases. Within the EMRP project Metrology for the characterisation of biomolecular interfaces for diagnostic devices, the measurement cell was used to successfully detect Alzheimer's proteins. It is now being patented prior to commercialisation.

Using this simple cell and an easy-to-use optical microscope, important molecular information is now readily available where complex sample preparation by trained staff using specialised equipment was previously needed. Early adopters of this innovative measurement cell are medical researchers and a major drug company, investigating the interaction of biological particles and potential uses of proteins in drug delivery mechanisms.

The measurement cell has the potential to be further developed into a simple diagnostic tool for a range of diseases including cancer and infections such as HIV and Hepatitis.



New bio-sample cell for vacuum analysis

A new method for robustly sealing 'wet' biological and organic samples in a measurement cell for vacuum analysis techniques has been rigorously tested. The cell was successfully used for x-ray spectroscopy analyses during measurements of proteins attached to the cells x-ray transparent window in the EMRP Project Metrology for the characterisation of biomolecular interfaces for diagnostic devices.

Until now the most accurate measurements of bio-samples required 'wet' samples to be freeze-dried so they can be placed in a vacuum, a process which changes their chemistry and has potential to introduce errors. This new measurement cell allows samples to be measured without the need for freeze drying, making measurements more meaningful since the original chemical structure is unchanged.

It is expected this will lead to more reliable techniques for spotting early stage diseases and for distinguishing between strains, supporting new drug research and paving the way for the development of new diagnostic methods.

Speeding up drug discovery

A new drug development template developed by the EMRP project Metrology for biomolecular origin of disease has enabled Oxford University and Malvern Cosmeceutics to cost effectively identify new drugs for application through skin using an advanced skin penetration system (Lipodisc®). This research team were one of the first to use the project's template based computer model that can identify potential compounds for use as new antimicrobial drugs.

The EMRP project Metrology for biomolecular origin of disease successfully showed how and where an antibiotic attaches to a microbe's cell membrane using high resolution spectroscopy and used this information to synthesise a single generic computer-based template that enables the prediction of antimicrobial action and resistance.

The Oxford and Malvern Cosmeceutics research team is currently seeking funding for a clinical trial to test their novel skin-based drug-delivery technology as an alternative to drug delivery via the digestive system or the use of injections just under the skin.

Reducing drug development costs is crucial to encouraging increased research into the new drugs urgently needed to fight an ever rising microbial resistance to our current drug armoury. The EMRP project's new template offers an example of how 'big data' computer modelling can assist pharmaceutical research.

Further information

More detailed information on the EMRP Health projects' outputs and the contact details for each project can be found at:

https://www.euramet.org/emrp-health-2011

Case studies for the EMRP Health Theme projects can be found at:

http://www.euramet.org/health

Other projects in the EMPIR Health theme can be found at:

https://www.euramet.org/empir-health-2015

Other EMRP projects can be found at:

https://www.euramet.org/research-innovation/emrp/emrp-calls-and-projects/

Europe's National Measurement Institutes working together

The majority of European countries have a National Metrology Institute (NMI) that ensures national measurement standards are consistent and comparable to international standards. They also investigate new and improved ways to measure, in response to the changing demands.

While traditional metrology stakeholders in manufacturing demand ever-increasing scope and greater accuracy, there is also a greater demand for accurate measurement in areas which support food safety, clinical medicine and environmental quality, as well as emerging areas such as biotechnology and nanotechnology. This requires resources beyond the scope of most national metrology systems and therefore it makes sense for NMIs to significantly increase the level of collaboration with each other. **The European Association of National Metrology Institutes (EURAMET)** is the body that coordinates collaborative activities in Europe.

EURAMET has implemented the European Metrology Research Programme (EMRP), a project programme organised by 23 NMIs and supported by the European Union, with a value of over €400M. The EMRP facilitates the formation of joint research projects between different NMIs and other organisations, including businesses, industry and universities.

EURAMET e.V.
Bundesallee 100
38116 Braunschweig
Germany

Phone: +49 531 592 1960
Fax: +49 531 592 1969
Email: secetariat@euramet.org

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