IN BRIEF

PERSONAL CHOLESTEROL DIAGNOSIS STEP CLOSER

Researchers report progress in the development of a personal cholesterol diagnosis.

Many people take cholesterol-reducing drugs. At the start of any treatment it is often a matter of trial-and-error to determine the right dosage for a patient. Not only that but whereas previously the total cholesterol content was measured, new techniques nowadays have discovered twenty different kinds of cholesterol. However, doctors are confronted with the problem of interpreting this new information, which means that in the clinic little use has been made of these new facts to date.

For this reason researchers from TNO and the universities of Leiden and Amsterdam have developed a mathematical model to help doctors interpret the data coming from these new techniques. It gives the doctor more insight into the cause of poor cholesterol values and allows the doctor to provide patients with personal advice and get the right drug prescribed more quickly for each patient.

The ultimate goal of the project is to give doctors an impression via this model of the liver function and fatty tissue function of lipoproteins (the cholesterol-containing particles in the blood). However, before that stage is reached, the computer model needs further development. It may take another few years before the technique is ready for use in the clinic.

An initial version of this model was published in a recent edition of the *Journal of Lipid Research*.

Info: daan.vanschalkwijk@tno.nl; www.jlr.org/content/vol50/issue12/

TIM OFF TO THE US

The American company Seventh Wave will be using TNO's *in vitro* gastrointestinal model TIM in North America for (bio-)pharmaceutical research.

Seventh Wave is a consultancy and contract research company whose field is comprehensive pre-clinical pharmacokinetic, toxicological and pathological research. At its lab in Chesterfield, Missouri, the company will be using two TIM systems to study the behaviour of orally administered dugs and drug ingredients during their passage through the gastrointestinal system.

The *TNO gastroIntestinal Model*, or TIM, is an accurate simulation of the gastrointestinal tract that enables the 'behaviour' of drugs and formulations to be studied while they are in that part of the human body. Different gastrointestinal conditions can be simulated, for instance for intake of drugs with water or a meal and for conditions related to age, health or disease.

Both TIM systems will be installed during the first quarter of this year. In a joint agreement between TNO and Seventh Wave, both parties will be performing contract research as well as developing new applications for the system.

Info: info-pharma@tno.nl

STUDY OF COMPOSITE SHIPS

TNO is a partner in an international research project into composite as material for frigates.

The aim of the CONVINCE *(COping with Naval Vulnerability through INnovative Composite Engineering)* project of the European Defence Association (EDA) is to develop frigates built of composite, a material composed of different components like fibre-reinforced plastic, resin and foam. Composite is interesting ship designers due to its very light weight, minimal maintenance and possibilities for signature management (flat panels, low heat conduction and the use of 'frequency selective surfaces' which allow the ship to use its radar while remaining 'invisible' to enemy radar). Twenty-eight research institutes and companies from six countries (Sweden, Norway, Netherlands, Great Britain, France and Italy) are cooperating in the project, with the Dutch consortium composed of TNO, Damen-Schelde, Solico and 2mv-composites.

CONVINCE focuses specifically on two issues that an earlier project revealed required further research: fire and explosion resistance. For the first aspect, the 'equivalent' approach will be taken instead of the 'prescribed' method; both approaches are permitted within the International Convention for the Safety of Life at Sea (SOLAS). Sweden will use the blast knowledge developed by TNO for ship vulnerability research.

Most participnting countries will design a composite superstructure on a steel hull but Sweden wants to develop a 110 metre long complete composite frigate. The project has to find a tangible application for the next generation of ships, such as the successor to the M frigate in the Netherlands.

The Dutch consortium will design and test multifunctional panels, or sandwich panels, that have a structural capacity and are blast, shock and fire resistant. To this end TNO's failure models will be expanded and used. Derivatives of such panels could also be used for cruise liners, buses and trains.

Info: andre.vanerkel@tno.nl, cornelis.vanthof@tno.nl

Operational Swedish Visby class of 70 m, made entirely out of composite.

STUDYING TELESCOPES FOR LISA

ESA has asked TNO to determine the thermal expansion coefficient of the LISA telescope.

The European Space Agency, ESA, intends to simultaneously launch three satellites containing the LISA (Laser Interferometer Space Antenna) instrument at the end of the present decade. These telescopes will measure gravitational waves (gravitational phenomena) in space that emanate from massive black holes or other astronomical phenomena in the frequency range of 10-4 to 10-1 Hz. The satellites will be at a distance of five million kilometres from each other The laser interferometer therefore has to operate across five million kilometre, and be able to capture a two-Watt laser beam that still has sufficient photons to reveal an interference pattern – a real technological challenge!

It is vital that the on-board optomechanical systems are extremely accurate and stable otherwise it is not possible to measure very precisely the gravitational waves. In tangible terms, this means that the telescopes' components must not be susceptible to deformation or temperature variations. In other words, they must have a thermal expansion of virtually zero.

TNO has been asked by ESA to determine the thermal expansion coefficient of the telescope systems designed by Astrium GmbH (Germany) and produced by Xperion (Denmark). This will be done in a specially constructed test set-up with the requisite accuracies in one of TNO's laboratories.

Preparations are under way for this two-year project whose budget for the TNO component is 1.2 millions euros.

Info: harm.hogenhuis@tno.nl

IN BRIEF

INVESTING IN MICRODOSING

TNO has invested in a sophisticated tool to allow more efficient testing of drugs.

TNO is the first European organisation to have purchased an Accelerator Mass Spectrometer (AMS) thereby allowing human microdosing studies to be performed for pharmaceutical and biotech companies. This innovative technology can generate human kinetic data on prospective drugs faster than other current methods and, therefore, accelerate the drug development process at lower cost. A key benefit is the drastic reduction this means in the number of animals needed for pre-clinic studies. The AMS enables TNO to offer industry a more comprehensive range of services (microdosing, toxicological and analytical research).

In microdosing volunteers are given a ^{14}C labelled drug whose extreme low dose guarantees safety. Blood that is taken at set intervals is analysed by the AMS. Since the AMS can detect traces of ^{14}C, concentrations of the drug and its metabolites are determined and used to acquire data on the absorption, the metabolic conversions and elimination. This information is essential for companies in deciding on their prospective drugs and allowing them to more quickly direct their development programmes towards prospective drugs that have the most suitable genetic profile in humans.

The major investment in the AMS, supplied by High Voltage Engineering Europe, has been facilitated by a subsidy from the Ministry of Economic Affairs. The AMS is available for research purposes from the beginning of 2011.

Info: wouter.vaes@tno.nl

CLOSER STUDY OF CO_2 TRAFFIC EMISSIONS

A TNO-led consortium will be studying the CO_2 standardisation for passenger cars and delivery vans.

In 2008 the EU decided that from 2015 the CO_2 emissions for new passenger cars may not exceed an average of 130 grams per kilometre; a comparable standard for delivery vans has recently been proposed. The new legislation is crucial if the European climate targets are to be met. The development of new technologies for fuel-efficient vehicles is promoted by the setting of such standards.

The European Commission has assigned TNO the task of leading a consortium to undertake studies over a period of four years to investigate the CO_2 standardisation for passenger cars and delivery vans in respect of:
- the reduction potential and costs of technologies for fuel-efficient vehicles and alternative powertrains and energy carriers;
- the costs, benefits and other consequences of far-reaching CO_2 standardisation for passenger cars and delivery vans;
- a comparison of the policy options to substantiate more stringent standardisation for 2020 and beyond;
- analysing developments in the market that influence CO_2 emissions;
- amendments to test procedures in relation to new technologies.

This four-year project may also deal with engineering and policy issues related to reducing polluting emissions.

The TNO-led consortium is composed of AEA and Ricardo (Great Britain), CE Delft (Netherlands), TML (Belgium), IHS (France) and Ökopol (Germany).

Info: richard.smokers@tno.nl, gerben.passier@tno.nl

INNOVATIVE EQUIPMENT FOR SURGERY

In the context of the IGIT4Health project, TNO is focusing on the development of innovative, diagnostic surgical equipment.

Surgical operations are increasingly being undertaken using minimal invasive methods since these both reduce the costs and boost the quality of life for the patient. In such operations the surgeon needs to have the right information (like good internal images of the patient) at his disposal. In the IGIT4Health project (*IGIT* stands for *Image Guided Intervention and Therapy*) a consortium is working on imaging, diagnostic and therapeutic tools and overall system architecture. The consortium includes a number of major medical-industrial parties (like Philips and Nucletron) and several SMEs and knowledge institutions (like the Netherlands Cancer Institute NKI, UMCs and TNO). The project, which began last autumn, comes under the SenterNovem HTTP (High Tech Top Projects) scheme.

TNO's role within the project is to expand existing MRI, CT and x-ray techniques with additional imagery (intravascular imaging, 'from the inside out'), *in situ* cancer diagnosis using spectroscopy such as developed for the Raman/LIBS instrument for use in space, patient dosimetry in cancer treatment, the development of real-time 3D navigation on the surgeon's endoscope, and contribute to the field of workflow and information management for IGIT instrumentation.

The TNO share of the IGIT4Health project is worth 3.4 million euros and the project runs until December 2010.

Info: nadine.wennersbusch@tno.nl

CONFRONTATION WITH NON-LETHAL WEAPONS

How do people react when confronted with (the threat of) non-lethal weapons?

TNO and the Royal Military Police are collaborating to study behaviour influenced by non-lethal means. The project aims to investigate the effects of non-lethal weapons (or the threat of these weapons) on human behaviour. To this end a behavioural model has been developed and tested in two experiments – in Aruba in October 2009 and a month later at Amsterdam Schiphol international airport, the latter as part of an inter-regional exercise.

The Schiphol scenario was a group of soccer fans wanting to see their team play in the European Cup final but denied entry to the host country. A crowd was confronted four times by a new unit of control forces that responded either harshly (escalating) or as non-violently as possible (de-escalating). In two of the four conditions the crowd contained a small group of ringleaders. The crowd comprised intermediate college students from Rotterdam and Amsterdam (two coaches full) while the control forces were members of an anti-riot squad of the Royal Military Police at Schiphol.

The results of the study will be used to check whether the crowd's behaviour is influenced by the presence of a few aggressive individuals and by the way the control forces respond. An interesting observation was that the crowd containing the few ringleaders formed a single front against the enforcers, even when they responded with full force in riot gear (helmet, long truncheon and shield).

The entire experiment was recorded on film and questionnaires circulated so that the effects observed could be explained as fully as possible.

Info: inge.wetzer@tno.nl

STUDYING THE IMPACT OF PHOTONICS

What is the significance of innovation and research in the field of photonics for European industry?

Photonics (or opto-electronics) concerns the exchange between light (photons) and electronics. It is an important sophisticated technology that can be used in a whole range of applications like health, ICT, lighting, optical systems and energy.

TNO has been assigned the task by the European Commission of analysing the impact that photonics has or may have on European industry. This study, 'Leverage of the Photonics Industry', involves several TNO disciplines. In addition, TNO is collaborating with SAGENTIA (for the quantitative market analysis) and the UK-based Photonics and Plastic Electronics Knowledge Transfer Network (PPE KTN), which enables access to a large-scale European network of experts.

The results of this analysis can be used by the European Commission to ascertain its policy with regard to the Seventh and Eight Framework Programme.

Info: christophe.hoegaerts@tno.nl

As an independent organisation, TNO turns knowledge into practical applications and so contributes to the innovative capacity of business, both at home and abroad, as well as social and international organisations.
TNO has a broad package of products and services, from advising on policy, products and services and performing contract research to the testing and evaluation of products and systems and certification according to international standards. In addition, TNO focuses on future knowledge issues through the TNO Co-financing programme, with co-financing through business that helps establish the direction of this knowledge development. Finally, TNO provides licences to some 700 inventions in its patents portfolio.

The expertise of nearly 4,300 employees has been brought under five core areas:
- TNO Quality of Life
- TNO Defence, Security and Safety
- TNO Science and Industry
- TNO Built Environment and Geosciences
- TNO Information and Communication Technology

The TNO Companies holding company brings innovations to the market via its specially founded subsidiary companies.

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Coordination
TNO Corporate Communications Department
P.O. Box 6050
2600 JA Delft
The Netherlands
phone +31 15 269 49 90
fax +31 15 262 73 35
e-mail redactie@tno.nl

Editors
Jan van den Brink
Renée Heijligers

Text production
CPLS text & copy, Goirle

Art direction
Onnink Grafische Communicatie b.v., Oudenbosch

Lithography and printing
Koninklijke de Swart, Den Haag

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TNO Infodesk
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T +31 15 269 69 69
F +31 15 261 24 03
E infodesk@tno.nl
www.tno.nl/wegwijzer

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