HIGH TECH FOR THE MEDICAL LABORATORY

VDGH

Verband der Diagnostica-Industrie

VDGH

1. We seek dialogue
2. We protect life
3. We identify disease risks
4. We research for people
5. We ensure quality and safety
6. We are partners for physicians
7. We are competitive
8. We are a strong team

We seek dialogue

In the early detection and diagnosis of disease, one branch of industry plays an all-important role. While its products and services may not be known to the general public, they are a crucial factor in modern medicine. We mean the diagnostics sector — an enormously innovative, high-tech industry that constantly drives forward medical science, enabling physicians to provide targeted care for their patients at an early stage of illness.

Blood glucose self-testing

Diabetes is on the rise — dramatically so. In Germany, for instance, the number of people suffering from diabetes has soared by about 50 percent since 1988. Today, there are some eight million diagnosed diabetics in Germany. That's ten percent of the population.

For more than 20 years now, diabetics have been able to measure their own blood sugar levels with easy-to-use blood glucose meters. The test results form the basis for determining the therapeutic dosage for insulin-dependent diabetics. For diabetics who are not insulin-dependent, the readings provide information on the impact of changes in lifestyle habits. More exercise and a healthy diet are considered the therapy of choice in this type of diabetes (type 2). Self-testing of blood sugar levels considerably reduces both the risk of diabetes-related diseases and mortality rates.

ABOUT 150 COMPANIES in Germany develop and manufacture reagents and analysis systems, known as in vitro diagnostics. Community-based doctors and hospital laboratories, and in some cases even patients themselves, can use in vitro diagnostics to examine body fluids or tissues. Driven by advances in molecular biology, miniaturization and automation, ever more powerful diagnostic methods have made great headway in laboratories.

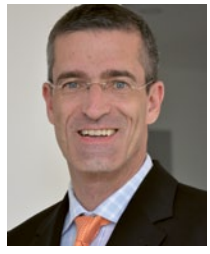
Sensitive detection systems, in particular biomolecular research reagents, chip technologies and detectors for research labs, are also needed in basic research and in applications such as pharmacy, biotechnology, food analysis and forensics. This is a growing market for the hundred or so life science research companies in Germany, which manufacture a large proportion of their products to the specifications of research institutions. These efforts make the latest findings from genomics and proteomics research available to patients and the healthcare system early on.

Laboratory diagnostics have long since become a crucial factor in modern medicine. Clinical laboratory testing plays a decisive role in two thirds of all clinical diagnoses. These tests can now be offered inexpensively in all areas of medicine as a result of industrial production and standardized analyses.

The real potential for efficiency in laboratory diagnostics, however, is not in its lower prices. In vitro diagnostics makes it possible to avoid the need for treatment altogether or to start it early. The earlier a disease is diagnosed, the more successful and inexpensive the therapy as a general rule.

The innovativeness of the diagnostics industry is not only pushing back the frontiers of science but is also raising societal issues. For instance, who is allowed to know the results of a test that predicts a serious disease for a particular person? For which new tests should the health insurer pay, and for which not? These are questions to which only dialogue within society can provide satisfactory answers.

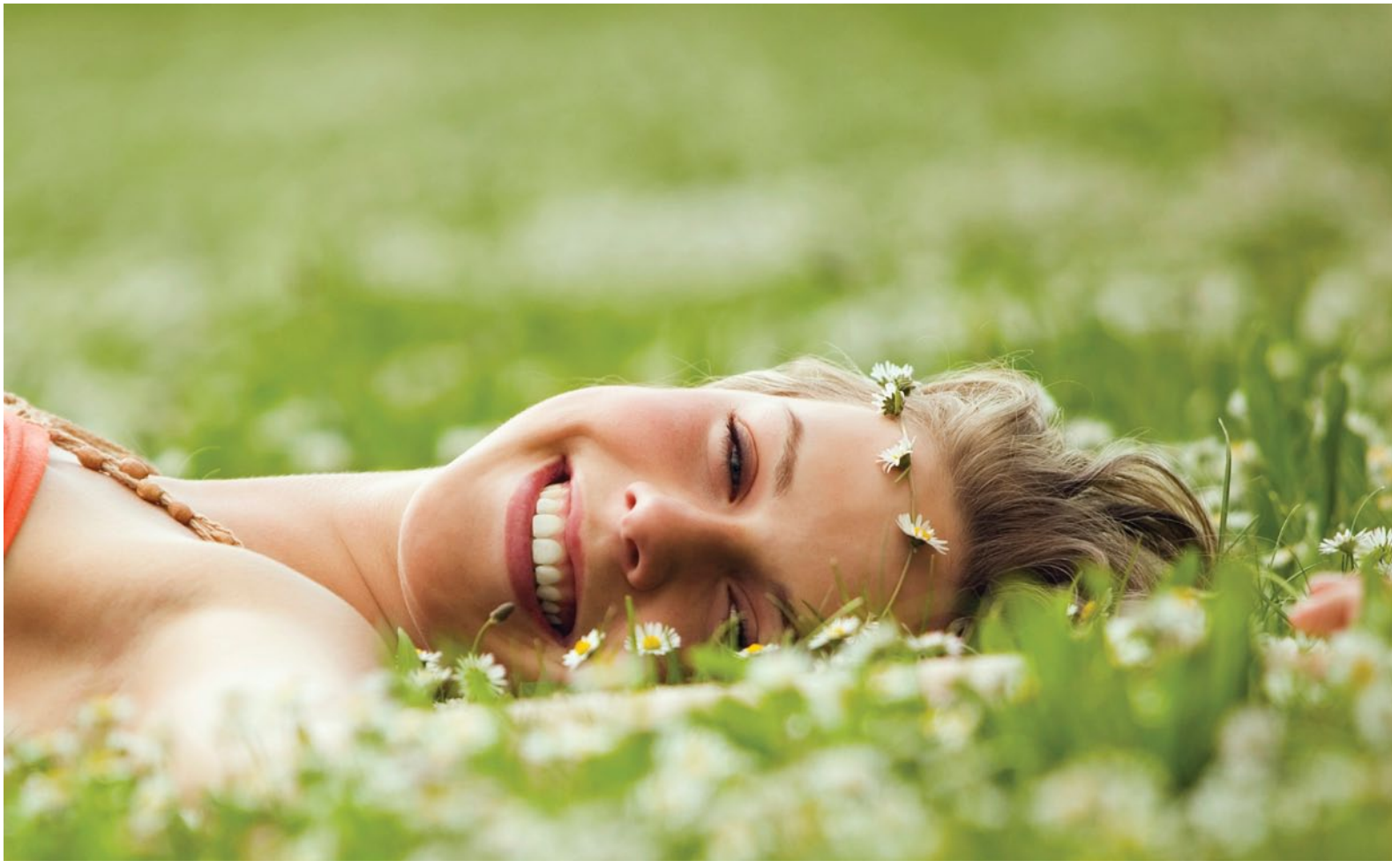
The Diagnostics Industry Association VDGH seeks this dialogue. Pursuing open and frank communication, it strives to ensure that the opportunities arising from laboratory diagnostics are recognized and systematically used — for the benefit of patients, social systems and Germany as a center of scientific and business endeavor.



Dr. Martin Walger
Managing Director
VDGH

We protect life

People benefit throughout their lives from laboratory diagnostics. Before and shortly after birth, laboratory tests reveal the risk of complications and provide evidence of serious metabolic diseases. The information is obtained early enough so that suitable therapy options, dietary measures and changes in lifestyle can largely prevent disease or at the very least reduce the consequences to a tolerable level.



WHAT STARTS AT birth may continue later in life. Laboratory testing reveals evidence of cardiovascular disease, liver or kidney ailments or the threat of cancer at an early stage.

Through targeted monitoring, testing also indicates during therapy whether the treatment the physicians have chosen is having the desired effect. Laboratory testing is used, for instance, to monitor immunosuppression after] transplants, follow the progress of therapy with cardiac glycosides, **check blood glucose levels** (which patients have long been able to do themselves with blood glucose meters), and monitor cancer therapy by detecting tumor markers in the body.

In Germany, about 60,000 people a year die from heart attacks. The presence of a heart attack can be confirmed or ruled out by measuring the activity and concentration of various blood components, so-called serum markers. Using serological techniques — in which blood samples are examined for their immune status by means of antigen-antibody reactions — laboratory clinicians can detect the **AIDS virus** or **hepatitis pathogens.** Contagious diseases can be demonstrated by means of microbiological investigations. Samples of different origins are applied to culture media and incubated at 35°C in order to multiply bacteria and fungi.

A problem of growing proportions is that of **hospital-acquired infections,** which affect around 600,000 patients every year, according to statistics from the German Society for Hospital Hygiene. As many as 30,000 people a year die from such infections. One of the causes is bacteria that have become resistant to particular antibiotics. The faster a hospital can identify such bacteria, the less likely it is that they can spread in the hospital setting. The time needed for screening can now be reduced from a full day to a few hours thanks to modern molecular methods. The bacteria suspected of being resistant to various antibiotics are first cultured to demonstrate resistance. Procalcitonin (PCT) is also a reliable marker for the detection and monitoring of bacterial septicemia. With the help of procalcitonin, hospital physicians can keep a close watch on infections that require antibiotic treatment. Laboratory testing thus contributes to the sparing use of antibiotics and to the prevention of resistance.

Hospital-acquired infections

Antibiotic resistance is becoming a major threat, especially for patients in hospitals. About six percent of all hospital patients in Germany fall ill with so-called nosocomial (hospital-acquired) infections. These are often caused by strains of Staphylococcus aureus that have become resistant to antibiotics (strains known as MRSA). Treating these infections is very difficult. That makes it essential to prevent these strains from spreading, which is only possible through complex hygiene measures that are both time-consuming and costly. Early detection of MRSA carriers is therefore very important because it helps protect other patients against infection.

Identifying staphylococci strains is not difficult under normal circumstances. The pathogen is spread on a culture medium and incubated overnight at 35 °C. By the following day, it will grow in characteristic shapes. The time factor, however, is crucial, and often another day is lost in identifying and determining resistance.

That's why it makes good sense to combine several different test procedures involving both cultures and molecular biological methods. At the same time, however, hospitals have to keep their costs under control. Nowadays, chromogenic media are offered in order to simplify the gold standard, i. e. a culture. They contain special antibiotic combinations that prevent the growth of the accompanying flora, in other words the non-relevant pathogens. Chromogenic media use color differentiation to detect and identify the relevant bacteria. Identification is fast, and the pathogens can often be pinpointed within the first day.

AIDS

AIDS is a chronic, life-threatening disease that is caused by the human immunodeficiency virus (HI virus, HIV). This virus damages or destroys particular cells in a person's immune defenses, so that the body can no longer effectively combat microbes such as bacteria, viruses or fungi and is thus more susceptible to infections that it would otherwise fight off with no difficulty. The acronym AIDS, which stands for acquired immune deficiency syndrome, is the most advanced stage of an HIV infection. There are two ways of detecting an HIV infection: detecting antibodies to the HI virus or detecting the virus itself. When we speak of HIV tests, we usually mean detection of the antibodies. The test will confirm the presence of antibodies which the infected person's immune system has developed against the virus. These antibodies usually develop within three to twelve weeks of infection with the virus.

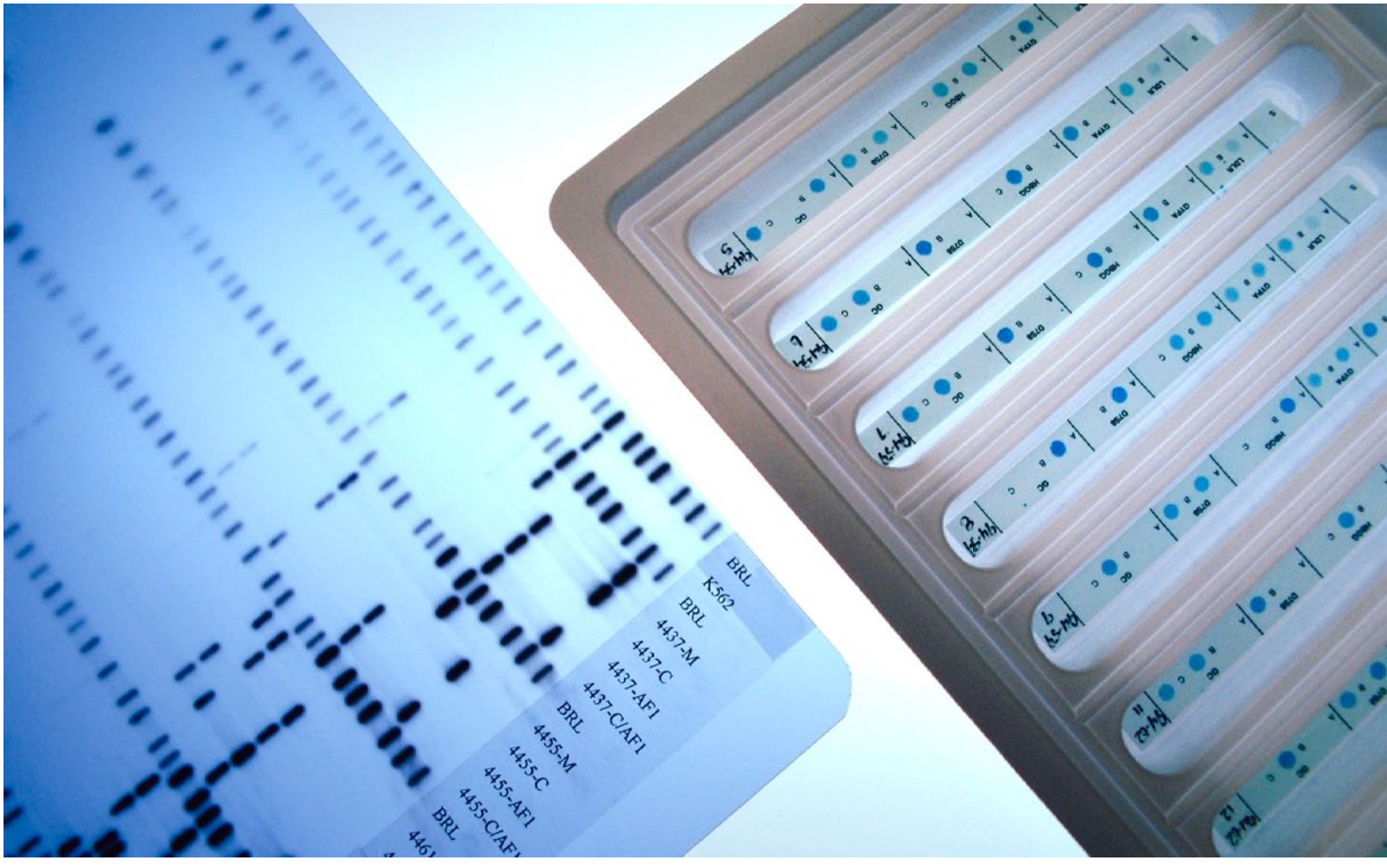
Three months after suspected infection, testing can reveal with a high degree of probability whether HIV antibodies have developed or not (the patient is then either HIV positive or HIV negative). However, an infection is regarded as certain only when the positive result of an initial test (screening test) is confirmed by another, more complex test (confirmatory test). Early detection of an HIV infection is of utmost importance in order to prevent the transmission of the disease but also in order to take full advantage of the treatment options. With the development of new medicines, therapy of HIV and AIDS has made huge strides and substantially improved both the life expectancy and the quality of life of people with HIV and AIDS.

However, there is no cure for HIV infection. In order to monitor the course and success of treatment, molecular methods are used to detect the viral RNA directly and thereby determine the viral count in the blood (the so-called viral load). The aim of HIV therapy is to reduce the viral load below the detection limit.


Display Results
Maintenance
System Setup
Shutdown

We identify disease risks

Diseases cost least if they don't occur in the first place. That's why politicians and health insurers prioritize prevention. In an aging society, prevention is an ideal way of stemming the seemingly unstoppable rise in healthcare costs.



Hemochromatosis

One in ever ten people in Northern Europe suffers from hemochromatosis. This disease of iron storage is hereditary and, if undetected, can in time destroy the liver. In such cases, survival depends on a liver transplant. A blood test costing only a few euros can detect this disease. The best treatment is regular phlebotomy, i.e. removal of blood from the body.

THE DIAGNOSTICS INDUSTRY makes an important contribution to this treatment. For one thing, blood tests to detect genetic defects can identify the risk of disease. For another, innovative laboratory tests make it possible to discover diseases in such an early stage that targeted therapy holds out great promise of success.

For instance: heart failure

The severity of heart failure can be determined even in patients who do not yet have any symptoms by performing tests to detect natriuretic peptides (BNP, NT-proBNP and MR-proANP tests). In addition, the latest biomarkers expand the range of medical options that allow doctors to make a more accurate prognosis and better manage the patient during consultations for heart failure.

For instance: kidney disease

Disorders of renal function do not cause any symptoms at first. They are often only noticed when the damage to the kidneys is no longer reversible. The patient may well even end up on dialysis and has to wait years until a donor kidney becomes available. This worst-case scenario can be prevented thanks to an innovative blood test: deterioration in renal function can be detected at an early stage by measuring the concentration of the protein Cystatin C in the blood.

For instance: cervical cancer

Some subtypes of human papillomavirus (HPV) are known to cause cervical cancer. If detected early, the danger can be eliminated. The high-risk types of the pathogen can be identified by means of the polymerase chain reaction (PCR), in which the viral DNA is first amplified and then examined.

The molecular HPV test illustrates just how inadequately the potential of laboratory diagnostics is exploited for the early detection of disease. Although the value of PCR is undisputed, it does not figure on the list of screening measures approved by Germany's statutory health insurers. The former Federal Association of Health Insurers initiated discussions about inclusion back in 2003, but consultations within the self-administration of the health sector have still not been completed.

If we are to benefit in full from the medical and economic advantages of preventive medicine, politicians and the industry's self-administration body self-administration of the health sector face the challenge of paving the way for diagnostic innovations to be included in standard care provision faster than in the past.

Allergies

Allergies are rising dramatically. Whatever their origin — allergic asthma, food allergies or insect venoms — allergies not only impair quality of life but can also be life-threatening. And they cost society huge sums of money: the direct and indirect costs of allergies in the European Union are put at around 25 billion euros a year. These soaring costs can be contained. The steady worsening of the allergic reaction can often be prevented by means of early diagnosis of the allergens causing the hypersensitivity and by targeted treatment, beginning in childhood.

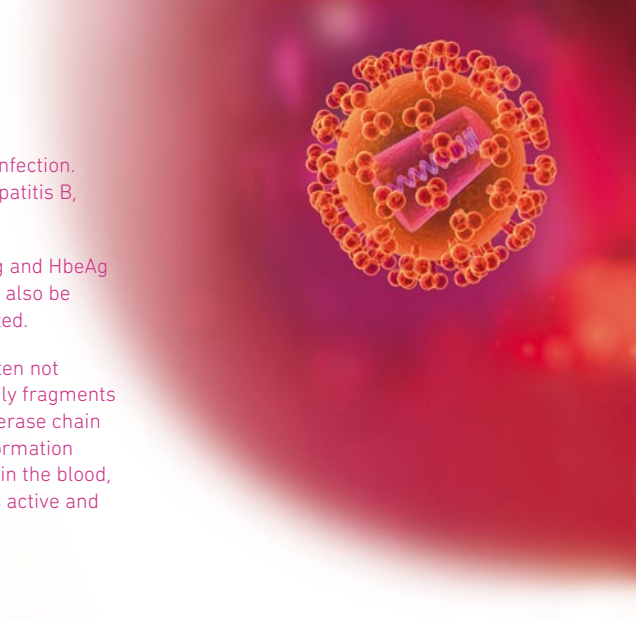
The skin prick test is the classic diagnostic method. The physician pricks the person's skin with a needle containing the potential allergen. If the test produces redness or a rash, this indicates that the patient reacts to the allergen. A more specific diagnosis can be achieved with modern laboratory tests in which antibodies are detected in a blood sample. Immunoglobulin E (total IgE) provides a first clue: the total amount of IgE in the serum (the clear portions of the blood) is often elevated in patients with, for example, hay fever, neurodermatitis or food allergies.

Specific immunoglobulin E (specific IgE) is assayed in the serum in order to find out to which specific substances the body has a hypersensitive reaction. Diagnostics manufacturers now offer more than 700 different allergens, far more than are available for the skin prick test. The allergens are formulated together with a solid or liquid excipient (depending on the manufacturer), which is brought into contact with the serum. Allergen-specific IgE can be determined on the basis of the typical color that the liquid displays at the end of a multi-stage process.

Diagnosis with allergy tests performed in specialized laboratories has another advantage besides the large selection of allergens. Unlike allergy testing on the human body, laboratory tests do not constitute any danger for the patient because the allergens only come into contact with the serum sample and not the patient himself. Even tiny amounts of an allergen can trigger potentially fatal anaphylactic shock in sensitized persons. This is particularly true of bee or wasp stings, of various foodstuffs such as peanuts or shellfish and of a number of antibiotics. Anaphylaxis simply cannot happen when IgE is assayed in the laboratory.

We research for people

The diagnostics industry is research-intensive. 13 percent of its workforce is active in research and development. This puts diagnostics companies, along with pharmaceutical manufacturers, at the top of the list in terms of their research commitment. An enormous financial and intellectual investment is needed to develop a new product.



Hepatitis B

Cirrhosis of the liver and liver cancer are frequent sequelae of a chronic hepatitis B infection. The chronic form develops unnoticed in a small proportion of patients from acute hepatitis B, from which most patients make an uneventful recovery.

Acute hepatitis B can be detected in the blood by identifying the viral antigens HBsAg and HbeAg in the blood. The antibodies (anti-HBs) produced by the body's immune defenses can also be detected in the blood and indicate whether recovery has already begun or is completed.

Chronic hepatitis B, though much rarer, is far more dangerous but the condition is often not recognized for a long time. It is diagnosed by examination of the viral DNA. Even if only fragments of the viral DNA are found in the blood, they can be amplified by means of the polymerase chain reaction, which makes it possible to identify them. A viral load assay will provide information about the patient's condition and the required therapy. If there is only little viral DNA in the blood, the infection is said to be dormant; large amounts of DNA means that the hepatitis is active and chronic.

THE DIAGNOSTICS INDUSTRY studies the findings of basic research for their suitability in diagnostics: great hopes are being placed in nanotechnology and genetic engineering. Nanotechnology in particular is currently achieving scientific breakthroughs that make it possible, for example, to build tiny biosensors with hitherto undreamt-of applications.

The diagnostics firms have high expectations of **genomics, proteomics and metabolomics research.** While genomics research concentrates on the genetic "blueprint", proteomics and metabolomics research focuses on the genetic building blocks — proteins and their substrates. Research is continually coming up with new findings on the molecular processes that take place in individual cells. These processes often provide the explanation why a particular treatment is successful in some patients and not in others. Thanks to research in these fields, we are on the way to personalized medicine, treatment that is "tailored" to the individual patient or to a small group of patients.

For instance: medicines

No drug has the identical effect in all people. Some patients need a higher dosage of their medicine, others a lower one. The reason is that the enzymes that break down the drug in the body have genetic differences so that the medicine is metabolized more quickly or more slowly. The consequences can be dramatic. A dosage that works perfectly well for the vast majority of patients may be too high or too low for certain people. If the enzymes in question are less active, the patient can be expected to have more side effects with a normal dose because the drug's active substance builds up in the blood.

For instance: HER2 biomarkers

Breast cancer patients will respond to therapy with the highly effective cancer drug trastuzumab only if their tumor overexpresses the growth receptor HER2. The drug is ineffective in all other patients. HER2 is therefore a good example of the ideal tumor marker: it is specific for one type of tumor, it is not present in healthy persons, it correlates in terms of quantity with the size of the tumor, and it shrinks under suitable therapy.

Marker- and biochip-based tests that seek genetic factors responsible for causing the disease have become the "gold standard" in biomedical research. Two biomarkers, for instance, are now used routinely in any diagnostic procedure: the HbA1c test, which shows the mean blood glucose level over the preceding three months, and the PSA test, which provides evidence of prostate cancer.

Proteomics research

Proteins are the building blocks of life. Whether as enzymes or hormones, as protective or transport substances, they keep life going; either as key elements of life or as "messengers", they are important starting points for pharmaceutical active ingredients and diagnostics. Scientists estimate the number of different proteins at several million. Which proteins are produced in a cell — a process that is directed by the genes — will have a major impact on cell function and may be decisive for whether a person remains healthy or falls ill.

Researchers are therefore trying to identify proteins that will allow them to distinguish between healthy and diseased cells at an early stage. These are known as marker proteins. A systematic comparison is made of the protein profiles of diseased and healthy cells, and discrepancies are carefully noted.

In most cases, groups of proteins are found to be typical for a disease. In order to identify these protein groups in routine diagnosis, multiparameter test panels are needed that detect a number of suspect proteins at one go.

Protein researchers, engineers and IT specialists are therefore developing special diagnosis chips for use in laboratory diagnostics that recognize different protein markers in one step.

The target proteins are bound and visualized by means of fluorescence labeling, and the results are analyzed on computer systems. The ultimate goal is to identify complex diseases at an earlier stage and to improve prognostic statements about the severity and course of the disease.

We ensure quality and safety

Laboratory diagnostics says it all: the diagnosis of body fluids and tissues is not performed in human beings but outside the body in laboratories employing highly complex analytical systems. The laboratory reagents needed for the tests do not come into contact with the body and therefore cannot cause any damage, unlike incorrectly used medicines.

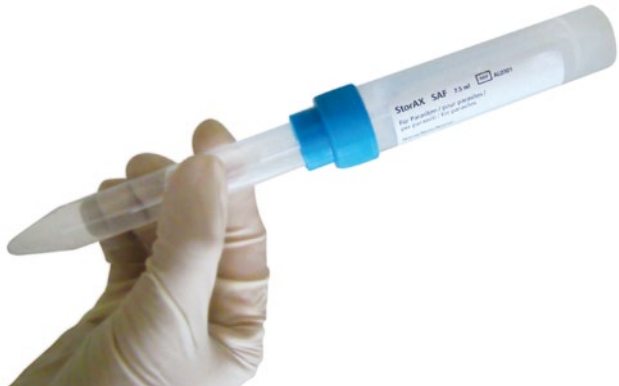
WHAT MAKES LABORATORY reagents safe is that they provide reliable test results. The reagents and analyzers used in a laboratory must guarantee precise (repeatable) and reliable results. Inaccurate test results that lead to incorrect treatment may endanger the patient or cause him to worry about an illness that he does not have.

In 1980, therefore, long before legal standards were defined, the diagnostics industry agreed on compliance with strict quality requirements for the manufacture of its products. Subsequent legislation was based on these industry standards, stipulating requirements for quality and safety that encompass both production and marketing.

For instance, the manufacturers of certain products are obliged to have their quality management system checked at regular intervals by external specialists, so-called "designated bodies". Another stipulation is that at regular intervals production batches have to be tested and approved for release by these designated bodies.

In Germany, these regulations are governed by the Medical Devices Act, which implements the European in vitro diagnostics (IVD) directive. Compliance with legal stipulations is monitored by the relevant authorities at federal state level, together with the two federal authorities, the Federal Institute for Drugs and Medical Devices (BfArM) and the Paul Ehrlich Institute (PEI).

The CE mark, with which diagnostics also have to be labeled, reflects European conformity as well as representing a common safety standard throughout Europe. The CE mark indicates that the product has undergone all the necessary conformity evaluations and complies with the legal requirements. It is not only a safety mark but also a seal of quality.



We are partners for physicians

From the test to diagnosis: many community-based doctors have their own laboratory in which they can perform simple tests. However, such laboratories in the doctor's office are becoming less significant. The vast majority of laboratory tests, especially complicated and rare procedures, are now performed in suitably equipped laboratories and are analyzed and interpreted by specialists for laboratory medicine or for microbiology.

IN THE HOSPITAL too laboratory tests play an important role. Rapid results from such laboratory tests are essential when treating patients in a medical emergency or for assessing the status of a patient, for instance during surgery. Major hospitals therefore have large-scale laboratory departments, which are operated in some cases by external laboratory service providers.

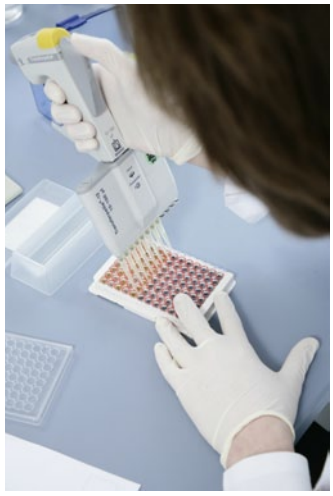
Whether done in the doctor's office or in the hospital, the procedure for handling urine, blood, stool or tissue samples is basically identical. The sample transport tubes are labeled with bar codes and a request form and are transported by courier vehicle, if necessary in climate-controlled containers, to the lab. There the samples are automatically logged in, split up for different tests, and sent to the analyzers by computer.

The analysis results are collated, and a report is sent to the patient's doctor, usually with a medical evaluation by the specialist for laboratory medicine or for microbiology. The lab findings are an important element in the patient history that helps the physician to diagnose the condition and manage the treatment.

The large number of samples that have to be analyzed every day are a great challenge for the laboratories: samples must not be mixed up, and the lab results have to be assigned to the right patient. The labs meet this challenge with the aid of highly sophisticated computer systems.

We are competitive

If you look for laboratory diagnostics in the expenditure statistics of Germany's Statutory Health Insurance (GKV), you'll look in vain. The costs of laboratory tests are included in the bill for the physician's fees. Germany's statutory health insurers spend less than three percent of their claims expenses (including physicians' fees) on laboratory tests, even though, in two thirds of cases, such tests either form the basis of all treatment given in hospital or else confirm the diagnosis. The costs of the necessary reagents and analyzers that are provided by the diagnostics industry account for barely a quarter of this percentage amount.



Competition on price

The diagnostics market is one of the few areas of the healthcare sector in which price has always been the decisive factor for success. The doctor's bill to the health insurer does not distinguish between his services and the costs of reagents. They are both lumped together in the fee. The cheaper a doctor can purchase these materials, the more profitably he can operate. The result is fierce competition between the diagnostics companies.

IN AN INTERNATIONAL comparison the fees paid for medical laboratory services in Germany are among the lowest in the world. In some cases, the very same test in the USA or Australia as well as in many Western European countries costs more than ten times as much.

Competition on price among manufacturers, which is propelled by low fees, has driven the trend to ever more efficient production and greater automation of the analyses. The number of tests performed has doubled in the past twenty years, but the proportion of spending on laboratory medicine in the GKV has fallen in the same period.

The diagnostics companies have mixed feelings about this trend. They have hardly any scope for further price cuts since they have now largely exhausted the efficiency reserves in the areas of production and automation. Some firms are starting to leave Germany as a place to do research and manufacturing. One reason is that access to areas that are relatively profitable, such as new and innovative tests, is all too frequently blocked by the lengthy procedure required for inclusion in the healthcare benefits covered by Statutory Health Insurance. Statutory health insurers and the medical profession are often hesitant to include innovative laboratory diagnostic tests in their services catalogue. The decision whether patients in statutory health insurance schemes will benefit from a new and innovative test rests with an evaluation committee consisting of health insurer representatives and the medical profession. However, the process can take years, which means that a long time may elapse before patients in the statutory health insurance funds in Germany reap any benefit from these new tests. Thus the potential of laboratory diagnostics is being largely underutilized.

We are a strong team

The German Diagnostics Industry Association (VDGH) is the trade association of the manufacturers of in vitro diagnostics and life science research firms active in Germany. Founded in Frankfurt in 1977, the VDGH is now located in Berlin from where it represents the interests of its members. The number of member companies is growing steadily. The Life Science Research section, whose membership has tripled in the past six years, is responsible for much of this growth.

GERMANY'S HEALTH CARE sector is highly regulated. In no other sector are industry's operating conditions determined by so many legal restrictions and decisions of the self-administration partners. The VDGH therefore seeks a fact-based dialogue with representatives of the health insurers, the medical profession and the hospitals, the relevant federal ministries and the German parliament. The association is committed to obtaining research and innovation-friendly conditions, clear rules for the inclusion of new laboratory tests in the statutory health insurers' services catalogue, and suitable remuneration for these tests.

The Life Science Research section at the VDGH focuses on the topics of scientific dialogue, analysis of research funding, electronic customer communications, and cooperation with trade fair organizers. It is driving forward the services for regular market surveys.

The VDGH offers its member companies up-to-date information on political, regulatory and business trends and developments. It organizes seminars and conferences for specific target groups. Additional services include corporate benchmarks, market forecasts, tender surveys, and trade compendiums.

Bundling knowledge

How can prevention ease the burden on social systems? What can we do to prevent the spread of hospital-acquired infections? What are the laws for approval of in vitro diagnostics in Malaysia? What information has to be provided in a request for reimbursement eligibility for a laboratory innovation?

More than 20 advisory committees of the VDGH collect and assess the relevant information. Based on this data, the Association develops joint positions that support the day-to-day work of its member firms and serve as the basis for dialogue with political decision-makers.

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