bio logical

Greiner Bio-One
customer magazine

Issue N° 1 ▪ Autumn 2016

The Dark Side of Sweet ness

Dear readers,

It took us a while to find a suitable name for our new publication, but we reached a decision in the end. '**bio**logical' (the name) will do so much more than just tie in with our company's name. We have had a long time to build up extensive subject area knowledge, with over 50 years of experience as your partner in the field of biology and medicine. From now on, we would like to share this knowledge with you in our customer magazine.

biological will be published biannually and provide you with the latest findings on current topics and information about relevant innovative product developments – content designed specifically to appeal to you as a medical professional, laboratory researcher or academic. It was also important to include tips on how to get the best out of our products in the magazine.

The first edition of our new magazine will give you advice, information and tips for diabetes prevention and the megatrend that is E-health. A great deal of effort has gone into it so we hope you like the results!

Happy reading!

Doris Gintner

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Diabetes mellitus

Diagnostics

Author

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Diabetes mellitus is one of the most common metabolic disorders in the world. There are an estimated six to eight million cases in Germany, and up to 400 million with the condition around the world, which does not include the many unreported cases that are believed to exist. It is a widespread disease in other words, and one that deserves our utmost attention.

We distinguish between different types of diabetes mellitus, but type I and type II account for the majority of cases. Ten percent of those with the condition have type I, or IDDM (insulin-dependent diabetes mellitus) as it is also known, an autoimmune disease which leads to the destruction of the pancreas islet cells and an absolute insulin deficiency. The condition presents itself during childhood or adolescence. Type II diabetes, or NIDDM (non-insulin-dependent diabetes mellitus), accounts for 85–95% of cases, presents itself with advancing age and can be attributed to insulin resistance and a relative insulin deficiency[1, 2].

One specific form of diabetes mellitus is gestational diabetes (GDM), diagnosed in women who develop diabetes mellitus for the first time during pregnancy. Risk factors include being aged over 30, being overweight, a family history of the condition and previous births where the child weighed more than 4500g. The condition has a prevalence of around 4% in Germany, which equates to roughly 25,000 cases per year. The patient's metabolic status usually returns to normal after childbirth. In Germany, 'mothering guidelines' [3] stipulate that every pregnant woman in which diabetes mellitus is not known to be manifest be offered a screening for GDM. This takes place between the 24th and 27th weeks of pregnancy, with blood sugar determined one hour after oral administration of 50g glucose. If the result ≥ 135mg/dL (≥ 7.5mmol/L), a normal OGGT (oral glucose tolerance test) must be conducted.

'Abnormal fasting glucose', or IFG (impaired fasting glucose) as it is also known, and 'impaired glucose tolerance', or IGT, are preliminary stages observed for diabetes mellitus[1, 2].

An early diagnosis and prompt treatment are essential.

Concomitant diseases and secondary effects of diabetes mellitus

Diabetes mellitus often goes hand in hand with severe metabolic disorders and their long-term effects, such as hyper- and dyslipoproteinemia, hyperuricemia, obesity, high blood pressure, arteriosclerosis and vascular damage. Macroangiopathy (coronary heart disease, stroke and arterial obstructive disease), microangiopathy (retinopathy and renal diseases) and diabetic neuropathy as well as diabetic foot syndrome are all long-term life-threatening effects of the condition[2, 4].

Hence, early diagnosis and prompt treatment are essential. National and international professional associations and other committees have been working intensively to address this issue, giving the medical profession invaluable support in the form of guidelines, recommendations or similar, while also advising doctors to exercise particular caution especially with regard to diagnosis and the preanalytical handling of blood.

Diabetes mellitus diagnosis

Cases of diabetes mellitus are confirmed via raised levels of blood glucose, a pathological OGTT (oral glucose tolerance test with 75g glucose) and raised values for HbA1c (glycated haemoglobin A_{1C} in EDTA blood) and, where applicable, also via glucose in the urine. Two guidelines are applicable when it comes to determining glucose and evaluating results: the DDG's guidelines[5], updated in 2012, which relate to diabetes diagnostics, and the GDM guidelines, which relate to gestational diabetes[6]. These guidelines cover determination of glucose specifications for the test material as well as for preanalytics, analytics and for evaluation of findings (determination of decision limits)[7, 8].

Test material

Various articles from experts[5, 6] describe determining venous plasma glucose as the best way of diagnosing diabetes mellitus. When doing so, care must be taken to avoid glycolysis (i.e. a further decomposition of glucose) in the blood collected, with literature stressing that fluoride alone is not a sufficient additive and recommending further action be taken[5, 6]. All the concentrations and threshold values specified in the guidelines for glucose apply to venous plasma. Whole blood is an alternative test material to venous plasma, in which case the measurement results have to be multiplied and adjusted with a factor of 1.11 (plasma equivalent). Conversion of capillary plasma

or whole blood values into venous plasma values, on the other hand, is not reliable and no longer permitted[7].

Video about the **VACUETTE®** FC Mix Tube from Greiner Bio-One

https://www.youtube.com/watch?v=tKw4fT91VWQ

Preanalytics

The GDM guidelines cover possible errors in preanalytics and look at the problem of incomplete inhibition of glycolysis by fluoride[5]. Inhibition of glycolysis by NaF only, without further additive presence, does not begin until two hours after blood collection, and is not complete for four hours. Due to this, blood glucose decreases on average by 6% within the first hour after collection and by 7% within 24 hours. By contrast, the glucose values measured with blood collection systems (in addition to NaF and EDTA),

which thanks to a buffer also ensure a suitable pH value in the acid range is possible, decrease by 0.3% after two hours and by just 1.2% after 24 hours compared to the baseline value[7]. When sending samples, the GDM guidelines recommend that only sample collection tubes fulfilling the preanalytical conditions for glycolysis inhibition according to these guidelines should be used. The manufacturer's exact usage instructions (e.g. the dilution factor) must be observed here.

The GDM guidelines recommend using only collection tubes which meet preanalytical requirements regarding glycolysis inhibition when sending samples.

Analytics

Standardised and quality-assured laboratory methods are prescribed both for determination of glucose and for HbA1c. This means that the requirements set out under Preanalytics have to be observed, as should statutory provisions concerning precision and accuracy, to be guaranteed by internal and external quality assurance in line with German Medical Association guidelines (RiLiBÄK)[9]. Classic laboratory methods aside and contrary to previous regulations, the GDM guidelines allow the attending physician to use unit-use reagents in combination with point-of-care techniques (POCT) in the initial diagnosis of GDM. For this purpose the measurement equipment and the reagents have to be specifically declared for use by physicians in diagnostics and screening in the manufacturer's recommendations. Furthermore, the RiLiBÄK provisions (internal quality assurance and participation in

inter-laboratory tests by registered medical practitioners) need to be observed. A recommendation made jointly by the DGKL (the German Joint Association for Clinical Chemistry and Laboratory Medicine) and the DDG (the German Diabetes Association) sets out in greater detail what is required from this procedure. This includes both what is required from the manufacturers (quality and quality control for measurement equipment and test strips) and from users (internal quality control with two concentrations on each day of testing)[10]. The measurement equipment intended for self-use by patients should not be used for diagnostics, however[7].

Evaluation of findings

The following threshold values are specified for glucose in venous plasma in the guidelines[5, 6] for evaluating metabolic status and diagnosing diabetes mellitus and gestational diabetes. Europe and the USA vary slightly in their evaluation of plasma glucose and HbA1c when diagnosing diabetes mellitus. Koschinky and Luppa[7] have something to say about this.

Pathological values for glucose in venous plasma

Impaired fasting glucose (IFG)

	100-125mg/dL (5.6-6.9mmol/L)

Impaired glucose tolerance (IGT)

OGTT 2-hr value	140-199mg/dL (7.8-11.0mmol/L)
When fasting value	< 126mg/dL (< 7.0mmol/L)

Diabetes mellitus (D.m.)

Casual plasma glucose	≥ 200mg/dL (≥ 11.1mmol/L)
Fasting plasma glucose	≥ 126mg/dL (≥ 7.0mmol/L)
OGTT 2-hr value	≥ 200mg/dL (≥ 11.1mmol/L)
HbA1c	≥ 6.5% (≥ 48mmol/mol Hb)

Gestational diabetes (GDM)

Fasting plasma glucose	> 92mg/dL (> 5.1mmol/L)
OGTT 1-hr value	> 180mg/dL (> 10.0mmol/L)
OGTT 2-hr value	> 153mg/dL (> 8.5mmol/L)
Screening for GDM 1 hr after oral administration of 50g glucose	≥ 135mg/dL (≥ 7.5mmol/L)

About the Author

Prof. Dr. Dieter Meißner

After studying chemistry, graduating and completing his PhD at the Dresden Technical University, and taking further education as chemistry expert in medicine, Prof. Dieter Meißner officially became clinical chemist and took a teaching qualification for clinical chemistry.

His extensive expert knowledge has been used in a variety of ways that have served to underline his professional profile in his chosen area. He has been active in medical preventive care as director of the Institute for Clinical Chemistry and Laboratory Medicine at the city clinic of Dresden-Friedrichtstadt, in education as professor for clinical chemistry at the medical faculty of the Technical University in Dresden, in research in the area of trace elements and in addition to this in further education as well as on the committee of the German Society of Laboratory Medicine.

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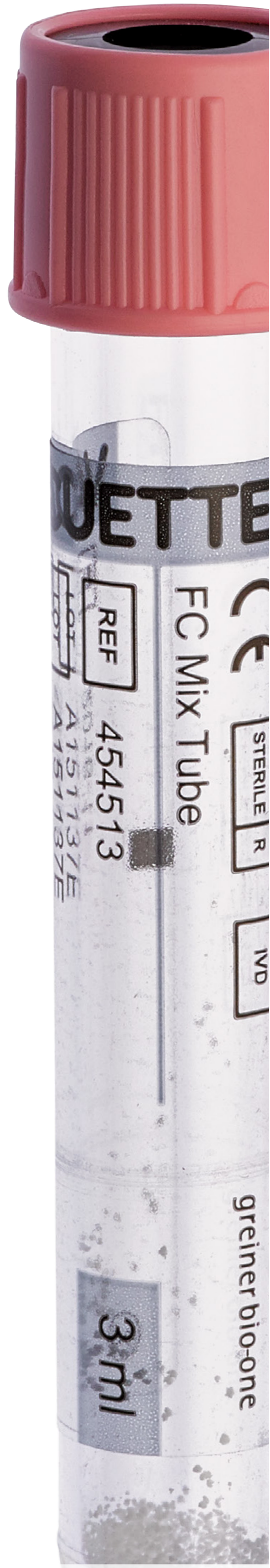
Following Glucose Tube Optimi-sation 'Guidelines'

The publication of new GDM guidelines means that Greiner Bio-One has had to introduce a new glucose collection system, thereby ensuring that falsification of glucose concentration become a thing of the past.



Following glucose tube optimisation 'guidelines'

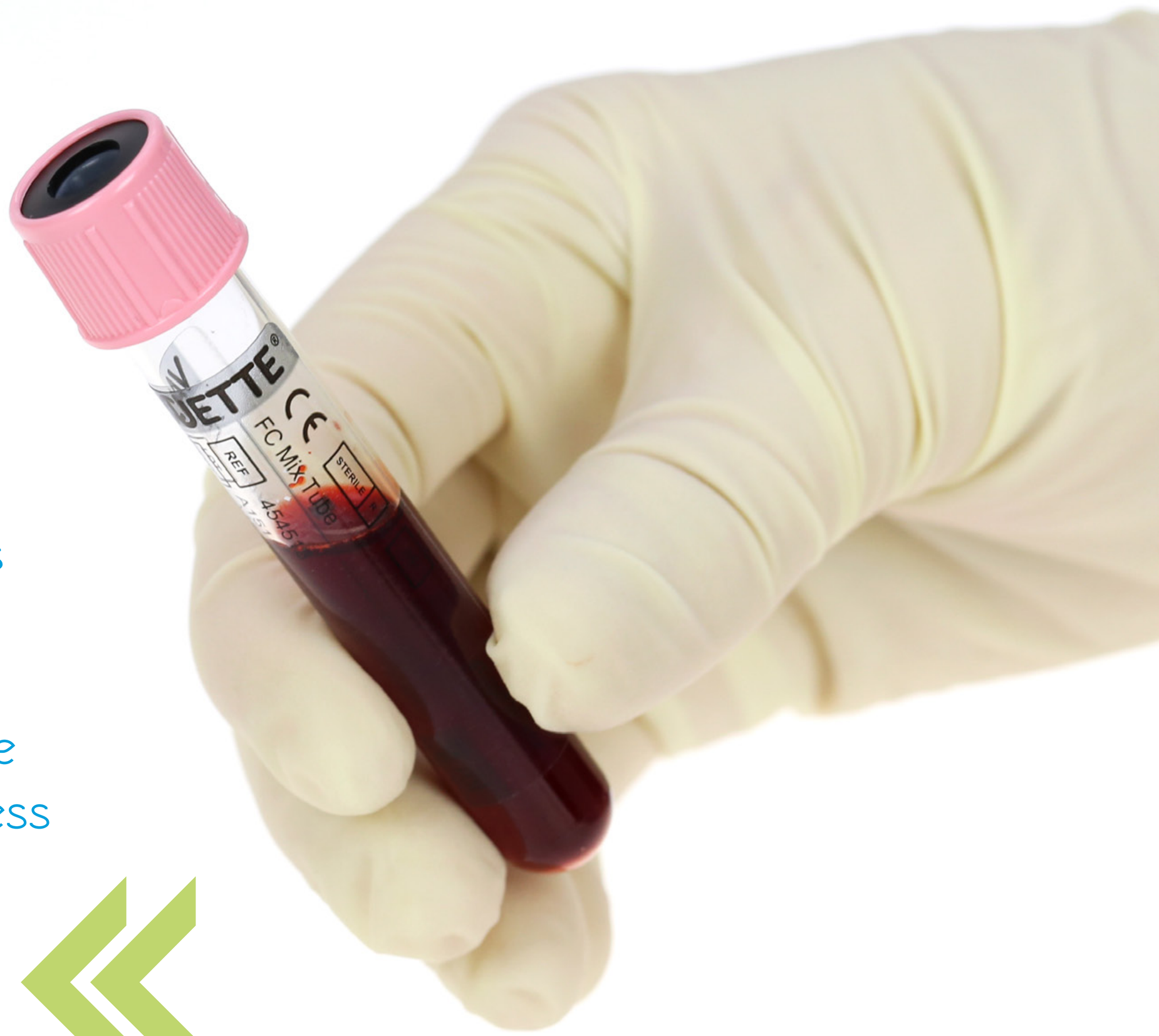
High blood sugar during pregnancy is harmful for both mother and baby. The DDG (the German Diabetes Association) advises against using blood collection tubes which contain sodium fluoride (NaF) only: "In our opinion, doing so is grossly negligent," explains Kiel based Dr Helmut Kleinwechter in a DDG statement in their medical journal of 25/08/2014 [1, 2].

The GDM guidelines state that test tubes should include a citrate/citric acid buffer as well as sodium fluoride (NaF) to prevent immediate glycolysis in the event of delay between the collection of blood and measurement in the lab. NaF alone is not sufficient as an additive because it takes two hours to begin to stop glycolysis and needs around four hours to complete this process. In this time, the concentration of glucose in the blood decreases, which leads to incorrect low results during diabetes diagnosis[3]. The powder additive in the **VACUETTE®** FC Mix tube contains both additives and as such meets the requirements outlined above.

What does the additive do in the new glucose collection system?

The citrate/citric acid buffer reduces the pH value in the sample. As a result, enzymes needed for the glycolysis process are inhibited and the actual 'in vivo level' is stabilised from the start. "This means that longer transport distances no longer pose any problems either, as the sample remains stable for 48 hours, even without centrifugation, when stored between 4°C and room temperature," according to Thomas Ehrenfellner, Product Manager for the new **VACUETTE®** FC Mix tube.

The sample remains stable for 48 hours, even without centrifugation, when stored between 4°C and room temperature.



The almost full inhibition of glycoloysis means that diagnosis is a much more reliable process than before.

Initial surprise at raised glucose values

The "higher glucose values after introduction of new blood sampling tube" phenomenon observed is correct. It should be pointed out, however, that none of the high values measured were incorrect, but rather were the concentrations actually prevalent in the blood of patients[1]. The almost full inhibition of glycoloysis in the **VACUETTE®** FC Mix tube means that diagnosis is a much more reliable process than before. The stabilisation is carried out in the whole blood and therefore does not require immediate centrifugation. Unlike in tubes where liquid is added, the finely granulated additive does not cause a dilution effect. There is no need to convert the measurement result.

As such, the **VACUETTE®** FC Mix tube is the ideal tool for reliably detecting diabetes and taking appropriate measures to combat the condition.

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Further information on the FC Mix tube by Greiner Bio-One as well as ordering details can be found on our webshop:

https://shop.gbo.com/en/row/articles/catalogue/articles/0010_0010_0070_0040/

MEGATRENDS

E-Health

'Megatrends' are not something you predict, as they are already there and are markers of change that have already been shaping our lives for a long time and will continue to do so for a long time into the future. They are the major 'winds of change'.

Christoph Rampetsreiter, Head of Greiner eHealth-Technologies, is very familiar with E-health as a megatrend and has been grappling with the topics in this field for many years.

As the development constants of global society, megatrends span several decades. They change the world, albeit slowly, but make a radical difference in the long-term[1].

E-health (electronic health) is one such megatrend and a collective term for the digital networking of service providers and the involvement of customers (i.e. patients). The term refers to all tools and services which use information and communication technologies (ICT) and which are used for prevention, diagnosis, treatment, monitoring and management in the field of healthcare[2].

Already we are confronted by elements of E-health technology in our daily life, for example in the form of different apps or test kits for home use. We met our E-health expert Christoph Rampetsreiter to ask him about this megatrend.

Why is the E-health trend important for our society?

Information and communication technologies are having more and more of an impact on our lives, which also includes healthcare. Technology is being used more and more in medicine and this, coupled with an ageing population, means costs are increasing in this field around the world, with the cost of hospital treatment accounting for the majority of these.

This is in part caused by a lack of transparency and data availability, as well as problems at the interface between healthcare service providers, which harbour the risk of less efficient treatment. These aspects have an adverse effect on treatment times, which in turn impacts on costs.

Many patients like to avoid playing the role of 'sick person' and would rather be a proactive 'contributor' to the treatment process. What options does E-health offer for this trend?

E-health makes it possible for the patient, for the first time ever, to securely access personal diagnostic findings regardless of physical location and time. Different providers such as KIWENO now offer people the option of taking capillary blood samples using test kits in the comfort of their own four walls, which they can then send off to the laboratory. Subsequent to examinations, the diagnostic findings can then be retrieved conveniently via an app on the person's smartphone, tablet or on a web platform.

What are the main objectives of E-health?

Increasing mobilty, free choice of doctors as well as increasing specialization in healthcare necessitate that data is available regardless of time or location.

E-health initiatives at national and international level are aimed at making the provision of healthcare treatment more efficient, thereby lowering costs and at the same time ensuring high-quality care for patients.

The availability of relevant patient data at the right time and in the right place is becoming increasingly important for the diagnostic process. This is because people are becoming more and more mobile and have a choice of doctor, but also because healthcare service providers are specialising increasingly. If their data (which is often obtained from analytics) is available, this can avoid multiple examinations and shorten treatment times.

What E-health apps are available? Can you give us a few examples?

Health apps also encompass functions and devices that you would not necessarily place in this category. These include diagnostic finding apps with easy-to-use encyclopaedias, body fat scales that collect different data, as well as monitors of high-risk pregnancies and glucose levels. Training apps such as Freeletics and Runtastic also count as E-health applications.

Greiner e-Health Technologies also provide a well-thought-out and comprehensive system in this area, with the option to optimise and increase the level of transparency of the pre- and post-analytical process through the use of pre-barcoded tubes and different E-health applications.

freeletics.com

runtastic.com

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Greiner eHealth Technologies

GeT to know it

Nicole Pingitzer, Project and Process Manager for Greiner eHealth Technologies (GeT), studied Process Management and Health and Social Care at university in Austria and has been part of the Greiner Bio-One family for four years.

What was your first impression of GeT?

When I joined Greiner Bio-One in 2012 working as a project administrator for GeT alongside my social care degree, I knew straight away that this business division had a big future. It was a wonderful opportunity for me to work on this kind of innovative project from the very beginning and to be actively involved in setting up something completely new.

2 How does GeT deal with the matter of e-health as a trend and offer process-controlled solutions for healthcare?

Increasing the reliability and efficiency of the diagnostic process is our top priority. GeT combines the latest software solutions, such as the automatic assignment of barcode tubes to the patient, with the tried and tested premium laboratory products made by Greiner Bio-One.

3 Which customers are you targeting with GeT?

Our customers include institutions such as hospitals and laboratories, but also individuals such as registered medical practitioners and healthcare professionals who take blood samples. Patients also benefit from our system because they can retrieve their blood test results quickly and easily using an app. As we offer a complete range of services, we are in a position to put together the right package for any customer.

We put together the right package for any customer.

4 Could you tell us more about the interesting pilot project at an Upper-Austrian hospital?

It was an exciting time and we got to know a lot of interesting people, who were very open and positive towards our new system. One of my lasting memories of that time is the collaboration amongst staff at the hospital, who were very proactive in providing helpful suggestions and input and helped to keep optimising processes.

5 What is the main advantage of GeT over existing processes in the healthcare system?

We support our customers step by step.

Aside from the unique combination of software products and lab accessories, the likes of which the market has never seen before, service components are very much our focus. We support our customers step by step en route to even higher quality standards and efficiency. Our main goal is to have satisfied customers who are happy to recommend us. We also have strong partners such Stiwa and Labuniq on our side, who enable us to develop innovative and customer-orientated solutions.

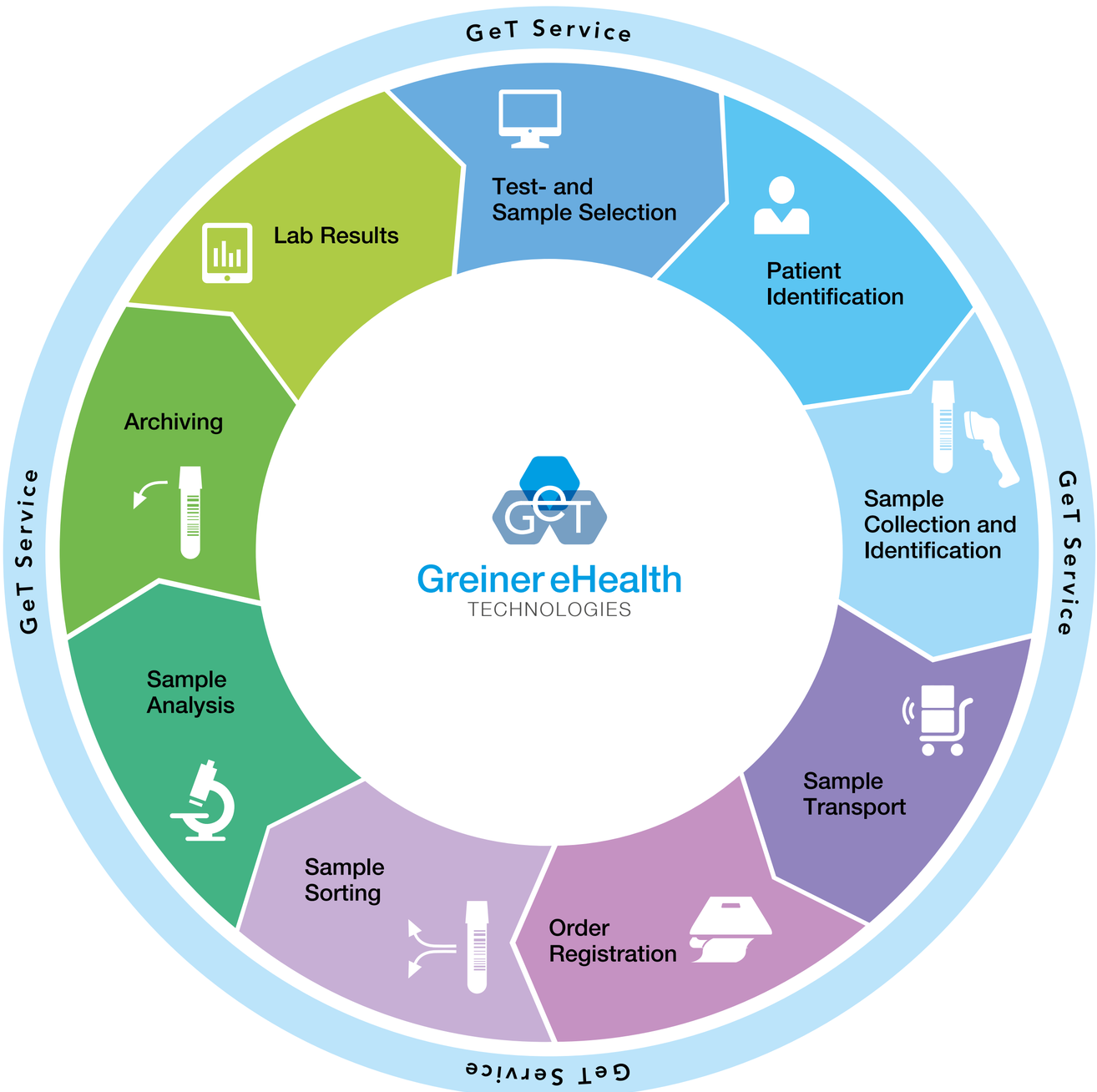
6 Does GeT reduce your customers' costs?

We are in a position to show our customers exactly where they will save money with GeT in comparison to their current system. The calculation system we use enables us to accurately forecast when the customer will be able to start benefiting financially from using the solution. Our new GeT micropage can be used to get an initial estimated analysis. It also provides interested parties with all the information they need in order to take the next steps in the process. We also have a Facebook page where we regularly post our news, ensuring our customers never miss anything.

7 Accreditation is an important aspect of healthcare systems. What does GeT do to help institutions with this?

What strikes us time and time again during visits to customers and when investigating processes is how low the level of transparency is in many areas of preanalytics and postanalytics. One example here is a lack of documentation detailing who collected the blood sample and when, i.e. the time of collection. These parameters are required to meet standards, however. The time of collection and the person who collected the blood sample are recorded automatically with GeT. This guarantees the kind of seamless documentation that makes it much easier to gain accreditation.

8 In your opinion, what would be the perfect GeT process flow?



Ideally, the institution would be using all GeT modules, and without any doubt these would be perfectly coordinated and optimise the entire process in every respect. Complete conversion of the entire process is a major undertaking, however, and requires a certain amount of time to take shape.

The GeT modules fit together perfectly, optimizing the entire process.

9

What would be the first step to take? What would you advise your customers to do?

We recommend beginning with one module and aiming towards the GeT Best Practice model. Customers could for example start by implementing pre-barcoded tubes in the sample collection process. This cuts out one whole step of the process, i.e. preparing tubes, which leaves more time for the patient.

Pre-barcoded tubes help free up time for other matters.

10

What has been your greatest success so far with GeT?

Last year we were able to create an international network of healthcare providers and experts for individual software solutions. It's a big success for us, to see GeT developing more and more on the market into an independent business division of Greiner Bio-One.

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