# Dear Customer,

We are thrilled that we could raise your interest in **in.vent Clinical Services (ICS)**!

Please allow us to provide you with a quick introduction to the service portfolios of **in.vent Diagnostica** and **ICS** followed by some case examples of previous diagnostic studies.

## in.vent Diagnostica – Biobank and targeted procurement:

**in.vent Diagnostica GmbH** is Europe's leader in human biosample procurement with 20 years of experience in the IVD market as both biobank and CRO.

We understand our biomaterials as the basis of high-quality IVD products. Our inventory permanently comprises over 500,000 aliquots of ethically acquired and clinically defined commercial samples (blood products, urine, faeces, sputum, saliva, swabs, tissue). We have established a dense cooperation network with thousands of physicians, hospitals, and other medical institutions to fully comply with the demands of our clients. These demands mirror the challenging requirements of the diagnostic market, ranging from thousands of liters of normal human serum to a few millilitres of sample with highly specific clinical background.

Not every demand can be supplied by what we have in stock, of course. Therefore, we specialised in acquiring project-specific samples hand-tailored to the customer's needs. This is what we call **targeted procurement**. Our capabilities in acquiring specific clinically defined samples are unmatched in the European market. This is what made us the number one sample source on the continent!

Naturally, our products are subject to meticulous quality management and control before being shipped all around the globe. We are certified according to **ISO 9001:2015** and **ISO 13485:2016**.

## in.vent Study Site:

We run a **company-owned** and fully equipped **study site** just half a kilometre away from the in.vent premises. Together with our well-trained personnel this allows us to conduct on-demand donation days and to be in full control over all steps of pre-analytics.
Additionally, of course, this institution serves as a controlled surrounding for IVD validation which leads us the second part of this introduction: **in.vent Clinical Services (ICS)**.

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## in.vent Clinical Services (ICS): Making CE possible

**ICS** is the newest expansion of our service portfolio. We have harnessed our 20 years of expertise in diagnostic studies to conceive a new level of IVD-services: A complete all-round package covering every step of diagnostic **assay validation**, including all performance studies, study protocols, and reports.

### Diagnostic Studies from A to Z

**Our All-round services**

- Project Planning & Cost Calculation
- Communication with Ethics Committee & Legal Authorities
- Sample Procurement
- Donor & Subject Recruitment
- Study Site Initiation & Coordination
- Monitoring
- Performance Evaluation Plan
- **Analytical & Clinical Performance Studies**
- Data Management
- Biostatistics
- Performance Evaluation Report
- CE-marking
- Post-Market Surveillance / Post-Market Performance Follow-Up

**ICS** was founded with regard to the major challenges for the European diagnostics industry that arise with the implementation of the **EU regulation 2017/746 on in vitro diagnostic medical devices (IVDR 2017/746)**. It is our goal to help global IVD developers and manufacturers to master this challenge.

Therefore, we offer a one-stop service covering every relevant step of the IVD validation and marketing process. Our services range from ethical considerations and sample procurement to the complete **Performance Evaluation** (Performance Evaluation Plan, Analytical and Clinical Performance Studies, Performance Evaluation Report) and all the way to CE-marking and Post-Market Surveillance. Micro-services such as Logistics or Storage are of course included.

Place your trust in our expertise: We know which and how many samples will be required for the validation of your assay. We will perform, manage, and document the analytical and clinical validation in an IVDR-compliant manner. **We will get your assay CE-certified.**

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# Case studies:

In order to provide you with an idea of what we can do and which roles we are able to play in your projects we would like to provide you with a quick glimpse into some of our previous work regarding diagnostic studies.

We are contractually prohibited from disclosing the names of our clients or detailed information about the projects' background, so please understand that this information will not be mentioned in the descriptions below. Do note, though, that the list of our clients comprises the top ten of global players in IVD as well as major pharmaceutical companies. Annually, we perform about 5-10 assay validations.

## Example 1: Multicentric Cohort Study

In a large study with multiple international study sites we validated an endocrinological diagnostic assay system for the monitoring of an important sexual hormone. We conducted a sample collection of healthy men, women in reproductive age, and children, as well as umbilical cord blood. The samples were then used for a reference value assessment study. The duration of the project from the recruitment of the first proband to the study report was ca. 24 months. All in all, more than 3500 probands were recruited for the study.

in.vent calculated the necessary sample sizes, elaborated inclusion (e.g. healthy nutritional status, normal differentiation of genitals, regular menstrual cycle) and exclusion criteria (e.g. thyroid disease, endocrinological disease, post-menopausal), wrote the study protocol, acquired a positive opinion from the ethics committee, took responsibility for study coordination, data management, and logistics, recruited 20 different study centres in 5 different European countries, and monitored the sample collection and processing.

The sample procurement was an international process including on-site monitoring and source data verification. Informed consent and case report forms were generated by us and archived at in.vent. This means that the documentation needed to be registered and checked for completeness. The data were introduced into a validated study data base and verified for plausibility by our data management team.

After all required changes and corrections had been implemented, a central monitoring of the data was conducted before the data and the samples were released for shipment.

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## Example 2: Development of a POC Rapid Test

In this project we were contracted to develop a Point-of-Care (POC) rapid test in the autoimmune disease segment. The purpose of the assay is to allow physicians to immediately stratify patients in cases that need to be hospitalised and cases that can be treated ambulatory. The fact that the test's matrix is whole blood posed an interesting challenge in this project.

After acquiring a positive opinion from the ethics committee, we procured the blood samples from healthy individuals, a panel of samples from patients with increasing severity of the indication, as well as human samples with different interfering factors. Experiments were conducted in our in-house laboratory. Also, the whole study was meticulously documented by us. We generated, distributed, and archived the patient information and informed consent forms, investigator brochures, and study protocols, monitored the study sites, and wrote the corresponding reports. The assay has reached marketability and is currently in authorisation phase.

## Example 3: CDx Development

We clinically validated a companion diagnostic (CDx) medical device in the immunology segment. The sponsor wanted a test that could stratify patients into responders and non-responders for the corresponding medicinal product. This included the prior identification of a suitable biomarker.

The procurement of samples was conducted by us which included ethical clearance and the generation and management of case report forms. The study required patients (75% women) that were starting a therapy with one of three different therapeutics without having been under this kind of therapeutic agent before. Samples were collected before (t0) and during the treatment (after 10-14 weeks, t1; after 20-28 weeks, t2). A validation panel containing serum from patients with at least 15 different autoimmune diseases was produced to analyse the effect of possible interferences for the CDx. Quartets of serum, K3-EDTA-, Na-citrate-, and Li-heparin-plasma were collected from donors.

After identification of the biomarker, large-volume samples (500 ml) were required as standardisation material which were collected at our company-owned study centre in Hennigsdorf. Furthermore, we conducted stability experiments with the marker in our laboratory. The result of our work is a CDx medical device that will allow a personalised treatment of patients. Currently, the assay is in authorisation phase.

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