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SusFE

# D1.2.2 Market Analysis Report

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| **Description** | Document describing the current European market of flexible electronics, including various points such as market segmentation, competitors' analysis, current differentiation strategies, drivers, barriers, trends and opportunities. | | |
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# Abstract

This 2nd market analysis report was written collectively by all partners of the SusFE consortium, according to their roles, use case leaders and technology providers.

For all healthcare applications – ie. blood sampling, wound monitoring, Point-Of-Care (POC), wearable cardiometabolic monitoring –, an overview of the current market and trends has been provided. It has clearly shown that all use cases developed by the SusFE consortium are well positioned, fulfilling the market needs.

Technology providers for batteries, flexible electronics and plasma surface treatment bring cutting-edge innovations to support the development of proof of concepts for the different cases. Innovations are technological and very complementary to each other. But they also should deliver more sustainable electronic devices.

# Statement of originality

This deliverable contains original unpublished work except where clearly indicated otherwise. Acknowledgement of previously published material and of the work of others has been made through appropriate citation, quotation, or both.

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# 1 Electronics for healthcare applications

## 1.1 Blood sampling use case (CAP)

Each year, 890 million tests of clinical biomarkers are conducted in Europe and the US* [Extrapolated data based on population from Swedish laboratory statistics, Ingvar Rydén, Kalmar Regional Hospital, Sweden, 2017]. and the total blood testing market is anticipated to reach USD 140.3 billion by 2028 according to a report by Grand View Research [1] [Shortened length of stay at hospitals, reduced contact between patient and concerned physician coupled with the rise in outpatient services are given as factors for the increased demand of blood testing services. Approximately seventy percent of all medical decisions are based on laboratory results. These tests are essential tools in both medical decision-making and diagnosis.

Traditional blood sampling is done through venipuncture by a trained nurse at a health care facility. Standard approaches collect several millilitres of blood, of which less than 10 percent is typically used for analysis. After a sample has been collected, it needs to be sent by cold chain transportation to a laboratory for analysis.

Blood sampling is associated with high costs of healthcare and inconvenience for patients. For low mobility patients, patients relying on frequent monitoring and patients in remote or low resource areas, blood analysis can constitute a considerable obstacle in everyday life or not be accessible at all.

Blood sampling through venipuncture also entails considerable limitations in many other sectors, e.g. patient monitoring in clinical trials by pharmaceutical companies, alcohol and drug tests by employers and police enforcement authorities, and doping tests.

Of the samples taken from non-hospitalized patients, a large proportion is possible to switch to home sampling. With the developing possibilities of telemedicine and digital follow up consultations, this proportion can also increase. The self-sampling blood collection and storage device market is expected to grow at a CAGR at 11.9% from 2021 reaching US$310.6 by 2031 [2].

In standard care and pharmaceutical clinical trials with phlebotomy, a time stamp when the sample was taken is usually printed when the tube labels are created at the sampling event. This time stamp is lost in traditional home sampling. An automatic time stamp as developed in this project, can overcome that loss of information in home sampling.

### 1.1.1 Clinical trials/pharma industry

Pharmacokinetics (PK) is the study of how the body interacts with administered substances for the entire duration of exposure and examines the Absorption, Distribution, Metabolism, and Excretion (ADME) of the substance. PK studies allow the characterization of ADME properties of a drug early in development. They also provide critical information including the impact of food interactions (in orally administered drugs), drug-drug interactions, and organ impairment on the disposition of a drug. As such, they are essential tools in drug development within the pharma industry. The global Pharmacokinetics services market size was valued at US$ 852.8 million in 2020 and is anticipated to grow at a CAGR of 10.3% during forecast period 2021 to 2030 [3]. AUC (area under the curve) is a measure to assess total drug exposure over time and is commonly used in PK studies. To assess AUC data, multiple blood samples are taken in timed intervals after administration of a drug. A full $AUC_{0\text{-}24h}$ can involve as much as 10-15 blood samples collected at distinct time points distributed over 24 hours after ingestion of the medication. With the trend in the pharma industry towards remote trials, the application of a self-sampling solution with an integrated function for registration of a sampling time will to be an enabler for such smart trials.

### 1.1.2 Health care

Home sampling is an attractive option for both screening on monitoring approaches. As an example, we take kidney transplanted patients. In the post operative monitoring program, the immunosuppressive drug level and kidney function is measured via a blood test (Drug level, Creatinine and Haemoglobin) approximately every 3rd week, which corresponds to 17 samples annually per patient. Annually, approximately 90 000 kidney transplants are performed worldwide, which results in approximately 15 million blood tests [4]. Given that the monitoring is life long, there is an accumulating number of patients being monitored over time and we can assume over 100 million blood samples per year, only for this patient group. The pharmacokinetic pattern on immunosuppressive drugs is well studied, and it is known that the time from drug administration to sampling has a clear impact on drug levels, giving important information for the monitoring. A full 24 h AUC immunosuppressive drug profile recording for every patient is often not feasible in clinical practice which is why simplified protocols often is used. There are however concerns on the safety and efficacy of these simplified protocols [5]. A time stamp on drug intake (such as that of like Pilloxa [6]) combined with a time stamp on the home sampling device, has the potential to exploit the full accuracy of 24 h AUC monitoring for kidney transplant patients at home. Considering that there are about 150 000 organs (kidney, liver, heart, lung, pancreas, small bowel) that are relying on similar treatment schemes, the use of a times stamp blood sampling card is substantial.

## 1.2 Wound monitoring use case (SOF, VTT & TU)

References: [7-10]

Electronics & Wound monitoring: Foreground

Electronics plays a pivotal role in modern healthcare applications, particularly in the field of wound monitoring. Wound monitoring is a critical aspect of healthcare, as it allows healthcare providers to assess the progress of wound healing, prevent infections, and optimize patient care. Electronics have revolutionized wound monitoring by enabling continuous, real-time data collection and analysis. Major components in the electronics for wound monitoring are sensors, connectors, power supply and data transfer.

Sensors are the heart of wound monitoring electronics and are used to measure parameters such as temperature, humidity, pH, and oxygen levels in and around the wound. For example, smart dressings embedded with sensors can provide real-time information about wound status. Similarly like to wearable electronic devices, such as smartwatches and activity trackers, these can track vital signs and transmit data to healthcare professionals, allowing for remote monitoring of wound healing.

Electronics are instrumental in the monitoring and management of chronic wounds, such as diabetic ulcers and pressure sores or post-operative wounds. Smart wound dressings equipped with sensors can provide continuous feedback on wound status, helping clinicians make informed decisions on time and prevent complications. These tracked parameters include wound temperature, inflammation, and drainage. Electronics also allow for the remote monitoring of patients' wounds, reducing the need for frequent inperson visits. This is particularly beneficial for patients in rural areas or those with limited mobility.

Market analysis & Trends

The wound healing market is evolving from traditional treatments to move towards more advanced forms of wound healing treatment, by integrating algorithms and artificial intelligence, smart bandages with monitoring capabilities, wearables for diagnosis and early detection of complications (e.g. infection) and by also increasingly include prevention to reduce the burden of chronic wounds.

The world market in 2020 for products for wound healing amounted to more than 20 billion dollars, therefore more than 35% for the most advanced forms of treatment. This last segment is in full evolution unlike the basic forms of wound treatments (i.e. bandages, dressings, negative wound pressure therapy) that should stagnate for years to come.

The leading players are those who will have the most influence on the wound care market trends. These companies (3M, Smith & Nephew plc, Mölnlycke, ConvaTec, Paul Hartmann AG, Medline Industries, Inc., Medtronic, B. Braun Melsungen AG, Cardinal Health, Inc.) represent approximately 80% of the current market. The market of wound care was valued at around 20 billion Euros in 2020 and is expected to increase at a CAGR of 6.7% between 2020 and 2030, mainly driven by the Advanced solutions, including the Monitoring solutions. A little less than a third of the market is generated in Europe (28%).

Advanced solutions cover two aspects, in terms of monitoring:

i) diagnosis and prevention: early wound detection, root cause analysis, diagnosis and prevention with portable scanners and wearables with sensors

ii) wound care: wound measurement and assessment, wound monitoring, remote wound monitoring with apps/software as solution portable scanners and smart bandages/dressings.

Current, sensor-based wearables and handheld devices are essentially tracking the mobility/position of patients and the risk of bedsores & pressure ulcers for chronic wounds (eg. Provizio® SEM Scanner, LEAF Patient Monitoring System, Masimo Centroid™, Sensor-based hospital garments or insoles: inPRO Medical, Orpyx® SI) and monitoring the moisture of wounds as a key driver of wound healing, but also as a risk indicator of pressure ulcers (eg. Provizio® SEM Scanner). For example, the Provizio® SEM Scanner (Bruin technologies) can analyze subepidermal moisture by biocapacity measurement which can be correlated with the risk of wound pressure sores, and which can then be used for early detection of these complications. At least, two other companies, Konica Minolta and Moleculight are developing wound monitoring solutions, based on the evaluation of moisture detection in wounds. These two companies are the most active in the field of wound diagnostic and monitoring technologies through their patent filings. More generally, the most investigated biosensors for monitoring solutions are used to measure humidity, pressure, motion, but also temperature and pH. As an example of commercial translation, Grapheal is on its way to develop WoundLab, a skin patch solution, for real-time and continuous monitoring of wound healing with biosensors (eg. pH) and leveraging the graphene technology (https://www.grapheal.com/woundlab). See the D1.1 deliverable for a review of the literature of biosensors-based solutions for wound monitoring.

Alongside solutions with biosensors, portable scanners, and screening devices are developed and marketed based on imaging technologies (eg. multispectral imaging, hyperspectral imaging, fluorescence imaging, and thermal imaging) and data analysis using machine learning and artificial intelligence algorithms. For example, MolecuLight i:X can visualize bacteria and measure wounds at the point of care, by using fluorescence imaging (excitation light at 405 nm and analysis of the fluorescence spectrum; green fluorescence coming from skin components, red & cyan fluorescence associated with certain bacteria found in contaminated wounds) (from https://moleculight.com/). Another example comes from the company Podimetrics which has developed SmartMat, a scanner, using thermal imaging and artificial intelligence to prevent the appearance of foot ulcers in diabetics which can lead to leg amputation (from https://podimetrics.com/).

Advanced solutions have received strong funding support from private investors and federal agencies, such as the National Institutes of Health (NIH) in the United States, and by the European Commission's Horizon 2020 & Horizon Europe Programmes.

Wound monitoring & SusFE solutions

SusFE consortium is currently designing and developing solutions to be integrated as part of smart dressings or be used in combination with conventional dressings. The intent is to integrate temperature, moisture and/or pH sensors with FlexIC and BeFC biofuel cell. The global architecture is given by the figure, below:

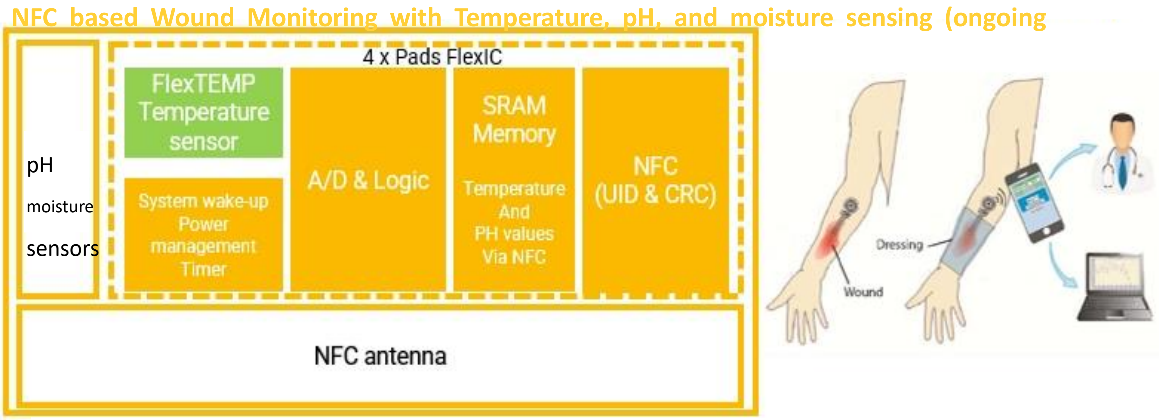


Figure 1 Temperature measurement within the FlexIC, external pH and moisture sensors, Low-Cost and flexible form factor

To note, BeFC has also their own proof of concept of a device, including temperature and moisture sensors, which may be adapted to wound monitoring. This device is powered by their biofuel cell battery. The information generated by the sensors are processed by an integrated microcontroller and data are transmitted wirelessly by Bluetooth.

## 1.3 POC Use Case (TU, VTT & SOF)

The global market for point-of-care diagnostics was estimated to be worth 45,4 billion dollars in 2022 and is forecasted to reach 75,5 billion dollars by 2027, growing at a CAGR of 10,7 % from 2022 to 2027 [11]. The growth of the point of care diagnostics market is driven by increasing prevalence of for example infectious diseases, aging population, increase of home testing and decentralization of healthcare. As an example, during the COVID-19 pandemic rapid lateral flow antigen tests became readily available and self-testing at home was widely accepted, also by the healthcare professionals. In fact, according to the

Market and Markets report, home care and self-testing is anticipated to have the highest CAGT.

According to the market report written by JouZeNet Consulting Ltd ordered by VTT in 2019, about 1/3 of the point-of-care revenues in 2017 came from lateral flow –based immunoassays. Another rapidly growing area (over 10%) of IVD was molecular diagnostics. The biggest product category was electrochemical sensing of blood glucose, while other large categories were cardiac and CRP testing.

According to the report, lateral flow remains to be important despite being an old technology, because it is easy and rapid to use, and the tests are relatively inexpensive to manufacture. Currently, there is a need to develop the lateral flow technology in the direction of more sensitive and quantitative tests. In addition, multiplexed lateral flow assays, able to detect multiple analytes from the same sample at the same time, are required.

From extensive market analyses and state-of-the-art publications, it is evident that PoC industry is moving towards more sustainable manufacturing with materials that have less environmental impact and are highly available (for example, the supply of LFA materials and PCR tubes were very limited during the COVID-19 pandemic), are produced closer to market areas (avoiding longer transport distances, changes in global disease threats and transportation). Demand will be increasing for mass producible, sensitive, and multiplexed PoCTs that can be used in decentralized set-ups and self-tests that are easy to be disposed by the end-users.

The point-of-care diagnostics research at VTT focuses both in traditional (LFA) and new technologies, the new developments including different antibody-based methods, microfluidic lab-on-chip devices and molecular diagnostics solutions. Electrochemical sensors are being developed by using new sustainable materials and manufacturing methods. In all R&D projects, sustainability is taken into consideration. Integrated systems is an important field of research, where for example quantifying electronics or reader systems are integrated onto POC tests.

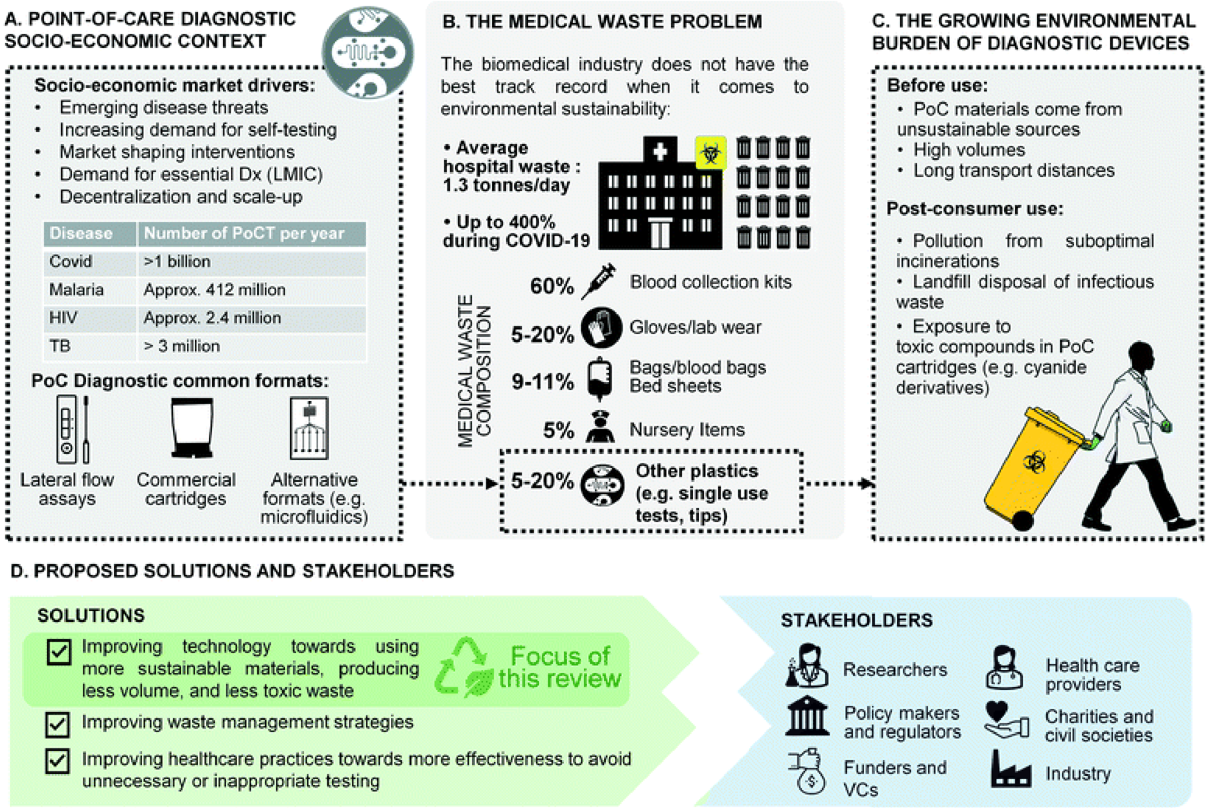


Figure 2 Overview of the challenges and solutions in single-use diagnostic devices. A) Point-of-care diagnostic socio-economic context. B) The medical waste problem. C) Growing burden of waste from diagnostic devices. D) Proposed solutions and stakeholders. [12]

## 1.4 Wearable cardiometabolic monitoring use case (TECSR)

The cardiometabolic disease market is expected to witness significant growth, according to a report by Market Research Future (MRFR). Projections show that the market could escalate from USD 155.37 billion in 2023 to USD 868.45 billion by 2032, marking a substantial growth rate of 24.00% within this duration[1]. This surge can be attributed to rapidly changing lifestyles and the increasing incidence of disorders such as diabetes, hypertension, cardiovascular disease, and high cholesterol.

Cardiometabolic disease (CMD) encompasses a range of health conditions. Notably, individuals with CMD have twice the risk of dying from coronary heart disease and three times the risk from heart attacks or strokes. Furthermore, cardiovascular disease, a subtype of CMD, is expected to contribute significantly to the market's expansion, given the high prevalence of CMD and related conditions like diabetes and obesity.

Globally, CMDs have emerged as a leading cause of death. Unhealthy lifestyles characterized by physical inactivity, smoking, and an improper diet are the predominant

[1] https://www.globenewswire.com/en/news-release/2023/05/10/2665742/0/en/Cardiometabolic-Disease-Market-Size-Worth-USD-868-45-Billion-by-2032-at-24-CAGR-Report-by-Market-Research-Future-MRFR.html

risk factors. According to WHO data[2], cardiovascular diseases account for 17.9 million deaths annually. Alarmingly, heart attacks and strokes represent 80% of these deaths, with a significant one-third of these fatalities affecting adults under the age of 70. Specifically focusing on coronary heart disease, which is the most common heart ailment, there were 360,900 reported deaths in 2019. Presently, about 6.7% of adults, equating to 18.2 million individuals aged over 20, are afflicted with CAD. Notably, almost 20% of CAD-related deaths involve those younger than 65 years. With the escalating incidence of CAD, there's an anticipated demand surge in the cardiometabolic monitoring products market.

In the realm of medical wearables, the global market is on an upward trajectory. Forecasts suggest a growth from €14.3 billion in 2020 to a staggering €95.6 billion by 2028, translating to a CAGR of 26.8%[3]. This growth is fueled by factors such as an aging global population, the proliferation of Home Health Care (HHC), and the advancements in Remote Patient Monitoring (RPM). A rising trend of personal healthcare coupled with the recognized benefits of consistent health monitoring further underpins this growth.

However, with progress comes challenges. In a study of e-textiles impact on recycling and disposal, Kohler et al[4] analyze a scenario of a simple ECG sensor shirt for daily health monitoring, massively adopted by the market. In case of a significant market adoption in the population segment older than 55 years, they estimate that this would provide up to 24 kt/year of e-textile waste for Germany alone. Extrapolated to EU market, for every 1% of the target market reached, 1 kt of additional e-waste would be produced each year.

In addressing these challenges, the SusFE approach stands out. The focus revolves around minimizing durable waste by pioneering biodegradable printed textile electronics. The advantages of SusFE's technology are multifaceted:

**Increased Wearability** – unlike the current product which are based on hard electronics, and worn as accessories specifically for the monitoring purpose, SusFE cardiometabolic monitoring system is foreseen as a garment embedded device. Part of everyday clothing, it will allow unobtrusive continual monitoring.

**Multimodal integration** – while current solutions largely rely on summing up data from individual sensors, suffering from issues like cumbersome cabling and sensors' placement, the data corruption due to noise and electric coupling, or fusing the data from spars sources, the SusFE cardiometabolic monitoring system is designed for multimodal sensing from the beginning, significantly increasing both usability and reliability of the system.

**End-of-life impact** – as prevalence of textile monitoring systems increases the end-of-life implications on the electronic waste will grow at an accelerated rate. The SusFE solution will be based on a part of durable electronics compliant with current e-waste regulations and a textile integrated part, which is expected to be a multi-use consumable. The later will be made with printed electronics, using biodegradable inks, leading to a sustainable solution.

[2] https://www.who.int/health-topics/cardiovascular-diseases#tab=tab_1

[3] https://www.grandviewresearch.com/industry-analysis/wearable-medical-devices-

[4] Köhler, Andreas R., Lorenz M. Hilty, and Conny Bakker. "Prospective impacts of electronic textiles on recycling and disposal." *Journal of Industrial Ecology* 15.4 (2011): 496-511.

# 2 Battery (BeFC)

We live in a digital and connected world, but the portable handheld devices we use are typically powered by coin or button cell batteries, which are complex, expensive and unecological to collect, process and recycle. As a consequence, approximately 15 billion primary batteries, and 97% of miniature batteries, disposed of each year end up in landfill or are incinerated.

BeFC produces paper-based biofuel cells that use enzymes (biological catalysts) to convert glucose and oxygen into electricity. This is a departure from conventional battery technologies that use reactive metals to store energy.

With a thickness of around 600 microns, the biofuel cell can be easily integrated into patches, or packaging, or applied as a label. Activation can be performed using a biological fluid (e.g., blood, urine, sweat), or through an integrated liquid reservoir (blister) that can be actuated by a thumb or finger.

Once activated, the cell voltage (nominal 0.75 V) typically develops in the order of seconds (depending on total size and activation mechanism). Constant discharge power is in the order of a few hundred microwatts per square centimeter, with short pulses of tens of milliwatts per square centimeter possible capable of powering microcontrollers and/or wireless transceivers. Such performance characteristics are ideally suited to quasi-continuous sensing applications with analog sensors paired with an ADC, or digital sensors with minimal processing and bandwidth.

The selected organic materials permit disposal via internal industrial composting, significantly reducing environmental impact. In short, providing data opportunities without the downsides of battery disposal. Disposal can also be achieved through incineration, a common disposal route for medical single-patient and single-use digital devices. Generally contaminated by contact with skin or biological fluids, they should be incinerated to avoid cross contamination and associated risks.

BeFC uses a paper-based construction that allows customisation of shape and size, and therefore power and energy. The use of bio-sourced and biodegradable materials results in an ecofriendly energy solution that can be composted. Internal tests have shown that more than 50% mass reduction in 45 days with industrial composting to ISO 20200 standards (see Figure 3) using a variety of biofuel cell materials (see Table 1).

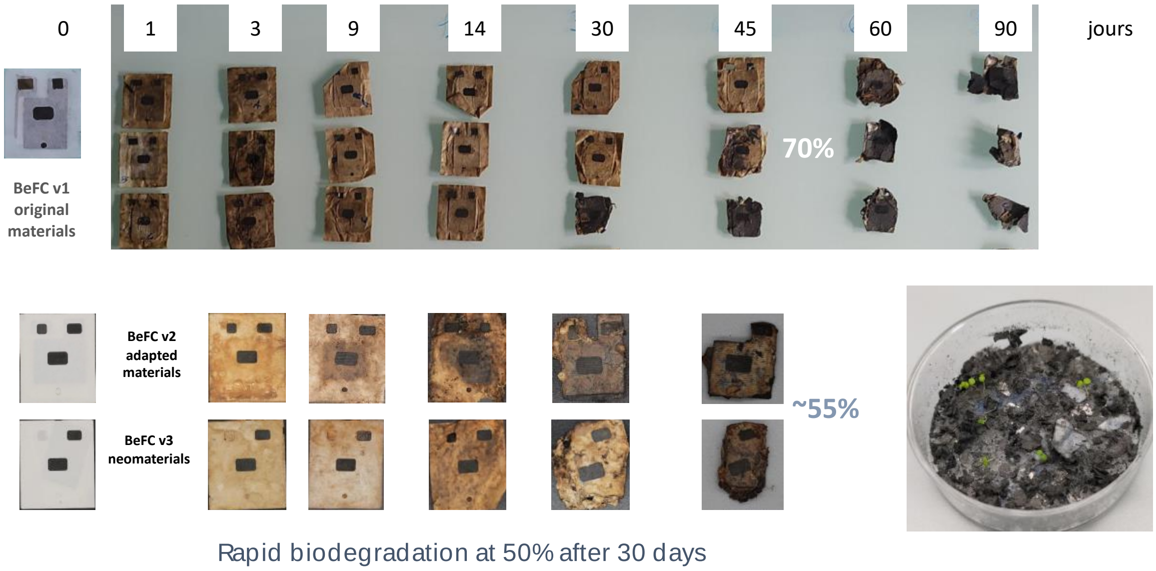


Figure 3 Highlights the use of different materials used in the construction of BeFC's biofuel cell that permit composting (industrial composting following ISO20200).

Sustainability is a key focus for the next generation of products and can be achieved using bio-sourced and/or biodegradable materials.

Table 1 Highlights the different materials used in the construction of BeFC's biofuel cell that permit simple disposal, possible recycling, and composting.

| Type | Disposal route |
|---|---|
| Cellulose | Composting. |
| R-PE | Recycling. |
| R-PET | Recycling. |
| BioPP | Biosourcing. Recycling. |
| PLA | Composting. |
| Carbon paper | Disposal. Recycling. |

# 3 Flexible electronics

## 3.1 Flexible Integrated Circuits (PRAG)

Pragmatic Semiconductor has developed an integrated circuit (FlexIC) platform that doesn't rely on silicon. Our revolutionary technology uses thin-film semiconductors to create flexible integrated circuits that are thinner than a human hair, and are significantly cheaper and faster to produce than silicon chips. This provides a compelling alternative for many mainstream electronics applications, as well as enabling new applications not possible with silicon. Pragmatic's ultra-low-cost, ultra-thin, flexible integrated circuits make it possible to embed our chips into almost anything, bringing connectivity and intelligence to everyday objects. Example applications include radio frequency identification (RFID) and near field communications (NFC), where our chips cost less than a penny and allow these everyday objects to be given unique digital identities as well as interact with their environment. This brings game-changing benefits to the entire product lifecycle, including inventory reduction, traceability, counterfeit detection, proof of provenance, and customer interaction. Pragmatic's technology is a key enabler for a circular economy and supporting sustainability goals, preserving valuable resources by allowing organisations to effectively reduce, recycle and reuse products and materials. Examples include: • Reducing food waste. By adding our chips to food packaging, retailers can use RFID and sensors to determine freshness, better controlling supply chains and enabling dynamic use-by dates. • Recycling materials. Our technology can be used to significantly improve the return and recycling of single-use packaging, for example through Deposit Return Schemes (DRS), which can now be deployed with automated identification to increase availability, convenience and return rates. • Reusing packaging. Our chips enable item-level traceability of multi-use assets within a universal system for recapture, sorting, cleaning, and return.

Underpinning these mass-market use cases, Pragmatic is the world's most sustainable semiconductor manufacturer. Our technology uses 100x less energy and water and has 1000x lower carbon footprint than conventional silicon manufacturing. Pragmatic also offers rapid customization of functionality. We can deliver made-to-order chips from design to production in just a few days rather than several months. We enable designers to create their own application specific flexible integrated circuits at a fraction of the cost and time required to develop custom silicon chips. Our foundry service uniquely allows agile hardware design, exponentially accelerating solution development and time-to market. Examples include proprietary RFID protocols, time/ temperature indicators, fingerprint sensors, wearable smart patches for healthcare, flexible display drivers, and novel microprocessor architectures. We also offer a Fab-as-a-Service model that enables secure, dependable, localized semiconductor supply through manufacturing directly on a customer's site. This highly scalable distributed production allows cost-effective, high-volume fabrication of flexible integrated circuits. Compared to conventional silicon fabs costing billions of dollars, our fabs require 100x lower capital expense and have >100x smaller physical and environmental footprint. Our self-contained modular fabs can be located anywhere in the world, delivering onsite 'just in-time' chip production that meets changing local demand whilst minimizing inventory costs and ensuring continuity and security of supply at a local and national level. Pragmatic is headquartered in Cambridge, UK, with our first fab operating in Sedgefield, and a second fab under construction at our new 15-acre Pragmatic Park site in Durham. Pragmatic has secured over $180 million in funding from venture capital and strategic investors including Cambridge Innovation Capital, Arm (global leader in semiconductor design IP), Avery Dennison (global leader in RFID), and Amcor (global leader in consumer and healthcare packaging).

10 x Lower production cost than conventional silicon manufacturing.

100 x Lower capital expense than conventional silicon manufacturing.

1000 x Lower carbon footprint than conventional silicon manufacturing.

Creating a more sustainable future

"Our company aspiration is simple: to enable as many innovative people as possible to design and manufacture products that solve the global problems we face every day. As a team, we are enthusiastic about everything we do and work hard towards ambitious targets to improve the world by enabling a dramatically new approach to electronics that opens markets not accessible with conventional semiconductor devices."

In all that we do, we endeavor to be a force for good that creates long-term value for all our stakeholders. This includes innovating both in terms of the products we offer and in their manufacturing such that we have a positive impact on everything and everyone around us. We look to the United Nations' Sustainable Development Goals (SDGs) to guide us.

Creating a more sustainable future for our descendants is not a simple task, it will require a wide range of innovations, some of which we have not even thought about yet. We strive to engage with thought leaders that generate novel ways of using our technology to deliver solutions and we continue to be excited about the possibilities ahead. Here we outline just a few of the areas in which we are already making progress.

## 3.2 Roll-to-roll (R2R) processing – Focus on printing & lithography (VTT & FhG)

Roll-to-roll (R2R) processing is an inexpensive and high throughput manufacturing method used to achieve continues flexible electronics on a roll of flexible polymeric foil, particularly for niche markets such as healthcare application.

| Period | Individual/Organization/Location | Description |
|---|---|---|
| 3000 B.C. | Mesopotamia | Round cylinders were used to leave impressions on clay tablets. |
| 1439 | Johannes Gutenberg (Strasbourg, Germany) | Invented the printing press. |
| 1796 | Germany | Lithography was invented. |
| 1843 | Richard March Hoe (New York City, N.Y.) | Invented the first rotary press. |
| 1903 | Albert Hanson (Berlin, Germany) | Filed a patent for a flexible circuit on paper. |
| 1960 | Hoffman Electronics (Los Angeles, Calif.) | First flexible solar cells were manufactured by incorporating thin single crystal silicon wafer cells into plastic substrates. |
| 1968 | T. Peter Brody (Westinghouse Electric Corp. Pittsburgh, Pa.) | Created the first thin film transistors (TFT) on paper strips. |
| 1974 | Michael Foster (Salt Lake City, Utah) | Developed a R2R process for mass-production of holograms using a thermal embossing method. |
| 1976 | RCA Laboratories (Princeton, N.J.) | Researchers created a Schottky barrier solar cell on stainless steel substrate. |
| Early 1980s | - | R2R manufacturing for flexible circuits was introduced in Japan. |
| 1994 | Iowa State University (Ames, Iowa) | Researchers produced TFT circuits on flexible polyamide substrates. |
| Late 1990s | Princeton University (Princeton, N.J.) | Scientists discovered that small-molecules OLEDs could be formed on thin, flexible sheets of plastic. |
| 2005 | National Cheng Kung University (Tainan, Taiwan) | Researchers of the Electrical Engineering department revealed the fabrication of patterned flexible OLEDs on PET substrates using a roller imprint process. |
| 2011 | National Institute of Standards and Technology (NIST) | Nanofabrication was introduced for R2R processing. |
| 2017 | Technical Research Centre of Finland (VTT) | R2R over molding technology was introduced for flexible electronics devices. |
| 2021 | Fraunhofer Institute for Applied Polymer Research IAP | R2R-Net developed R2R production technology used to coat or modify flexible materials such as polymer films, membranes, textiles, ultra-thin glass or metal strips |

Source: BCC Research

Figure 4 Technological milestones for global market for R2R technologies for Flexible devices. Extracted from the BCC Publishing report [13]

The manufacturing of R2R flexible electronics can be accomplished using two specific techniques: lithography and printing. Both techniques are popular in the current market for fabricating flexible electronics on a large scale; however, they differ in their underlying principles and processes.

Lithography involves patterning light-sensitive materials on a substrate using a physical or digital mask and various chemical reactions. This method typically offers high resolution and precision, commonly used in the semiconductor industry for integrated circuits and thin-film patterning on flexible substrates.

Printing is a process of transferring inks or functional materials onto a roll of substrate to create a desired pattern. Although the achievable resolution with printing is lower than with lithography, the low cost of fabrication, higher speed of production, and ability to be applied to various substrates are the main advantages of this technique. Both techniques find wide application in the fabrication of flexible electronics for a variety of applications.

In some cases, a combination of lithography and printing techniques can be employed to leverage the strengths of both methods. Both processing methods are expected to be extensively used in the global market for R2R fabrication of flexible electronics.

Polyimide (PI), polyethylene terephthalate (PET), polyethylene naphthalate (PEN), and polyetherimide (PEI) are the majorly used substrates for the fabrication of flexible electronics in R2R format. These mentioned materials provide sufficient mechanical stability, flexibility, proper heat resistance, ultra-thin texture, and light weight at a low cost. Even though these materials are biocompatible, they are not biodegradable, which opens the door to alternative biodegradable materials in the future of R2R manufacturing for flexible electronics.

The market size of 31.7 billion USD is expected to experience a growth of 8.5% CAGR from 2022 to 2030. In this regard, the fabrication of the display segment accounts for up to 51% of the market due to its extensive use in various electronic devices such as monitors, smartphones, and laptops. On the other hand, flexible batteries are estimated to be the fastest-growing segment, and healthcare is projected to be the most opportunistic segment during the forecast period. This can be attributed to increasing investments in the research and advancement of diverse medical apparatus, including devices for patient monitoring, self-monitoring, and a variety of wearable medical tools. Escalating healthcare costs, coupled with the growing disease burden, are driving the adoption of cutting-edge and technologically sophisticated healthcare devices in healthcare facilities worldwide.

a) Sustainable processing

Sustainability cannot be ignored by any business or new product development process due to environmental impacts related to climate change, resource deficiencies and waste catastrophes. As a new developing industry Printed Intelligence has a valuable opportunity to implement sustainability in all levels. Sustainability could even be the main value proposition for the product or service in some cases.

Printed Intelligence solutions cover a wide range of applications and industries, and the opportunity how sustainability is induced varies. Printing technologies in general have many sustainable advantages compared to traditional production methods through materials, processes, and design. The sustainability aspects of printed intelligence include e.g. the following:

• Mass production is performed mostly in room temperature which can save energy

• Production is done in most cases in normal atmosphere and clean room is not needed

• Production process can be chosen to match the required volume and market demand

• Material consumption is lower compared to traditional processes due to printing of thin layers

• Products are often thin and lightweight, which saves fuel and space required in transportation

• The choice of using different materials as inks and substrates

• The manufacturing technology allows rethinking of the end-product design to minimize e.g. the size of the product or waste generated

Despite many the advantages mentioned above, there are also some generic challenges on ensuring sustainability of Printed products that need to be taken into consideration [14]:

• Material choice: Disposable products should be made of disposable/recyclable/

dissolving/composting materials.

• Often current components have been developed using plastic film PET as the substrate.

• In some applications lead or other harmful or rare metals are used.

• Toxic volatile solvents are needed in some cases which presents an occupational health issue in production.

• Some products require large production volumes to be economically viable, thus the market size should be secured to avoid waste products.

• Process and material development to increase the yield in production.

At VTT, the development of sustainable solutions for printed and flexible electronics market is one of the most important research topics in the electronics manufacturing area. Sustainability is considered starting from the product design to material selection, to manufacturing process and disposal of the end product (Figure 5). The development of sustainable materials is described in the next chapter. Especially important is to find bio-based options to replace traditional plastics as substrates in wearable products.

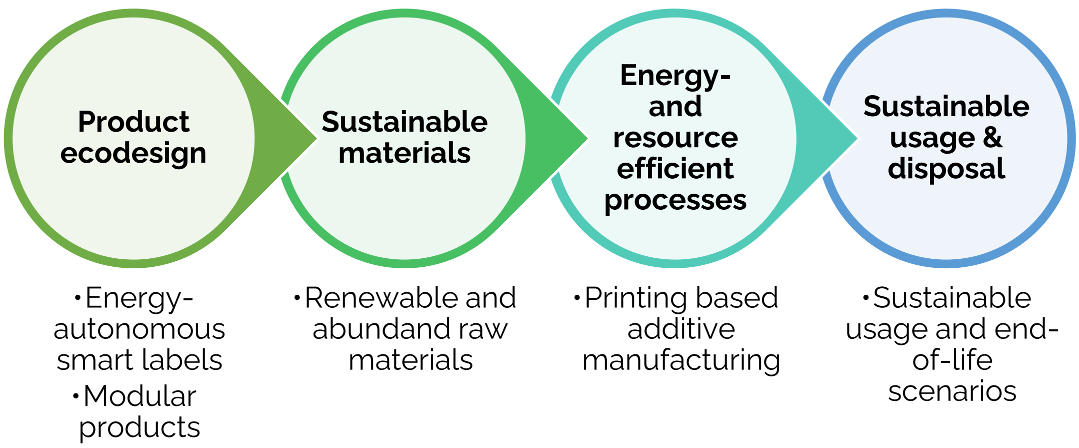


Figure 5 Sustainability aspects of printed electronics

A lot of effort and recent investments at VTT have been put into developing the roll-to-roll –based printing and converting processes further to enable better sustainability and better capability to serve the customers. Roll-to-roll processing enables consistency in quality and scale-up of manufacturing from pilot to manufacturing scale. The use of flexible materials in printing and integration can be performed on large areas by using alternative, sustainable materials. Recently the research focus has been shifted from actual printing processes more to integration processes, including roll-to-roll converting, component assembly and in-line quality control.

The fields of industry that VTT is working in include medical and wellness sector, especially wearable sensors, and diagnostics, with special emphasis on photonics based medical devices. Photonics-based technology breakthroughs and new medical devices enable more versatile, flexible sustained measurement of health, and they also consider comfort of use. With EU-funding, medical photonics pilot line "MedPhab" is active at VTT, together with several other EU partners. In pilot scale manufacturing of medical devices, special attention is addressed to medical device regulations and quality management during development and manufacturing work.

Another important field is the energy industry with organic photovoltaic batteries and integrated heating elements. Integrated electronics in automotive industry is also important.

b) Biodegradable options [15]

There is a constantly increasing number of applications for printed, flexible and hybrid electronic devices, including smart wearables, intelligent textiles, and health monitoring systems. Traditionally, these devices are manufactured by using fossil-based plastics. Due to environmental concerns, there is a high need for bio-based options to replace traditional plastics. Additionally, quantities of electronic waste need to be reduced by developing material recovery and recycling technologies.

VTT has developed a fully biobased and biodegradable substrate for printed flexible electronics. The material is based on nanocomposite of cellulose nanofibril and hydroxyethyl cellulose. On this substrate, it is possible to print conductive inks and assemble electronical components. In a published study, an electrocardiograph (ECG) device was fabricated on the substrate as a technology demonstrator and its performance was confirmed on human volunteers [16].

Table 2 Conventional materials for the fabrication of single-use POCT, LOC and microfluidic devices (adapted from [12]).

| Material family | Associated prototyping & fabrication method | Advantages | Disadvantages |
|---|---|---|---|
| Silicon and glass | Standard photolithography and soft lithography | • Thermal conductivity<br>• Stable electro-osmotic mobility<br>• Resistance to organic solvent | • Higher cost of fabrication<br>• Dangerous chemicals involved |
| Thermoplastics (e.g., PMMA, PC, PS, PET, PVC, ABS, COC, COP) | Injection molding, fusion deposition modelling, laser cutting | • Resistance to alcohols<br>• Mostly low cost<br>• Rapid prototyping<br>• Mechanical recycling | • Unsustainable source of raw materials<br>• Toxic fumes when incomplete combustion (e.g., during laser cutting) |
| Elastomers | Casting roll-to-roll | • Easy and low cost of microfabrication<br>• High elasticity<br>• Gas permeable | • Incompatibility with organic solvents<br>• Absorption of hydrophobic and small molecules |
| Hybrids | Combination of the above methods | • Integration of functionalities | • High cost of fabrication<br>• Complexity in manufacturing |

As other alternatives for traditional plastics for printed electronics, VTT has studied the applicability of several renewable-based substrates and based on the results, the transparency and printability of silver ink was good with all tested substrates [17]. The bio-based alternatives include bio-based PET, poly (lactic acid) (PLA), cellulose acetate propionate (CAP) and regenerated cellulose film NatureFlex TM. Bio-base PLA is currently used SusFE at VTT as the substrate for electrochemical sensors with promising results.

In printed electronics, the demand and need of low-cost highly conductive inks suitable for sustainable mass-production has increased annually. Silver nanoparticle inks are widely used due to high conductivity and good levelling property. However, silver is relatively expensive to be utilized for low-cost applications, but in comparison to gold or similar materials, less expensive. Conductive inks have the highest environmental impact in the printed electronics life cycle. To decrease this impact, commonly used silver inks could be replaced with less impactful materials such as copper or graphite. However, electrical conductivity of copper and graphite inks is lower than silver ink so this might limit the use cases. Furthermore, silver is often a byproduct of mining for other metals, including gold, lead, copper, and zinc. With our approach, we aim to limit the environmental impact by mass-manufacturing on sustainable materials with as green chemistry as possible and decreasing the amount of used materials.

Table 3 Sustainable materials for the fabrication of single-use POCT, LOC and microfluidic devices (adapted from [12])

| Material family | Associated prototyping & fabrication method | Advantages | Disadvantages |
|---|---|---|---|
| Re-cycled plastics (e.g., PMMA) | Injection molding, fusion deposition modelling, laser cutting, hot-embossing | • Readily available<br>• Compatible with conventional manufacturing<br>• Good transparency<br>• Low autofluorescence | • Not biodegradable<br>• Requires plasticizers that cause incineration pollution |
| Natural fibers (e.g., paper, wood, cotton) | Wax printing, coating, laser writing | • Low cost<br>• Readily available<br>• | • Typically limited to 2D microfluidic<br>• No transparency<br>• Limited volume capacity<br>• Fragility<br>• Material with inherent biological, chemical and mechanical variability |
| Bio-based polymers (e.g., CA, PLA) | Injection molding, fusion deposition modelling, laser cutting, hot-embossing | • Sustainable source of raw materials<br>• Resistance to alcohols<br>• Mostly low cost<br>• Rapid prototyping<br>• Mechanical recycling<br>• Good transparency<br>• Low autofluorescence<br>• Readily available | • Limited commercial suppliers for films (e.g., PLA films)<br>• Some manufacturing processes not possible due to degradation while processing |
| Hybrids | Combination of the above methods | • Integration of functionalities | • High cost of fabrication<br>• Complexity in manufacturing |

c) Supply chain

The research and development of R2R technology is carried out by global R&D centers such as CEA-LIT, Fraunhofer EMFT, VTT Technical Research Centre of Finland, Eurecat, Leibnitz Institute for Polymer Research Dresden, and RISE Research Institute of Sweden. The technology integrator companies that are in the intermediate stage after R&D centers are responsible for providing materials, designs, devices for the manufacturing of flexible electronics, components, and sensors for integration. These companies develop, manufacture, and distribute flexible electronic devices, related software, and services to improve the product value. Global companies like BASF, DuPont, and Merck are increasing their investments to enhance the manufacturing of flexible electronics.

The fabricated flexible electronics are used in flexible displays, flexible solar cells, the aviation industry, RFID tags, optoelectronics, and wearable sensors. Major end users or producers of these products are global companies such as NXP, Würth Electronics, Philips, Schneider Electric, Robert Bosch, Samsung Electronics, Solar Frontier, Palo Alto Research Center Incorporated, LG Corporation, Cymbet Corporation, Blue Spark Technologies, Enfucell Flexible Electronics Co. Ltd., Imprint Energy, E Ink Holdings, AU Optronics, and UMS-United Monolithic Semiconductors.

# 4 Cold Plasma Technology

## 4.1 Plasmas in industry: general considerations

Cold plasmas are non-equilibrium, near-ambient temperature excited (partially ionized) gases that can be generated at atmospheric pressure (AP) by applying high voltage (kV range). AP plasmas obviate the need for expensive vacuum systems and can thereby reduce costs. They are useful in numerous plasma-chemical reactions such as ozone synthesis, surface modification of polymers and textiles, abatement of pollutants, and those taking place in excimer lamps. Industrially, cold plasmas can be used to functionalize surfaces of sensitive materials due to their abundant production of reactive species, including high energy electrons, metastables, radicals, and UV radiation; the physicochemical properties of plasma discharges, which will govern the reactivity towards materials and chemical precursors of thin coatings, will strongly depend on the type of discharge, input power and feed gas.

Most of the commercially available industrial plasma systems are corona-type plasma sources. Corona plasmas, typically generated directly in air, comprise many ultra-rapid constricted micro-channels (streamers) that occur pseudo-randomly over the electrode (or dielectric) surface, a charge transfer occurring at each discharge site on the electrodes. The many highly reactive plasma species generated, some of very short lifetime, interact with substrates or chemical precursor molecules; these include "reactive oxygen and nitrogen species" (RONS), for example: hydroxyl $^{\cdot}OH$ and hydrogen $H^{\cdot}$ radicals, superoxide $O_2^{\cdot -}$ anion, singlet oxygen $^1O_2$, hydrogen peroxide $H_{-2}O_2$, nitric oxide $^{\cdot}NO$, nitrite $NO_2^-$ and nitrate $NO_3^-$ ions. The result from the interaction between RONS and substrate materials is the modification of the surface chemistry (functionalization) through incorporation of polar moieties. Resulting changes in surface energy are known to potentially promote adhesion, printability, or wettability of treated surfaces. The effect of surface modification is typically limited in time and is not always sufficient for optimal adhesion promotion. The latter is of course system-dependent (substrate-adhesive combination).

The following Table 4 gives an overview of MPG's competitive landscape. It should be mentioned that most of these companies focus on corona plasmas. Some of these (PlasmaTreat, Acxys, Inocon…) do claim that deposition of thin coatings is possible using their technology. This point will be further addressed in the next sub-section.

Table 4 Competitive landscape: industrial atmospheric pressure plasma systems manufacturers

| Manufacturer | Application of plasma | Turnover (in EUR) | Since | Location |
|---|---|---|---|---|
| Relyon plasma | Activation and cleaning | 6.8 M | 2002 | Regensburg, Germany |
| Femto science | Activation and cleaning | < 5 M | 2005 | Dongtan-daero, Korea |
| Tantec S/A | Activation and cleaning | 6 M | 1974 | Lunderskov, Denmark |
| Henniker plasma | Activation and cleaning | 6.3 M | 2008 | Runcorn, England |
| Diener Electronics | Activation and cleaning | < 1 M | 1993 | Ebhausen,Germany |
| Neoplas GmbH | Medicine - skin treatment - decontamination | 3 M | 2005 | Greifswald, GER |
| CPI (Coating Plasma Innovation) | Activation and limited coating/deposition | 142 k | 2001 | Fuveau, Fance |
| PlasmaTreat | Activation and limited coating/deposition | 40 M | 1995 | 18 sites in Europe, present worldwide, except for Africa |
| Inocon | Activation and limited coating/deposition | 16 M | 1994 | Linz, Austria |
| Acxys | Activation and limited coating/deposition | 6.3 mil | 2000 | Grenoble, France |
| SurfX technologies | Activation and limited coating/deposition | 4.3 M | 1999 | Redondo Beach, CA, USA |

## 4.2 MPG technology: not a traditional industrial plasma solution

Addition of precursors in discharges, using the right process parameters, can lead to the formation of an ultra-thin solid coating; this process is often referred to "plasma-enhanced chemical vapor deposition", or more specifically "plasma polymerization". Corona plasmas offer limited possibilities on that regard, provided the too energetic and too high temperature streamers generated. The latter will lead to excessive fragmentation of precursor molecules, resulting in massive loss or alteration of the functional groups that need to be incorporated in the growing coating.

Grafting of specific and sensitive functional groups on the substrate is rendered possible by MPG technology. This can be achieved by adding chemical precursors, bearing specific functional groups (carboxylic, amine, epoxy, thiol, cyanate…), or even biomolecules, to the plasma discharges. MPG's AP plasma technology is protected by 32 families of patents, for a total of 148 active patents in several regions of the world. MPG's plasma technology consists of a dielectric barrier discharge (DBD) jet designed for the deposition of ultra-thin coating using mostly nitrogen and argon, or less frequently air. It has been designed specifically for the deposition of thin functional coatings. The cold (near ambient T) and homogeneous (glow or Townsend discharges) plasmas generated by MPG jets are milder than the more traditional "corona" plasmas available on the market, both for the substrate and for the chemical precursors. This enables treatment of very sensitive substrates and deposition of truly functional coatings. The injection of chemical precursors – (mostly) in the form of aerosols – occurs only in the afterglow region, therefore preventing "poisoning" of the electrodes due to coating formation in the inter-electrode gap. Another unique and protected aspect of MPG technology is based on the design and manufacturing of nozzles to protect the reactive volume (afterglow) from the surrounding atmosphere, and to process samples with more complex geometries. These aspects differentiate MPG technology from the rest of the market.

The equipment includes atomizers that are used to generate aerosols from the chemical precursors. This permits use of many different types of either pure liquid precursors, or formulations, solutions, suspensions, etc. Compared to traditional plasma-enhanced chemical vapor deposition, the "aerosol-assisted plasma deposition" concept enables the plasma deposition of a significantly larger number of different chemistries, some of which could not be deposited otherwise. Another benefit of aerosols is the relatively high chemical feed compared to vapor deposition processes, leading to a notable increase in deposition rates (by a 10 factor of more), up to industrially viable ones.

A vast range of chemical precursors can be used, in the form of pure liquids, formulations, emulsions, suspensions, or even polymer/oligomer solutions. Families of precursors that can be deposited are numerous, among which: amines, hydroxyls, thiols, organic acids, epoxies, acrylates or methacrylates, aldehydes, silanes, isocyanates, fluorinates, organosilicons, ethers, quaternary ammonium. Biomolecules, such as proteins, antibodies, peptides can also be efficiently grafted onto surfaces, while preserving their integrity. It should be stressed that MPG technology is the only commercially available that can efficiently deposit such a range of precursors.

Other manufacturers (PlasmaTreat, CPI) do claim that deposition of chemical precursors is possible with their equipment, but these are typically limited to organosilicons such as hexamethyldisiloxane (HMDSO) or sister molecules. These molecules call for high energy-per-molecule input and are not to be considered "chemically functional". In this case, streamer-rich plasmas such as corona ones can be used. This is not the case when one wants to deposit sensitive chemical functions or biomolecules.

## 4.3 Objectives in the SusFE project

MPG technology will be used:

- To deposit **adhesion-promoting functional coatings** on flexible substrates
- To deposit **anti-biofouling coatings and biomolecules** such as CRP protein on sensor electrodes

It is too early at this stage of the project to try and position MPG technology versus more traditional corona plasma for adhesion promotion.

As per the deposition of biomolecules and of anti-biofouling coatings, it should be noted that MPG technology is the only commercially available that enables deposition of such nanolayers. Depending on the input plasma power, the process temperature varies. With nitrogen as plasmagen gas, the process temperature ranges from 35°C up to 80°C for very high input. Using argon, the temperature stays close to room temperature (max 35°C). This enables treatment of sensitive substrates and deposition of very sensitive functional precursors, including biomolecules (proteins, antibodies, peptides…).

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