Smart Integrated eXtreme environmenT Health monitor with Sensory feedback for ENhanced Situation awarEness

Deliverable 13.2

Safe-By-Design report

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EXECUTIVE SUMMARY

Background	Aim
The SIXTHSENSE will develop a wearable health monitoring system with closed loop tactile biofeedback, that allows first responders in hazardous situations to sense their current health status. It will allow early detection of risk factors that could lead to rapid deterioration of health or operation capabilities of first responders, by leveraging predictive models based on multimodal biosensor data. As a team management tool, it will enable real-time monitoring of all deployed operatives, helping increase team effectiveness and operational safety. To help accelerate the pace of technological advancements aimed at first responders, beyond the scope of the project, SIXTHSENSE will establish a novel research methodology for sustainable inclusion of first responders in a co-development process.	This report outlines the Safe-by-Design (SbD) concept, its principles and relation to a classic chemical risk assessment, and how it can be adopted within the SIXTHSENSE project, with a special focus on nano-related safety issues. By implementing the SbD concept, safety-related issues are considered already in the design phase from the very beginning, i.e., from the project start. This allows to design innovative materials/processes/products as safe as possible and prevents late development failures.

Approach

By applying the SbD concept, all project-relevant materials, processes and (interim) products that may pose a risk for human health and/or the environment will be assessed, through timely and close interaction with the technical developers. Special focus will be put on nano safety issues, i.e., used nanoparticles in the screen-printed inks.

Findings and results

In summary, the array of sensors described above represents a significant step forward in improving the safety and effectiveness of first responders, particularly those in roles such as firefighting and mountain rescue. The vest continuously monitors wearers´ vital signs, environmental conditions and physical state. The data is transmitted in real time to the central management system, providing a continuous assessment of the overall health and performance of first responders. This facilitates the timely implementation of risk mitigation measures that can potentially prevent accidents, injuries or health-related issues.

ABBREVIATIONS

ECG	Electrocardiogram
EHS	environmental, health, and safety
EU	European Union
HR	Heart rate
K^+	Potassium
Na^+	Sodium
PD	Panic disorder
PTSD	Post traumatic stress disorder
RR	Respiratory rate
SbD	Safe-by-Design
TRL	Technology readiness level

1 INTRODUCTION

This report outlines the Safe-by-Design (SbD) concept, its principles and relation to a classic chemical risk assessment, and how it can be adopted within the SIXTHSENSE project, with a special focus on nano-related safety issues. By implementing the SbD concept, safety-related issues are considered already in the design phase from the very beginning, i.e., from the project start. This allows to design innovative materials/processes/products as safe as possible and prevents late development failures. By applying the SbD concept, all project-relevant materials, processes and (interim) products that may pose a risk for human health and/or the environment will be assessed, through timely and close interaction with the technical developers. Special focus will be put on nano safety issues, i.e., used nanoparticles in the screen-printed inks.

1.1 Project overview

SIXTHSENSE is a multidisciplinary innovation and research action with the overall aim to significantly improve efficacy and safety of first responders' deployment in hazardous environments by optimising on-site team coordination and mission execution. Between the booming EU economy and the climate change, the number and consequences of disasters occurring in inaccessible rural areas is on a constant rise. First responder deployments in extreme conditions such as fighting wildfires or alpine search and rescue missions have gone from exceptional to regular events in only a couple of decades. As this trend is likely to continue, the risks for wellbeing of the engaged first responders continue to grow. To avoid the loss of life or lasting consequences on the first responders' health, it is important that the key physiological parameters of deployed operatives are monitored in a way that provides timely and actionable information, without hindering their operational capacity.

The SIXTHSENSE is a wearable health monitoring system with closed loop tactile biofeedback that allows first responders in hazardous situations to sense their current health status. It allows early detection of risk factors that could lead to rapid deterioration of health or operation capabilities of first responders, by leveraging predictive models based on multimodal biosensor data. As a team management tool, it enables real-time monitoring of all deployed operatives, helping increase team effectiveness and operational safety. To help accelerate the pace of technological advancements aimed at first responders, beyond the scope of the project, SIXTHSENSE will establish a novel research methodology for sustainable inclusion of first responders in a co-development process. A comprehensive framework will allow practitioners to significantly contribute in all stages of the development process, without excessively burdening the first responders with activities outside the domain of their expertise.

This report outlines the SbD concept, its principles and relation to a classic chemical risk assessment, and how it can be adopted within the SIXTHSENSE project, with a special focus on nano-related safety issues. By implementing the SbD concept, safety-related issues are considered already in the design phase from the very beginning, i.e., from the project start. This allows to design innovative materials/processes/products as safe as possible and prevents late development failures.

1.2 Purpose and scope of this document

This report addresses safety using two different approaches that are essential to advancing technology to improve first responder safety, integrates the advances made during the SIXTHSENSE project and gives an outlook on further possibilities. (1) The first approach focuses on mental and physical health and safety of first responder by identifying and analyzing challenges and key risk factors that first responders face both on regular duty and after incidents. These scenarios expose them to extreme physical and psychological stress. Subsequently the psychophysiological stress often manifests itself in mental disorders, such as acute and chronic stress, depression, and post-traumatic stress disorder (PTSD) (Jones, 2017). These stress-related disorders themselves have subsequent impact on the decision making during high-demand emergency situations and therefore impact on first responders' safety in a negative feedback loop (Regehr & LeBlanc, 2017). The Biosensors developed in the SIXTHSENSE project enable early detection of exertion and therefore can prevent extreme states by intervention and subsequently ameliorating the psychological burden followed by physical overexertion and stress. (2) In the second approach the safety of the used materials and articles was assessed by implementing the SbD principles. The development and improvements from alpha to gamma demonstrator were considered where applicable. Not only was the wearer of the demonstrator considered, but also the personnel involved in the production of biosensors. Key areas of this approach include a comprehensive evaluation of the intended purpose of the sensors: their detection capabilities, specific applications, and the risks they address. Additionally, it is essential to understand both the short-term and long-term improvements these sensors provide by monitoring, particularly in relation to physical dangers and the mental disorders. Furthermore, to ensure broad application beyond the specific use cases in SIXTHSENSE, this report will delve into an overview of strategies aimed at mitigating these risks at both the individual and institutional level.

2 METHODOLOGY

By applying the SbD concept, all project-relevant materials, processes and (interim) products that may pose a risk for human health and/or the environment will be assessed, through timely and close interaction with the technical developers. Special focus will be put on nano safety issues, i.e., used nanoparticles in the screen-printed inks.

3 SAFE-BY-DESIGN

Eliminating hazards at the design or planning stage is often easier and cheaper to achieve than making changes further down the process pipeline, when hazards have already become real risks. Thus, throughout the SIXTHSENSE project SbD approaches covering materials, processes and (interim) products respectively were considered.

SbD is advocated as a strategy to enhance innovation capabilities by minimizing late-stage development setbacks. Its effectiveness is evident through numerous ongoing initiatives related to nanotechnology's environmental, health, and safety (EHS) aspects, notably within the European Union (EU) NanoSafety Cluster at the European level. SbD initiatives prioritize the avoidance of hazards and risks rather than managing them as post-exposure concerns. By embracing the SbD approach,

innovators and regulators gain timely insights aimed at achieving minimal risks and preventing adverse product impacts, such as bans (Kraegeloh et al., 2018).

In this report the SbD concept was applied to SIXTHSENSE, a wearable device for first responders to improve safety by enhancing situational awareness. As physiological distress reaches a point of overstraining, it can lead to multiple impacts, including longer recovery time, long-term physical injury, and mental health impairment. Professions involving high levels of physiological stress, such as first responders, represent an example of these challenges.

3.1 Physiological and psychological stress in first responders

First responders are known to regularly experience high levels of physiological stress, often driven by adrenaline, which might cause them to overexert themselves by failing to recognize their own boundaries. This often results in work-related disorders and injuries (Friedenberg et al., 2022) and sometimes even death (Wohlgemuth et al., 2023). Current measures to prevent physical overexertion mainly address preventive actions like enhancing fitness levels (Le et al., 2020). Additionally, there is an intricate combination of mental, emotional, and occupational pressures behind the scenes, that have a negative influence on their general well-being, as well as on their professional performance (see also D6.3). Rajabi's extensive study offers an insightful categorization that addresses the numerous daily stressors first responders experience. From management challenges, including financial burdens and perceived neglect of workplace safety, to the perceived fear of explosions and exposure to life-threatening toxins. The gravity of these factors accumulates over time. The emotional toll of frequent exposure to crucial events compounds the effects of occupational pressures. Such traumatic experiences have a variety of consequences. Symptoms such as irritability, aggression, impulsiveness, and decision fatigue are the direct manifestations (Greinacher et al., 2019; Rajabi et al., 2020). Mental fatigue, which if untreated, progresses into burnout, is perhaps one of the most pervasive and debilitating consequences. A comprehensive study was conducted in 2018 which suggested that burnout is correlating with a substantial decline in compliance to crucial safety practices. This kind of negligence puts not only the affected individual first responder at risk, but also the people they have a duty to protect in danger as also their team joining them in active deployment (Smith et al., 2018). This common condition not only compromises first responders' health, but also negatively impacts their reliability, thereby jeopardizing the high standard of service that communities rely on (Wolkow et al., 2019).

Nevertheless, challenges with mental health are not solely attributed to burnout. There is a link between trauma exposure, highly stressful situations, inconsistent sleep habits, and the many mental health issues that first responders are confronted with (Wolffe et al., 2023). According to a recent study, the prevalence of depression and anxiety among UK firemen is roughly three times higher than that of the general population. These conditions are not exclusive as around 44% of those with mental health problems reported suffering from more than one condition. In this survey, more than 60% of firefighters who took part reported that they suffered from sleep difficulties. Other common mental health disorders which were reported included anxiety, prevalent in approximately 12%, depression in around 10% and PTSD in around 5%. Compared to the general English population, firefighters had significantly higher rates of self-reported depression and anxiety. The study also highlights the importance of understanding the complex relationships between multiple risk factors, such as trauma exposure, lifestyle, and occupational challenges, and how these lead to mental disorders and

impairments in firefighters. The research suggests that further support for mental health and focus on interventions may be required in first responder, emphasizing not only physical well-being but also mental (Wolffe et al., 2023).

In conclusion, there are many aspects which contribute to the relationship between physical exertion and mental health in first responder careers which can lead to a wide range of problems. By understanding these dynamics, it is essential to improve both individual well-being and the effectiveness of essential services such as firefighting. Resources to support and protect those in such roles can have a meaningful impact on their lives and the communities they serve.

3.2 SIXTHSENSE - impact on first responders

This is where SIXTHSENSE steps in, providing prevention support catered to the demanding requirements of first responders. Depending on the needs of the institution and the workforce's preparation, it can be employed in either a long-term or short-term approach. By targeting the specific factors SIXTHSENSE is addressing, it can play an instrumental role in enhancing physiological and psychological well-being without extensive calibration required. It provides a more immediate and streamlined method for dealing with first responders physical and mental health challenges, contributing to both their well-being and the overall performance and reliability (see figure 1).

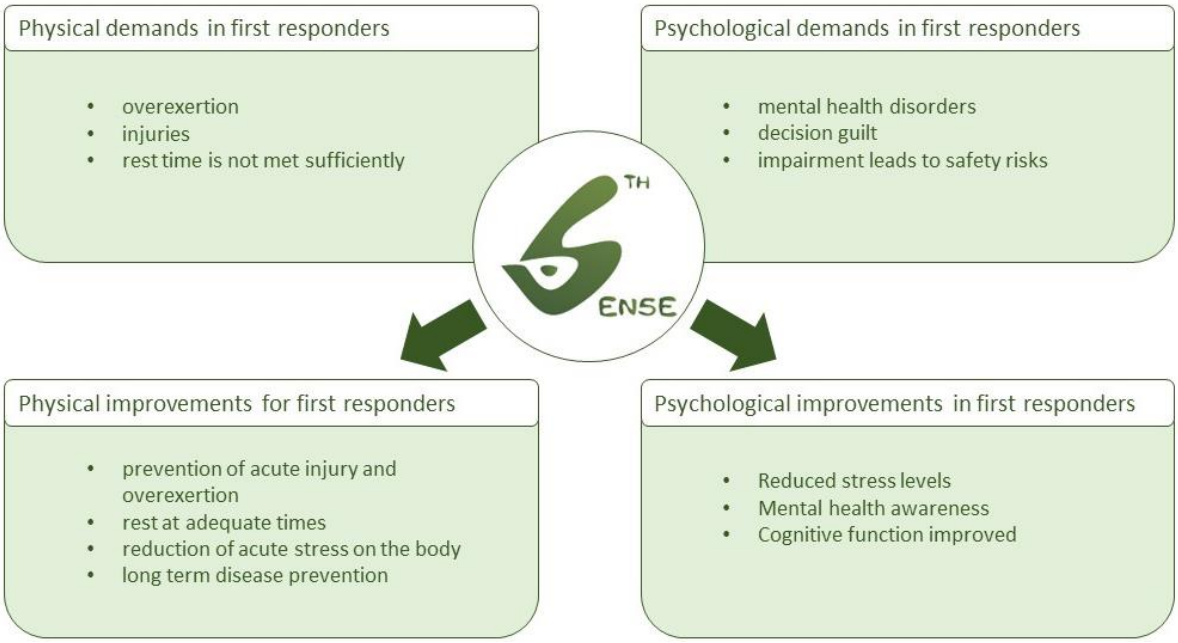

Figure 1: SIXTHSENSES´ impact on first responders physical and psychological safety and well-being

The report compiles observations drawn from multiple viewpoints, offering an overview of the developmental progress, and presenting recommendations for the safer development of innovative products as well as the impact on both direct user safety and mental health prevention due to sensor-based remote diagnosis. In the following segments, the functionality and significance of various sensors used to track crucial health parameters (as described in D9.7 showing the gamma demonstrator) are described and their safety is considered as well. Additionally, improvements from alpha – over beta – to gamma prototype are considered. The sensors in the gamma demonstrator include integrated sensors for electrocardiogram (ECG) acquisition, a temperature sensor, removable

bio sensing pad and stimulation electrodes pad. While the minimally invasive sensor for lactate measurements using a microneedle, is not part of any of the demonstrators, its safety was assessed within this report.

3.2.1 Non-invasive sensors for Cortisol, Lactate, Sodium (Na^+) and Potassium (K^+) monitoring to assess fatigue, stress and hydration

The specific concerns according to the SbD concept for the sensors developed by Tecnalia are described in the following table 1. The safety of first responders was set in a physiologically relevant context for emergency deployment describing the biosensors impact individually (table 2-5). The sensor is comprised of a patch, which is attached to the users´ chest.

Table 1: SbD considerations and development strives from all demonstrators for the biosensor for Cortisol, Lactate, Sodium (Na+) and Potassium (K+) monitoring to assess fatigue, stress and hydration)

SbD considerations for removable chest pad for Cortisol, Lactate, Sodium (Na^+) and Potassium (K^+) monitoring
The sensor has no direct contact to the users´ blood flow, but is attached via direct skin contact. The partner is aware that for determining the occurrence of exchange/absorption of particles from the sensor, a leaching test according to ISO 10993 is warranted. The same holds true for general dissolving of substances from the material, which requires further investigation to make a definite statement. All critical substances which were used are defined and classified according to ISO 14971 and 10993 in D9.11. Additionally, a concern the partner is aware of regards the use of solvents in the production process of screen-printed electrodes, hence safety precautions are taken to protect involved personnel at the relevant steps. The application of current for measurement of the biomarker lies in the mA to µA range, and is hence negligible and poses no safety concern. The beta demonstrator incorporated sensors for cortisol, lactate and Na^+ measurement. The gamma demonstrator incorporated lactate, Na^+ and K^+ sensors. During beta demonstrators´ biocompatibility tests (D9.6) cytotoxicity of materials was investigated and samples were classified. Even tough, after a structured biological evaluation plan considering a risk management process performed in D9.11, it was stated that for the biological evaluation plan and given the nature of body contact through the skin and contact duration of the gamma prototypes, the ISO 10993-1: "Biological evaluation of medical devices- Evaluation and testing within a risk management process" will recommend the following endpoints for the biological evaluation: Irritation according to the ISO 10993-Part 23. Following this recommendation, pHEMA-based material tested in D9.6 gave non-irritant results. While acrylamide showed no cytotoxicity, it was omitted as material of choice in the gamma demonstrator to omit possible safety concerns as it has been implicated in cancer genesis a (Klaunig, 2008; Rice, 2005). Instead, pHEMA-based material was chosen as protective layer because it was non-irritant in D9.6 and, even with a change in composition, after the analysis of risk performed in D9.11 it was stablished as a safe material. Na^+-ISM membrane was intended to be used in beta and gamma prototype. Cytotoxic assays were performed on a Na^+-ISM deposited on top of an electrode and it resulted cytotoxic. Although that fact, it was recommended to perform irritation assays instead of cytotoxic ones because of the nature of contact. and is listed along all other components that are in direct contact with first responders´ skin in D9.11. Regarding the sensor development the beta Na^+ sensor showed issues with correlation and reproducibly with iontophoretic extraction, hence was exchanged for the alpha electrode prototype in the gamma demonstrator. Also, as the reader is not capable to perform OCP measurements, the Na-ISM membrane is avoided. Instead of using a selective membrane, ions are

detected through changes in sweat ionic strength with impedimetric and voltametric techniques. Because of this change, non-irritation assays were performed in D9.11 for Na^+-ISM membrane. The used anti-cortisol antibody was replaced by a nanobody due to size issues in the technical application of the sensor. A certificate of analysis was provided by partner InnoProt for the Anti-Cortisol Nanobody. In this certification the plasmid construction, protein expression and the specificity to detect cortisol is detailed.

Table 2: Advantages and safety concerns regarding cortisol monitoring in first responders

Cortisol monitoring in first responders for enhancing safety in first responders	
Physiological description	Cortisol is causally involved as a stress hormone in human bodies´ reaction to acute and chronic stress. During the acute fight-or-flight response the sympathetic nervous system releases adrenaline, which leads to subsequent glucose release. If the body senses persisting danger/stress cortisol is released to keep the fight-or-flight response active. Once cortisol levels drop, the stress reaction and the effects on body function subside and the activation of parasympathetic nervous system follows (Russell & Lightman, 2019).
Relevance for first responders	While acute cortisol spikes are necessary first responders to physiologically adapt to high-demand situations, constant high levels of cortisol can reverse its beneficial effects and even contribute to the development of maladaptive processes, such as physical diseases (metabolic syndrome, cardiovascular disease and higher risk for infections), but also mental disorders (Russell & Lightman, 2019).
Suggested interference	Definition of maximum duration for cortisol peaks is suggested to avoid possible overexertion while a first responder stands under the influence of the fight-or-flight response. As an intervention it is proposed to communicate a command for more frequent breaks to the first responder once the high-alert status is not of utmost relevance for the emergency deployment and the situation allows to safely rest. Whatever intervention is chosen to be followed through with, one must consider the time of day when assessing cortisol levels as well. Cortisol levels exhibit a 24-hour circadian rhythm, with levels being at its lowest at the early phases of sleep (late evening) and a spike when an individual is waking up (early morning) (Mohd Azmi et al., 2021), which should be considered during monitoring.

Table 3: Advantages and safety concern regarding lactate monitoring in first responders

Lactate monitoring in first responders for enhancing safety in first responders	
Physiological description	Lactate, the salt of lactic acid, is produced during the anaerobic breakdown of glucose, particularly in skeletal muscles in physical high-demand situations. While it has been seen as the culprit and implicated in muscle fatigue, this concept is more recently being challenged (Cairns, 2006).
Relevance for first responders	Elevated lactate levels can indicate overexertion of skeletal muscle or oxygen deprivation. Monitoring lactate is vital in high-intensity environments, such as high-stress occupations. The role of lactate in the pathophysiology of delayed onset muscle soreness further highlights its significance (Sonkodi, 2022). Recognizing increased lactate levels early in their rise will aid decisions

	regarding rest and activity balance, potentially preventing injuries and ensuring continued optimal physical performance. However, there are some limitations regarding measuring Lactate in sweat, which may pose a safety concern if first responders rely on the measure too intensely. Sweat lactate has been shown to exhibit poor correlation to blood lactate levels (Derbyshire et al., 2012), making it a suboptimal biomarker for measuring physical exertion. Lactate in sweat is rather a byproduct from sweat glands and, hence, independent of blood lactate (Green et al., 2000). However, elevated **levels of lactate in sweat, alongside glucose, magnesium, creatinine, Na^+, K^+ and chloride were found in patients with panic** disorder (PD) (Kukumberg et al., 2009). Nonetheless, this makes sweat lactate an interesting target biomarker for detecting enhanced mental pressure, rather than physical exertion in first responders.
Suggested interference	It should be considered to develop a threshold of maximum lactate production in sweat over time. Additionally set strategies should be in place to allow for optimal recovery. The best-case scenario would be to prevent overexertion altogether by interfering before threshold levels are reached and hence avoiding an anaerobic state during demanding emergency deployment by downregulating first responders´ physical activity.

Table 4: Advantages and safety concern regarding sodium (Na^+) monitoring in first responders

Sodium (Na^+) monitoring in first responders for enhancing safety in first responders	
Physiological description	Na^+ concentration in the human body is maintained at 135 – 145 mM. If Na^+ concentration falls beyond or above this range severe organ damage is the consequence (Noda & Matsuda, 2022).
Relevance for first responders	High physical demand during emergency deployment goes hand in hand with sweating in the setting of thermoregulating. Via this path not only water is lost, but also Na^+. This is especially apparent in hot environments like those experienced by fire fighters (Bates & Miller, 2008). As it has been shown that Na^+ loss differs between environments regarding the surrounding temperature, the constant monitoring via the developed sensor will allow for targeted intervention.
Suggested interference	First responders should be closely monitored via the Na^+ sweat sensor and alerted in case of excessive Na^+ concentration in their sweat, indicating enhanced Na^+ loss. Counteract can be achieved by reducing physical activity, and therefore reducing the sweating rate, which will coincide with reduced Na^+ loss. Additionally, electrolytic beverages should be part of standard deployment equipment and consumed upon need (Shirreffs & Sawka, 2011). Importantly, the correct beverages should be chosen here, as consumption of plain water may lead to further aggravation by plasma dilution and put the first responder into hyponatremia, while consumption of high-sugar drinks would lead to excessive consumption of energy fuel (Bates & Miller, 2008). As Na^+ plays a crucial role in transmitting nerve impulses and muscle contractions, the stabilization of Na^+ levels ensures that nerve and muscle functions return to their optimal state. This means better reflexes, muscle coordination, and cognitive clarity (Bates & Miller, 2008).

Table 5: Advantages and safety concern regarding potassium (K^+) monitoring in first responders

Potassium (K^+) monitoring in first responders for enhancing safety in first responders	
Physiological description	K^+ has key functions in maintaining numerous cellular functions. Physiological levels under normal conditions are mostly controlled through excretion via kidneys in respect to changed K^+ intake. Further distribution of K^+ stands under hormonal control (Palmer & Clegg, 2016). Upon physical demand muscles release K^+, which consequently leads to an increase in plasma K^+ concentration (Palmer, 2015). However, under physiological conditions a balance is ensured.
Relevance for first responders	In hot environments the loss of K^+ is aggravated via excessive sweating, which is potentially causally involved in the development of heat illness (Malhotra et al., 1976; Palmer & Clegg, 2016). The condition of severe K^+ depletion is termed hypokalemia and leads to muscle weakness and fatigue, which poses a potential hazard in emergency deployment scenarios.
Suggested interference	Strategies for treating hypokalemia include administration of K^+, without additional glucose or bicarbonate administration to avoid unwanted distribution in cellular compartments. As cardiac emergencies are highly associated with K^+ depletion, the ECG should be carefully monitored to immediately spot tachyarrhythmias should they arise (Palmer & Clegg, 2016). K^+ excretion (at least via kidneys) stands under circadian control, which should be considered when evaluating measured levels by the sensor (Gumz & Rabinowitz, 2013).

3.2.2 Non-invasive sensors for body temperature, posture, and cardiopulmonary monitoring

The sensors for body temperature, posture and cardiopulmonary monitoring are independent of each other and SbD considerations are shown in table 6. The sensors comprise an electrode for body temperature (table 7), for electrocardiogram (ECG) acquisition, which can detect heart rate (HR) and HR variability, as well as a full the respiratory rate (RR) (see table 8). The sensor for monitoring body posture is described in table 9. In table 10 the electro tactile feedback system is considered

Table 6: SbD considerations and development strives from all demonstrators for the biosensor for body temperature, cardiopulmonary monitoring

SbD considerations for wearable sensors for body temperature, posture and cardiopulmonary monitoring
HR monitoring using ECG electrodes and body temperature measurements are well established methodologies that pose no safety concern for the user to the current knowledge. A questionnaire filled out by the developing partner confirmed that the electrodes will have direct skin contact, but are entirely noninvasive with no mentioned safety concerns in the use or production. Further as reportedly no nanomaterials were used in the production, there is no concern regarding nanosafety. However, it should be noted that the interference of materials with the environment are warranted to be subject of further investigation. The in D5.4 described sensor for ECG measurements (beta tests) was not part of the final product as the sensors described in D9.12 were chosen for integration in the final prototype. Regardless, the conductive layer of the not used sensor was made of Ag/AgCl (Henkel Electrodag 6037E SS), with an insulation coating (Henkel

Electrodag PF-455B) covering the conductive leads, while sensing working and counter electrodes are covered with a layer of conductive carbon (Henkel Electrodag 440 B). The contact part for skin would have been covered in a commercial hydrogel.

Table 7: Advantages and safety concern regarding body temperature monitoring in first responders

Body temperature monitoring for enhancing safety in first responders	
Physiological description	Physiological human body temperature is controlled at 37°C. Only little deviation is allowed which still allows for normal functioning without acute and lasting damages (33.2 to 38.2°C, if one includes even oral measurements making the spectra a bit broader than core temperature measurements) (Sund-Levander et al., 2002; Tansey & Johnson, 2015).
Relevance for first responders	First responders are often subject to extreme temperatures, ranging from extremely low temperatures for mountain rescuers during winter, to extremely high temperatures for fire fighters in active deployment during forest fires. Exercise-heat stress is a major disruptor of physiology, leading to impaired thermoregulation, hydration, ion balance and in extreme cases even cardiac homeostasis (Périard et al., 2021; Trangmar & González-Alonso, 2019). Recognizing early signs of hypo- and hyperthermia and other heat-related illnesses, such as heat exhaustion or heat stroke is crucial in ensuring first responders´ safety.
Suggested interference	If the biosensor detects changes in body temperature, behavioral adaptations are warranted immediately: Immediate cooling/controlled rewarming, rehydration, and pauses in better suitable environments (Flouris, 2011). Additionally, to improve the potential to act on imminent threats, first responders should be regularly made aware of prevention methods such as regular breaks, staying hydrated, removing heavy equipment when possible in educational trainings (Kenny & McGinn, 2017).

Table 8: Advantages and safety concern regarding electrocardiogram (ECG) monitoring of the heart rate (HR), its variability and the respiratory rate (RR) in first responders

Electrocardiogramm (ECG) for heart rate (HR) a respiratory rate (RR) monitoring for enhancing safety in first responders	
Physiological description	HR and HR variability provide vital information about the autonomic nervous response (Kleiger et al., 2005). It can be affected by different levels of physical exertion (Aubert et al., 2003). The RR is also a crucial indicator for pathological conditions and stressors (Nicolò et al., 2020) and a good indicator not only for actual exertion, but importantly perceived exertion (Nicolò et al., 2017). Resting and maximum HR and RR greatly vary from individual to individual and depend on multiple factors, including age, sex and fitness.
Relevance for first responders	HR and RR monitoring can add a new essential layer of safety for first responders in high-intensity situations, where rates surpass physiological ranges for an extended time frame, which can signal stress or overexertion. Moreover, regular HR monitoring assists in early detection of underlying heart issues and supports overall cardiovascular health and sleep quality if interventions are set in place. The relationship between impaired sleep and

	alterations in HR variability during stressful tasks emphasizes the intricate connection between sleep, stress, and heart function. This emphasizes the importance of comprehensive monitoring in maintaining a balanced physiological state (Chalmers et al., 2022). Rapid and/or shallow breathing can not only indicate distress or anxiety, but also be caused by environmental stress (Tipton et al., 2017). Fire fighters particularly have been shown to engage in voluntary hypoventilation during training and deployment (Hostler & Pendergast, 2018). Additionally, the sensor can detect the QRS complex, which could give further information on cardiac health during active deployment. However, that is currently not of interest for the involved partners.
Suggested interference	Being aware of first responders stress and physical exertion levels will aid in making better informed decisions. Exercise level adjustment during emergency events to keep HR and RR in a physiologically interval will help to prevent overexertion and subsequently reduce recovery times. Additionally, to interventions regarding the deployment itself, first responders should be trained in breathing techniques which can help in controlling HR levels acutely (Laborde et al., 2022; Malhotra et al., 2021).

Table 9: Advantages and safety concern regarding body posture and movement monitoring in first responders

Monitoring of body posture and movement monitoring for enhancing safety in first responders	
Physiological description	Posture is defined as the position of the body in its environment and relies on the human anatomy to maintain balance also during dynamic movements (Carini et al., 2017).
Relevance for first responders	Poor posture can lead to discomfort and eventually even to lumbar spine injuries (Du et al., 2023). Occupational low back pain is highly prevalent in professionals required to carry out heavy or repeated lifting (Pope et al., 2002). The predominant non-fatal injuries in first responders (specifically fire fighters) are stemming from overexertion resulting in musculoskeletal disorders. Misalignment or inefficient movement patterns can lead to overuse injuries and chronic pain, especially when firefighters are involved in physically demanding roles like repetitive motions or heavy lifting (Yunus et al., 2022). Monitoring the body posture and movement ensures correct body alignment and movement.
Suggested interference	Regular monitoring and real-time feedback can ensure correct body alignment and efficient movement patterns, which can prevent injuries in the long run.

Table 10: Advantages and safety concern regarding the electrotactile feedback module in first responders

Electro tactile feedback enhanced communication for first responders	
Technical description	The electro tactile feedback system consists of two main components: • stimulator device • electrode for electro tactile stimulation of the wearer

	Therefore, the system is divided into an active part with connection options for data transmission and energy supply and a passive counterpart in form of electrodes that perform the actual stimulation on the body.
Relevance for first responders	The basic principles are based on the idea of forwarding information via tactile feedback to the first responder, who can sense the information reflected to him. The electro tactile feedback module is connected via a patch on the upper body and used as a communication medium. The signal is generated by electrical stimuli that can be felt at direct skin contact. The electrodes on the patch can generate different patterns with different meanings, which can be interpreted by the first responder after initial training on the signals.
General safety of the system	Regarding the stimulation device and used current a dedicated regulatory roadmap was created and serves as a guiding document for further development towards higher TRLs of the described technology. Since the electro patch has direct contact with the skin, the materials must be skin-compatible to avoid skin reactions/irritations.
SbD considerations for the electro tactile stimulation system	Despite biocompatible raw materials, the production process may chemically/physically alter the materials, potentially negatively influencing their skin compatibility. For this reason, this should be addressed in a dermatological test using the final product (e.g., as part of the series launch and process validation). In this test there should be an additional phase considering potential impact of cleaning/sterilization processes, which can leave endotoxin residue on the product.

3.2.3 Minimally invasive sensors for monitoring lactate and glucose in interstitial fluid

SbD considerations regarding the microneedle-based sensor are shown in table 11. The sensor can measure lactate (for lactate-specific considerations regarding enhanced safety of first responders by continuous monitoring also see table 3) and glucose (table 12).

Table 11: SbD considerations and development strives from all demonstrators for the microneedle-based biosensor lactate and glucose monitoring

SbD considerations for microneedle-based monitoring of lactate and glucose
While the used microneedle used in this sensor is minimally-invasive and bares little risk for lasting damage, the following safety concerns should be noted: any damage to the skin harbors the risk for transmitting an infection, either via the inserted device, in this case a microneedle which was potentially mishandled and no longer sterile, or via pathogens on the recipients' skin, due to improper cleaning of application site, that entered the body with the device. While this poses a risk, *in vitro* studies have demonstrated that the risk for infection by microneedles is considerably lower compared to conventional hypodermic needles. They also showed that no microorganisms crossed the epidermis and therefore concluded that in healthy users, who are immunocompetent are at negligible risk to contract local or systemic infections (Donnelly et al., 2009). A recent review on the safety profile of microneedling (as a collagen and elastin proliferation stimulating technique) similarly concluded a minor risk, but highlighted the importance of caution regarding already infected users and darker skin types (Chu et al., 2021). Therefore, a two-way approach using preventive and aftercare interventions to minimize the risk of the use of minimally invasive

microneedles is proposed: (1) The application site should be properly cleaned by using suitable skin disinfectants (Boyce, 2019) and the person applying the device should be trained and sensibilized for aseptic techniques. Additionally, the device production should adhere to medical product legislation regarding aseptic production and packaging. (2) The application site should be monitored in predefined intervals by the user, who was previously trained in detecting signs of infection (redness, swelling, ulceration, pain)[1].

Table 12: Advantages and safety concern regarding glucose monitoring in first responders

Glucose monitoring for enhancing safety in first responders	
Physiological description	Glucose is the major energy catabolite for human cells and the control of glucose levels within a physiological range. Blood glucose levels vary throughout the day and depend on activity level and food intake. In high-demand scenarios, such as intense physical labor, the demand for glucose rises in the skeletal muscles. Hence glucose is mobilized to supply the emerging need (Suh et al., 2007).
Relevance for first responders	While variation of glucose levels is typical to a certain degree, levels reaching the upper or lower end of the physiological spectrum can potentially have harmful impacts. During prolonged exercise, as necessary during first responders´ deployment, the increased strain on skeletal muscles results in an increased demand for glucose, which is met by enhanced glucose mobilization and hence results in raised blood glucose levels (Suh et al., 2007). While acutely this is necessary to meet the physiological needs under enhanced physical strain, on the long-term elevated blood glucose levels, as also seen upon chronic stress (Chen et al., 2020; Lloyd et al., 1999), can lead to overall poor glycemic control and subsequently diabetes manifestation (Kabeya et al., 2012). Hypoglycemia on the other hand occurs rarely among the healthy population, with an exception being detected under extreme physical strain (Muneer, 2021). Measuring glucose in the interstitial fluid, which correlate closely with blood glucose concentrations (Jarvis et al., 2023), allows the continuous monitoring of first responders metabolism.
Suggested interference	High blood glucose: If the sensor detects elevated glucose levels a break should be taken as the immediate requirement for excess energy will decrease. Taking a break allows the body to stabilize and start using the glucose in the bloodstream, while not sourcing additional glucose through mobilization. Low glucose levels: An established form of restabilizing blood glucose is the consumption of easily available carbohydrates, hence first responders should be equipped with snacks or glucose gels to address any rapid drops in blood sugar.

3.3 Holistic impact of integrated monitoring on health and abilities in first responders

3.3.1 Injury prevention

With the physically strenuous nature of firefighting, amplified by psychological stress and increased occupational demands, first responders are particularly prone to overexertion injuries. Well-being and safety of first responders play an indispensable role in the protection of life and property. Overexertion and musculoskeletal conditions have been identified as the most frequently occurring impairment of health (Le et al., 2020). A more in-depth analysis revealed that two of the largest fire services in the USA underlined these findings, as they found 54.1% of occurring injuries were caused by overexertion. Continuous monitoring of health parameters during active deployment will eventually give rise and/or support a data-drive strategy for injury prevention, which will be crucial in preserving the well-being of first responders. In addition to the acute use of SIXTHSENSE in active deployment it could be considered to employ the product in regular physical testing for first responders, to possibly detect issues before they arise in an emergency.

3.3.2 Long-term prevention disease prevention

Shift workers and individuals exposed to high occupational strain, including first responders, are at higher risk of developing a set of adverse health outcomes. Individuals of the described category are more susceptible for developing cardiovascular disease (Frost et al., 2009; Moretti Anfossi et al., 2022), stroke (Brown et al., 2009), gastrointestinal issues (Knutsson & Bøggild, 2010) and prostate (Kubo et al., 2006) and breast (Manouchehri et al., 2021) cancers. Adjusting long-term stress levels and allowing for improved recovery time may improve the outcome for first responders regarding long-term disease events.

3.3.3 Sleep and recovery

High quality sleep can promote improved mood and overall health, while also reducing susceptibility to mental disorders (Palagini et al., 2022). For individuals in high-demand professions, such as first responders, sleep quality is not just a matter of wellbeing, but a key component of recovery and preparedness (Brown et al., 2020). The relationship between sleep quality and alertness emphasizes a potential risk: poor sleep can lead to reduced alertness and reduced productivity, affecting both safety and effectiveness in critical roles (Ganesan et al., 2019). A combination of monitoring techniques including cortisol provides a deeper understanding of the occurring stress during shifts, which has impacts on the quality of sleep (De Nys et al., 2022). Recent research by Wolffe and colleagues reveals a complex relationship between firefighters' exposure to trauma, irregular sleep patterns, and specific mental health disorders. Firefighters experiencing insomnia were found to have statistically significantly higher occurrences of mental disorders, such as PTSD and PD, along with increased risk for alcohol abuse (Wolffe et al., 2023).

3.3.4 Cognitive function and situational awareness

The occurring stress during shift work, as also the often-impaired quality of sleep, relates to tiredness during work, which ultimately poses a safety risk. Interrupted and irregular resting periods have impact on daytime function, in (Brown et al., 2020). Further it has been shown that sensory memory and attention is more often impaired in shift workers (Gumenyuk et al., 2010). Together, this results

in increased risk for work related accidents (Brown et al., 2020). Monitoring health parameters may give a better overview of current cognitive function, as numerous of the sensors are sensitive to parameters implicated here.

3.3.5 Mental health

Beyond the acute use of SIXTHSENSE as a direct preventive measure to reduce stress, it is advisable to implement healing methods once it becomes apparent that stress levels have escalated. Social support from supervisors and coworkers has been found to positively influence resilience, motivating firefighters by fostering a sense of belonging within the organization (Bernabé & Botia, 2016). However, there unfortunately is a lot of stigmata concerning mental health in the firefighter community (Huang et al., 2023). Therefore, it is crucial to address the underlying stigma that still prevents affected people from seeking and accepting required assistance. This includes presenting available options in a way that emphasizes the positive impact on their work and personal life.

Strategies on the individual level:
Rather than providing a universally applicable answer, it is essential to offer different options. It would improve the acceptance among individuals if they feel in control and not pressured into any sort of intervention or therapy. Offering online resources would also be an appealing option because they are easily accessible, often anonymous, and customizable. Considering the stigma that exists in this context, maintaining anonymity can be especially crucial. Regarding hands on teaching, learning techniques for managing anxiety, such as deep breathing, meditation, and progressive muscle relaxation, can be useful tools for individuals in high-stress jobs. However, regular psychological evaluations should be promoted and considered to become mandatory. First responders should also be able to detect early signs of stress, depression, or PTSD through these evaluations and partly individually by enhanced education in the field. Additionally, a healthy work-life balance with defined periods of adequate rest should be enforced.

Strategies on the institutional level:
Regarding the actual shift work, constantly changing, long or unpredictable shifts can be a significant source of stress. By providing more consistent or predictable shift rotations, work-induced stress can be managed in a better way on an institutional and individual level subsequently. To further improve physical and psychological safety and confidence, first responders should be adequately equipped in all situations and trained for high-risk situations, which can significantly reduce potential trauma and stress (Rajabi et al., 2020). Further, moral distress in the form of decision guilt, which often occurs in public safety personnel, as morally challenging decisions must be made quickly in stressful situations (Lentz et al., 2021), could potentially be ameliorated by improving “mental aftercare”. In regard of the institutional stigma for seeking mental health support the open participation of leadership personnel in mental health programs will reduce the associated stigma. An independent body that periodically reviews mental health provisions in these departments can ensure that the necessary care and resources are being provided, holding institutions accountable. Creating an open channel where professionals can share their feedback about their mental well-being or on areas, they feel need additional focus can be a valuable tool in understanding and addressing issues.

4 CONCLUSIONS

In summary, the array of sensors described above represents a significant step forward in improving the safety and effectiveness of first responders, particularly those in roles such as firefighting and mountain rescue. The vest continuously monitors wearers´ vital signs, environmental conditions, and physical state. The data is transmitted in real time to the central management system, providing a continuous assessment of the overall health and performance of first responders. This facilitates the timely implementation of risk mitigation measures that can potentially prevent accidents, injuries, or health-related issues.

The seamless integration between the vest and the central management system promotes improved communication and coordination between team members and command centers. This increased connectivity improves situational awareness and decision making. As a result, emergency response becomes more efficient and resource allocation in critical situations becomes more agile. This technology underlines the commitment to the safety and well-being of first responders and recognizes the physical and mental demands of their role. It equips them with the tools they need to maintain peak performance and minimize the risks associated with their duties.

In the field of emergency response, the development and adoption of such advanced technologies is essential to improve effectiveness and resilience. Continued research and development efforts in this area are essential to ensure the continued safety and well-being of first responders, who are an integral part of protecting and serving our communities and SIXTHSENSE is part of this journey.

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