KIFFIK Biomedical, Inc.

A Novel ISF Access Device for Continuous and Non-Invasive Biological Sampling

Medical Technologies Innovation Facility
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At the time of release, KIFFIK EXP is not FDA-cleared and are intended for investigational purposes only.

EXECUTIVE SUMMARY

UNMET NEED

Late diagnoses in oncology and chronic diseases lead to poorer patient outcomes and higher lifetime healthcare costs. Earlier detection through minimally invasive, repeatable sampling could enable earlier intervention, risk stratification, and broader-scale optimisation of therapy. Modern liquid biopsies and blood-based screening methods are effective. Still, they can be limited by low signal-to-noise ratios in early disease stages and logistical challenges associated with frequent testing (Passaro et al. 2024).

OPPORTUNITY IN INTERSTITIAL FLUID (ISF)

ISF, the extracellular fluid that bathes tissues, reflects local tissue biology and has a composition similar to that of plasma. It provides access to proteins, metabolites, nucleic acids, cytokines, and other biomarkers that indicate dynamic, site-specific molecular changes. Its proximity to the tissue microenvironment makes it suitable for early signal detection and long-term monitoring with wearable or near-patient methods (Wu et al. 2024).

BARRIER TO DATE

Routine ISF access has been limited by methods that are either invasive or operationally complex (e.g., suction blisters, microdialysis, microneedles), which restricts throughput, patient comfort, and real-world deployment (Saifullah and Faraji Rad 2023). These methods also pose a risk of sample contamination, with one study noting that applying a vacuum to the micropores created on the skin by microneedles can contaminate ISF with blood (Saifullah and Faraji Rad 2023)

KIFFIK'S APPROACH

KIFFIK's electroporation-based platform creates temporary microchannels in the outer skin, allowing non-invasive, repeatable ISF extraction through a compact, wearable system designed for remote or point-of-care use. Compared to traditional methods, electroporation offers improved comfort, ease of use, and scalability for frequent sampling and decentralised trials.

IMPACT FOR INVESTORS AND THE NHS

If validated in prospective studies, ISF access *via* electroporation could (i) broaden biomarker discovery in tissue-proximal fluid, (ii) improve early detection programmes, (iii) support decentralised clinical trials and remote monitoring, and (iv) complement blood-based diagnostics and liquid biopsies, potentially reducing system costs while expanding screening reach and compliance (Wu et al. 2024).

CONTENTS

1. INTRODUCTION

1.1 THE IMPORTANCE OF EARLY DETECTION

Across oncology and major chronic diseases, earlier detection improves survival and quality-adjusted life years while lowering downstream care costs; however, achieving frequent, acceptable sampling in non-acute care settings remains a challenge. Passaro highlights both the promise and persistent limitations of current blood-based biomarker strategies for the accurate early detection of diseases. (Passaro et al. 2024)

1.2 ROLE OF BIOMARKERS IN PERSONALISED MEDICINE

Biomarkers guide risk prediction, screening, diagnosis, therapeutic selection, and monitoring of treatment response. Yet many clinically used tumour markers lack sensitivity/specificity for early disease, motivating exploration of new fluids, new analytes, and higher sampling cadence to capture transient or low-abundance signals. (Savas and Coskun 2025).

1.3 WHY ISF?

ISF is a nutrient-rich, tissue-proximal fluid with a composition broadly similar to plasma. Because it directly interfaces with local cells and the extracellular matrix, ISF can reflect microenvironmental changes earlier or more dynamically than systemic blood. Growing evidence supports ISF's utility for proteins, metabolites, and other analytes, as the field of ISF wearables is advancing rapidly (Wu et al. 2024).

1.4 THE HISTORICAL BOTTLENECK: ACCESS

Traditional ISF collection techniques, such as suction blistering, microdialysis, and microneedle-based extraction, have enabled progress in research but face barriers to routine clinical deployment, including invasiveness/discomfort, technical complexity (e.g., catheters, pumps), cost, and workflow burden. These constraints limit the required sampling frequency for capturing early signals and remote monitoring (Saifullah and Faraji Rad 2023).

1.5 A NOVEL PATH: ELECTROPORATION-ENABLED ISF ACCESS

KIFFIK's platform utilises brief, controlled electroporation to create temporary epidermal microchannels and then gently extracts ISF, thereby achieving a non-invasive, repeatable, and wearable-friendly design. Publicly available materials describe a painless operation that avoids thermal damage, enabling sustained or intermittent sampling suitable for point-of-care and decentralised settings (Abbasi and Heath 2024). This approach has the potential to bridge the long-standing access gap and unlock ISF for real-world diagnostics.

1.6 SCOPE OF THIS WHITE PAPER

The biological basis and diagnostic potential of ISF are reviewed to synthesise the limitations of conventional access methods, and present electroporation-based access, including KIFFIK's platform and other emerging devices, as a practical route to scale. In addition, the implications for the pharmaceutical industry are outlined, with proposals for NHS deployment, regulatory translation, and a roadmap for validation and partnerships.

2. ISF

2.1 BIOLOGICAL COMPOSITION AND RELATIONSHIP TO BLOOD PLASMA

The ISF occupies the extracellular space between capillary blood vessels, lymphatic vessels and the parenchymal cells of tissues. ISF is a fluid phase of the interstitium; it bathes cells, mediates nutrient and waste exchange, and reflects the local tissue microenvironment (Wiig et al. 2010). From a compositional standpoint, ISF shares many solutes with plasma (electrolytes, small metabolites, proteins), but ISF differs in that it interacts directly with the extracellular matrix, cells, and local tissue secretions. For example, in tumour tissue, the ISF contains locally secreted proteins at higher concentrations than in plasma (Wagner and Wiig 2015). A crucial point is that ISF can reflect tissue-proximal changes that may not yet have been diluted into the systemic circulation, potentially leading to ISF superseding biomarker detection in blood (Wiig et al. 2010).

2.2 KEY BIOMARKERS IDENTIFIED IN ISF (EMPHASIS ON CANCER)

Although the body of literature remains smaller than for blood/plasma, there is growing evidence that tumour interstitial fluid (TIF) contains diagnostically relevant biomarkers. For example:

- Proteomic analyses of liver TIF identified proteins not readily found in matched plasma, highlighting the high local concentration of tumour-origin proteins in ISF (Sun et al. 2016; Wiig et al. 2010).
- Metabolomic work in murine pancreatic and lung adenocarcinoma models showed that nutrient levels and metabolite profiles in TIF differ significantly from plasma, reflecting tumour microenvironment metabolism (Sullivan et al. 2019).
- In human skin ISF/dialysate studies, significant positive correlations were observed between 39 metabolites in ISF vs plasma, including known early-cancer and chronic-disease biomarkers (e.g., 1-methyladenosine) (Oharazawa et al. 2024). Based on these findings, ISF is emerging as a source of biomarkers, including proteins, metabolites, and cytokines, owing to its spatial proximity to diseased tissue.

2.3 COMPARATIVE DIAGNOSTIC ADVANTAGES

2.3.1 TISSUE PROXIMAL SENSING

ISF is closer to the site of pathology (e.g., tumour or inflamed tissue) than blood, allowing local changes to be captured before systemic dilution. For example, secreted tumour proteins may be elevated in TIF before becoming measurable in plasma (Wagner and Wiig 2015).

2.3.2 DYNAMIC MOLECULAR CHANGES

Because ISF is linked to interstitial exchange and immediate cell-extracellular matrix (ECM) interactions, it may reflect more rapid or sensitive shifts in microenvironmental biology than blood does (Sullivan et al. 2019). The metabolite differences found in tumour ISF *versus* plasma support this (Sullivan et al. 2019).

2.3.3 POTENTIAL FOR FREQUENT OR CONTINUOUS MONITORING

The composition of ISF suggests that, if accessible, it could be used for serial sampling or wearable monitoring of biomarkers, providing a richer time series than infrequent venous draws (Yang, Jie et al. 2023). Therefore, ISF offers a compelling complement, and in some cases an advantage, to blood as a diagnostic biofluid, especially for early detection, localised disease monitoring and longitudinal sampling.

2.4 CHALLENGES IN ACCESSING ISF

2.4.1 LIMITATIONS OF CONVENTIONAL TECHNIQUES

While ISF holds promise, its widespread clinical adoption has historically been limited by challenges with sample access. Major methods include:

- Microneedles (MN), arrays or patches that penetrate into the dermal layers to access ISF. These have attracted increasing research interest due to their minimal invasiveness; however, they face challenges related to fluid volume, reproducibility, depth control, and integration into workflows (Samant et al. 2021).
- Suction blister technique, a method applying negative pressure to raise a blister and harvest ISF. While effective for research, it is time-consuming, causes tissue disruption, and is not suited for high-frequency sampling in routine clinical use (Wiig et al. 2010).
- Microdialysis, insertion of a semipermeable catheter into tissue to perfuse fluid, capturing molecules from ISF. This is technically complex, requires trained personnel, and is challenging for outpatient or wearable scenarios (Wagner and Wiig 2015).

2.5 QUALITY AND PURITY OF ISF

Previous ISF extraction techniques have faced significant challenges related to the quality and purity of the collected fluid. Conventional methods, such as suction blisters, micropores, microdialysis, and various microneedle-based systems, can inadvertently harm the skin or underlying tissues, leading to contamination, release of inflammatory particulates, and distortion of biomarkers in the samples. Studies have shown that suction blistering, micropores, and microdialysis can cause tissue damage, resulting in local inflammation and contamination of ISF samples (Sprunger et al. 2025). demonstrated that microneedle-based dISF collection required post-collection morphological assessment due to the risk of structural tissue disruption and explicitly noted that methods such as suction blisters and microdialysis "can damage the skin and introduce contamination." Similarly, Wu (Wu et al. 2024) observed

that techniques such as suction blistering and micropores might trigger inflammatory responses and alter biomarker levels, with hollow microneedles additionally prone to blockage from dermal tissue cutting, thereby further affecting purity. Recent reviews, including Chen (Chen et al. 2025), emphasise that poorly designed microneedles, or those with sharp edges or requiring repeated insertions, can damage capillaries and cause localised inflammation, compromising the biological integrity of the sample. These limitations in the quality of earlier ISF extraction methods highlight the need for approaches that preserve tissue structure, minimise trauma, and prevent the introduction of blood or particulate contaminants, areas in which the KIFFIK K, EXP™ platform is specifically designed to improve performance.

2.6 OVERVIEW OF KEY ISF CLINICAL AND RESEARCH STUDIES

2.6.1 LANDSCAPE OF ISF RESEARCH

A growing body of clinical and translational research has demonstrated the value of ISF as a diagnostic medium. Across pharmacokinetics, biomarker discovery, biosensing, and comparative physiology, modern ISF studies increasingly show a strong correlation between ISF and blood-based analytes, while also highlighting opportunities for continuous, minimally invasive monitoring.

Table 1. Summary of Key Studies on ISF for Biomarker Monitoring, Pharmacokinetics, and Wearable Sensing.

Point of Interest	**References**
PK/PD study: micro-needle ISF, Glucose & Metformin.	(Yang, Jian et al. 2025)
Real-time monitoring of biomarkers. In cancer treatment, MNs show potential for targeted drug delivery, gene therapy, anti-ageing, and the treatment of skin diseases. ISF Trauma with the old method.	(Chen et al. 2025)
ISF was compared to serum for inflammation, cardiac, and cytokine biomarkers and was found to mirror blood while providing additional tissue-level data, closely matching ISF Trauma to the previous method.	(Sprunger et al. 2025)
Compares ISF and blood for cortisol, hormones, lactates, drugs, cytokines, etc. ISF trauma with the traditional method.	(Wu et al. 2024)

Table 1 Continued. *Summary of Key Studies on ISF (ISF) for Biomarker Monitoring, Pharmacokinetics, and Wearable Sensing.*

Reviews ISF stability and resilience: non-clotting, haemolysis-free, and ambient-stable compared with blood.	(Friedel et al. 2023)
ISF has attracted significant attention across many fields due to its unique benefits, including portability, high accuracy, ease of operation, and excellent stability.	(Li et al. 2024)
Describes a self-sampling ISF patch enabling quick on-device quantification; supports logistical and point-of-care benefits.	(Wilkirson et al. 2024)
Compared ISF and blood for drugs, proteins, and metabolites, found near-total overlap plus unique ISF markers supporting PK and precision monitoring.	(Ma et al. 2023)
Demonstrates compartmental PK/PD modelling that includes extracellular and interstitial spaces as effect-site representations.	(Zou et al. 2020)
Suction Blister Fluid (SBF / ISF) vs Plasma. SBF/ISF reflects the local extracellular environment and provides a clinically relevant alternative to plasma for biomarker and PK analysis. It is acellular and largely free of haemolysis, enabling reproducible measurement of proteins, cytokines, and small-molecule analytes with good correlation with plasma levels while offering improved sensitivity to tissue-level dynamics.	(Sjöbom et al. 2020)
Shows that ISF is acellular, haemolysis-free and can be analysed directly for proteins and cytokines, comparable to plasma.	(Miller et al. 2018)
Wearable sensors have advanced quickly, but genuine innovation, especially in non-invasive chemical sensing, has been limited by the skin serving as an information barrier. This paper explains why most commercial success has resulted from adapting existing physical sensing methods and emphasises the need for new approaches that can overcome fundamental biochemical-access challenges.	(Heikenfeld et al. 2017)
ISF is better in PKPD: "Ultimately, the success of pharmacokinetic/pharmacodynamic integration depends on accurate assessment of unbound drug concentrations at the site of action, most accurately represented by ISF."	(Gonzalez et al. 2013)

3. BARRIERS TO WIDESPREAD CLINICAL ADOPTION

3.1 INVASIVENESS/DISCOMFORT

Even minimally invasive techniques may cause local tissue damage, patient discomfort, or an increased risk of infection, especially when repeated.

3.2 TECHNICAL COMPLEXITY AND WORKFLOW BURDEN

Methods such as microdialysis and suction blistering require specialised equipment and trained staff, which are not readily compatible with routine clinical settings or home use.

3.3 COST AND THROUGHPUT LIMITATIONS

Due to time, labour, and equipment requirements, existing ISF sampling methods are generally low-throughput and expensive when scaled.

3.4 SAMPLE VOLUME AND BIOMARKER SENSITIVITY

Small ISF volumes and potential dilution or variable recovery make detection of very low-abundance biomarkers challenging. Some studies indicate that although ISF correlates with plasma for many metabolites, concentrations are lower (e.g., in a ISF study, total protein was ~57% of serum), suggesting that sensitivity may be a limitation (Sprunger et al. 2025).

3.5 DEPTH, TISSUE HETEROGENEITY AND STANDARDISATION

ISF composition may vary with tissue location, physiological state, vascular/lymphatic dynamics, and local matrix properties. This heterogeneity poses challenges for consistent sampling and interpretation across patients and sites.

3.6 NOVEL ACCESS *VIA* ELECTROPORATION

Electroporation is a method in which brief, controlled electrical pulses are applied to biological membranes (or tissues) to increase permeability by creating transient micro- or nano-scale pores. While electroporation is more commonly referenced in therapeutic or gene delivery contexts (e.g., cell membrane electroporation for drug/genes), recent work has extended the concept to skin permeability and extracorporeal fluid access. For example, electroporation has been proposed as a means to access ISF non-invasively by briefly disrupting the epidermal barrier, thereby enabling fluid extraction without the use of conventional hypodermic needles. (KIFFIK Biomedical 2025)

3.7 MECHANISM OF ISF EXTRACTION

KIFFIK's K-EXP™ platform comprises a two-part system: a Skin Electroporator™ that generates temporary microchannels in the outer skin, followed by an ISF Extractor™ that enables controlled, repeatable ISF collection (KIFFIK Biomedical 2025).

- The Skin Electroporator applies a patented, low-voltage electrical pulse to the outer skin, creating temporary micro-openings (micro-channels) through the epidermis without thermal damage, pain or residual skin changes (KIFFIK Biomedical 2022).
- After the micro-channels are established, the Extractor component applies gentle negative pressure to draw ISF at a low flow rate through the created channel network into a collection reservoir. (KIFFIK Biomedical 2025)
- The system is described as wearable (e.g., on the arm and designed for repeated, comfortable sampling rather than a one-off invasive draw. (KIFFIK Biomedical 2025) This combination enables non-invasive, repeatable, and scalable access to ISF, moving beyond the limitations of legacy methods (microneedles, suction blisters, microdialysis).

3.7.1 OTHER EMERGING DEVICES

While KIFFIK is perhaps the most mature in electroporation-based ISF access, broader research is underway into minimally invasive ISF extraction and sensing. The following provides a brief summary:

- A review of ISF-based wearable biosensors notes sampling techniques, including microfluidic microneedle patches, which obtain ISF for biomarker detection but frequently still require insertion or perforation (Wu et al. 2024; Yang, Jie et al. 2023).
- A study using a tilted microneedle system increased ISF extraction efficiency *via* mechanical penetration rather than electrical permeabilisation (Kim et al. 2021). In comparison, electroporation offers the promise of needle-free access, potentially reducing patient discomfort and improving adherence.

3.7.2 TECHNICAL BENEFITS

Non-invasive/minimal invasiveness: Because the epidermal barrier is temporarily and reversibly modified, the skin returns to normal post-extraction. KIFFIK describes the process as "painless, non-heat generating, and reversible" (KIFFIK Biomedical 2025).

The device's KIFFIK features are the following:

- Repeatable sampling: The ability to generate micro-channels without damaging the skin means multiple sampling episodes are feasible. This supports longitudinal monitoring.
- Wearable-friendly form factor: KIFFIK's device can be integrated into user-friendly formats that could be used in outpatient, at-home or decentralised settings.
- Scalable for high throughput/remote settings: unlike suction blistering or microdialysis, which require clinician time and infrastructure, a wearable electroporation platform

may scale more rapidly across populations, enabling broader biomarker screening programmes or remote trial monitoring.

3.7.3 HOW ELECTROPORATION IMPROVES ON CURRENT METHODS

Comparison of conventional ISF sampling methods with KIFFIK's electroporation-enabled platform Table 2. Controlled electroporation overcomes key limitations of existing techniques, microneedles, suction blistering, and microdialysis, by reducing invasiveness, improving patient comfort, and enabling simplified, decentralised, and repeatable sampling suitable for real-world and remote applications. In essence, electroporation offers a bridge: the bio-rich sampling of ISF combined with the usability and scalability needed for real-world diagnostics and monitoring.

Table 2. Comparison of conventional ISF sampling methods with KIFFIK's electroporation-enabled platform. The table highlights how controlled electroporation overcomes key limitations.

Conventional Method	**Key Limitations**	**Electroporation *via* KIFFIK Platform**	**Improvement**
Microneedles	May require penetration, be semi-invasive, have variable volume, and cause patient discomfort. (Kim et al. 2021; Yang, Jie et al. 2023)	No or minimal penetration (*via* micro-channels), lower discomfort	Increased patient acceptance, better adherence
Suction blister	Slow, disruptive to the skin, not suited for frequent sampling, and uncomfortable. (KIFFIK Biomedical 2025)	Rapid micro-channel creation + gentle extraction	Faster, less burdensome
Microdialysis	Complex equipment, trained staff, not suited to home use, limited throughput.	Simplified device, wearable form, minimal staff support	Enables decentralised sampling, remote use

3.8 IMPLICATIONS FOR THE PHARMACEUTICAL INDUSTRY

The non-invasive, repeatable access to ISF enabled by KIFFIK Biomedical Inc.'s platform offers a number of strategic opportunities for pharmaceutical developers and diagnostics companies as described in the sections below.

3.8.1 BIOMARKER DISCOVERY & VALIDATION

Because ISF more closely reflects tissue biology (rather than solely systemic circulation), it may uncover novel biomarkers (proteins, metabolomics, nucleic acids) associated with early

disease, therapeutic target engagement, or microenvironmental changes. For the pharmaceutical industry, this means enriched endpoints, improved translational insights, and differentiation in crowded therapeutic classes.

3.8.2 EARLY DIAGNOSTICS & SCREENING ASSETS

Integrating ISF sampling into diagnostic workflows could enable earlier disease detection (especially in oncology and chronic disease), leading to more effective interventions. For diagnostic companies, this platform enables non-blood-based screening, potentially reducing barriers to uptake (e.g., fear of needles and the need for frequent sampling). KIFFIK cites a total addressable market (TAM) of ~US$1.8 trillion for their platform's use cases by 2035 (KIFFIK Biomedical 2025).

3.8.3 REMOTE & DECENTRALISED TRIAL/MONITORING MODELS

The wearable-friendly, non-invasive format supports frequent or continuous sampling outside the clinic, ideal for decentralised clinical trials, real-world evidence generation, and longitudinal monitoring of therapeutic response or toxicity. KIFFIK's platform explicitly supports trial decisions ("Earlier visibility into efficacy signals, safety indicators, and patient stratification") through ISF monitoring (KIFFIK Biomedical 2025).

3.8.4 COMPLEMENTING LIQUID BIOPSIES AND STANDARD DIAGNOSTICS

ISF has great promise, but it does not aim to replace blood or imaging diagnostics entirely; rather, it aims to supplement them, providing earlier tissue-proximal signals that can guide when conventional approaches should be deployed, thereby making diagnostics more innovative and potentially more cost-efficient.

3.9 STRATEGIC LEVERAGE FOR THE NHS AND HEALTH SYSTEMS

For health systems like the NHS, the technology offers potential system-wide benefits:

- Improved patient uptake and adherence (less invasive sampling means higher participation, especially in screening or monitoring programmes).
- Shift from episodic sampling to continuous or high-frequency monitoring, which may reduce hospital admissions, detect deteriorations earlier, and enable outpatient or home-based management.
- Potential cost savings through earlier detection (smaller, more treatable disease), reduced reliance on invasive procedures, and less clinical staff time for phlebotomy or complex sampling.
- Scaling of biomarker-driven programmes across chronic disease, oncology surveillance, and remote patient care, aligning with the NHS's ambitions for digital health, home monitoring, and preventive care.

3.10 CONSIDERATIONS FOR PHARMA/DIAGNOSTIC PARTNERSHIPS

Pharma–diagnostic partnerships represent a major opportunity to accelerate therapeutic development, improve patient stratification, and unlock new commercial models. By integrating ISF-based sampling and biomarker analysis across drug development, diagnostics, and healthcare delivery, collaborations with KIFFIK can support more precise, data-rich decision-making from early clinical trials through to routine clinical use. The following considerations outline key partnership models and deployment pathways for maximising clinical and commercial impact.

- Co-development of companion diagnostics: Pharma companies developing therapies (especially in oncology, immunology and chronic disease) can partner with KIFFIK to create ISF-based biomarker panels that accompany a therapeutic, improving patient stratification and response monitoring.
- Early-phase trials: Incorporating ISF sampling in Phase I/II studies could provide richer data on pharmacokinetics (PK), pharmacodynamics (PD), target engagement and microenvironment response, shortening development timelines and de-risking assets.
- Diagnostics business model: Diagnostics companies may license or integrate the platform into existing workflows or create new ISF-specific assays, generating new revenue models.
- Health system roll-out: For broad adoption, scalable manufacturing, ease of use in home or primary care settings, and integration with electronic health records (EHRs) will be key strategic enablers.

4. REGULATORY AND TRANSLATIONAL PATHWAYS

4.1 CLINICAL VALIDATION AND ADOPTION

- Rigorous clinical validation is required: Prospective clinical studies comparing ISF biomarker performance (sensitivity, specificity, reproducibility) to established standards (blood/plasma, imaging) are essential.
- Device regulatory approval: KIFFIK's platform is currently described as "not FDA cleared. Investigational use only" (KIFFIK Biomedical 2025). For full deployment, the device must meet regulatory requirements (e.g., CE mark in the EU/UK, FDA 510(k) or de novo in the US) for safety, usability, accuracy, and reliability. As no suitable predicate device exists for this type of ISF extraction technology, KIFFIK plans to pursue the FDA De Novo classification route, which is intended for innovative, low- to moderate-risk medical devices without an existing comparator.
- Companion diagnostic regulatory alignment: If ISF biomarker assays are developed for therapeutic selection or monitoring, regulatory pathways for companion diagnostics (CDx) apply, including analytical validity, clinical validity and clinical utility.
- Health technology assessment (HTA) and reimbursement: For the NHS and other health systems, evidence of cost-effectiveness, clinical benefit and patient-outcome improvement will drive adoption and reimbursement decisions.

4.2 COMPATIBILITY WITH CURRENT DIAGNOSTIC WORKFLOWS AND STANDARDS

- Integration with existing lab/clinical systems: The ISF workflow must align with sample handling standards, bio-analysis, data management, quality control, and accreditation (e.g., ISO 15189 labs in the UK).
- Harmonisation with biomarker analytics: Assays developed for ISF must meet the same analytical performance (limit of detection, precision, stability) as conventional fluids. User-friendly interfaces and data interpretation modules will support clinician acceptance.
- Data management and interoperability: For continuous or remote monitoring applications, data security, privacy (GDPR, UK Data Protection Act), connectivity and EHR integration are crucial.
- Clinical pathway fit-in: The platform must demonstrate where it improves or complements existing pathways (screening, monitoring, diagnosis) rather than duplicating them. Early stakeholder engagement (including clinicians, NHS decision-makers, and diagnostics labs) is advisable.

4.3 TRANSLATIONAL ROADMAP SUMMARY

- Pilot feasibility studies (healthy volunteers, biomarker detection in ISF)
- Early clinical studies (target disease cohort, correlate ISF biomarker with disease outcome or response)

- Larger multicentre validation (sensitivity/specificity *versus* standard of care)
- Regulatory submission of device + assay
- Reimbursement/HTA submissions, rollout in research programmes
- Commercial adoption in screening, monitoring, and decentralised care.

5. NHS BUSINESS CASE FOR INTEGRATING KIFFIK TECHNOLOGY

5.1 BACKGROUND AND RATIONALE

The NHS faces sustained pressure from late diagnoses, workforce shortages, and increasing treatment costs across oncology and chronic disease pathways. Earlier detection is consistently associated with improved survival and reduced care costs (Coleman et al. 2020). Blood-based screening, while powerful, remains limited by systemic dilution of early biomarkers and logistical challenges of frequent venepuncture in population programmes (Laubach et al. 2019).

KIFFIK Biomedical's non-invasive ISF electroporation platform provides a scalable, repeatable, and patient-friendly alternative for accessing biomarkers. The technology enables near-patient or at-home sampling, reducing dependence on phlebotomy infrastructure and freeing valuable clinical workforce capacity (Samant et al. 2021). This aligns with NHS England's Long-Term Plan (2019), which calls for earlier diagnosis, prevention-led care, and digitally enabled health monitoring (NHS England 2019a).

5.2 QUANTITATIVE COST–BENEFIT MODEL

A base-case economic model was constructed using publicly available NHS cost benchmarks and published health-economic studies. It assumes deployment to a 200,000-patient cohort for routine screening or chronic disease monitoring: model assumptions and supporting sources for the economic analysis of home-based ISF sampling.

Table 3. Summarises key parameters used to estimate the potential cost savings and diagnostic impact of replacing conventional venepuncture appointments with KIFFIK's electroporation-enabled ISF sampling platform. Assumptions include cohort size, healthcare costs, appointment non-attendance (DNA) rates, projected improvements in early-stage cancer diagnosis, and associated differences in treatment costs.

Parameter	**Assumption**	**Supporting Source**
Cohort size	200,000 participants	(NHS Screening Programmes 2023)
Draws replaced per person per year	2 venepuncture appointments	(NHS 2025)
Phlebotomy cost per draw	£6.00	(National Clinical Guideline Centre 2015)
Nurse appointment cost	£10.75	(NHS Employers 2025)
Missed appointment (DNA) rate	5%	(NHS England 2019b)
Cost per missed appointment	£160–£165	(Esendex 2025)
Reduction in DNAs with home sampling	50%	(Souza et al. 2022)
Annual cancer incidence in the cohort	1%	(Cancer Research UK 2025)
Early-stage diagnosis improvement	+2% absolute	(Coleman et al. 2020)
Cost difference: early vs. late-stage	~£8,000	(Hofmarcher et al. 2020; Luengo-Fernandez et al. 2013)

5.3 BASE CASE RESULTS

This section presents the base-case economic impact of implementing KIFFIK's electroporation-enabled ISF sampling platform as an alternative to conventional venepuncture. Using conservative assumptions, the analysis quantifies potential annual cost savings across key areas of healthcare delivery, including workforce efficiency, reduced missed appointments, and earlier disease detection. The results illustrate the scale of system-level value that ISF-based home sampling could deliver, alongside an attractive per-patient saving and a rapid payback period following deployment.

Table 4. Estimated annual cost savings from implementing KIFFIK's electroporation-enabled ISF sampling platform. The table presents the projected financial impact of replacing conventional venepuncture with ISF-based home sampling, including savings from reduced phlebotomy costs, decreased nurse appointment time, fewer missed appointments (DNAs), and earlier-stage cancer diagnoses. The total estimated annual saving of £10.3 million equates to approximately £51.50 per patient, with an expected payback period of 18–24 months post-rollout.

Category	**Annual Saving (£)**
Avoided phlebotomy costs	£1.1 million
Nurse appointment time saved	£4.3 million
Reduced DNAs	£1.7 million
Earlier-stage diagnosis savings	£3.2 million
Total estimated annual savings	£10.3 million

These assumptions correspond to a per-patient annual saving of approximately £51.50 and a payback period of 18–24 months after device roll-out.

5.3.1 SENSITIVITY AND SCALING

A conservative scenario (100,000 patients, +1% early-stage shift) still yields approximately £3 million in savings per year, while an ambitious roll-out (300,000 patients, +3% shift) approaches £25–30 million annually. Health-economic modelling of stage migration supports these figures: earlier cancer diagnosis reduces NHS treatment costs by 50–70%. (Luengo-Fernandez et al. 2013; Round et al. 2015)

If applied across multiple NHS screening and chronic disease programmes, national integration could generate >£100 million per year in combined clinical and operational savings.

5.4 QUALITATIVE BENEFITS

Beyond direct financial savings, adopting KIFFIK's electroporation-enabled ISF sampling platform offers a range of important qualitative benefits for patients, healthcare systems, and society. These benefits include improvements in patient experience and equitable access, enhanced workforce efficiency, richer longitudinal health data, better clinical outcomes through earlier detection, and progress towards sustainability goals. The following table summarises the key non-monetary advantages of ISF-based remote sampling, supported by evidence from the literature and policy sources.

Table 5. Qualitative benefits associated with KIFFIK's electroporation-enabled ISF sampling platform. This table summarises the broader system-level and societal advantages of adopting ISF-based remote sampling, including improved patient experience, greater equitable access, greater workforce efficiency, richer longitudinal health data, better clinical outcomes through earlier detection, and reduced environmental impact from lower travel and hospital utilisation.

Domain	**Expected Benefit**	**Supporting Source**
Patient experience	Non-invasive, painless sampling improves adherence and satisfaction.	(Yuan et al. 2023)
Equity and access	Remote sampling improves inclusion for rural, mobility-limited, and working-age groups.	(Petretto et al. 2024; Yu and Meng 2022)
Workforce efficiency	Free nurse and phlebotomy capacity for high-acuity care.	(NHS England 2023a)
Data richness	High-frequency ISF sampling enables longitudinal tracking of biomarkers.	(Samant et al. 2021)
Clinical outcomes	Early detection improves survival and QALYs; delays worsen prognosis.	(Coleman et al. 2020)
Sustainability	Reduced hospital visits and travel lower carbon emissions.	(Greener NHS 2025)

5.5 IMPLEMENTATION PATHWAY

5.5.1 PHASE 1 – PILOT (YEARS 1–2)

- Feasibility and validation across 3–5 NHS Trusts in oncology and metabolic disease pathways.
- Integration with existing NHS digital monitoring platforms and EHR systems.
- Economic and patient-reported outcome data collection.

5.5.2 PHASE 2 – SCALE-UP (YEARS 3–5)

- Expansion into national screening programmes (e.g., Diabetes Prevention, Bowel, Breast).
- Joint NHS–industry consortia *via* the Accelerated Access Collaborative (AAC).
- Outcome-based commissioning linked to early detection metrics.

5.6 ROI AND VALUE PROPOSITION

At an estimated deployment cost of £100–150 per patient (analysis) and recurring annual savings of £50–80 per patient, the payback period is two years, followed by sustained yearly savings. This supports NHS financial sustainability goals under the Long Term Workforce Plan and Innovation & Life Sciences Vision (GOV.UK 2024)

5.7 STRATEGIC ALIGNMENT

The KIFFIK platform supports the NHS's Quadruple Aim of:

1. Enhancing patient experience;
2. Improving population health;
3. Reducing per capita cost;
4. Improving staff experience.

It directly aligns with:

- NHS Long Term Plan (GOV.UK 2025): earlier diagnosis and prevention-led care.
- NHS Digital Transformation Strategy (NHS England 2023b): adoption of at-home monitoring and diagnostics.
- UK Life Sciences Vision (GOV.UK 2021): fostering diagnostic innovation within the healthcare system.

5.8 SUMMARY

Integration of KIFFIK's ISF technology could enable the NHS to deliver substantial system-level benefits. Modelling suggests annual savings of approximately £10–30 million, depending on scale of deployment and pace of adoption. These savings are driven by a combination of reduced in-clinic phlebotomy, shorter nurse appointment times, fewer missed appointments (DNAs) enabled by at-home sampling, and downstream cost reductions from earlier disease detection and stage-shifting.

In addition to financial impact, ISF-based remote sampling has the potential to improve early diagnosis rates, reduce outpatient burden, and alleviate workforce pressures, while also supporting NHS decarbonisation and digital transformation objectives. Collectively, these impacts create a compelling value proposition for pilot deployment and partnership through Innovate UK and NHS Innovation Accelerator pathways.

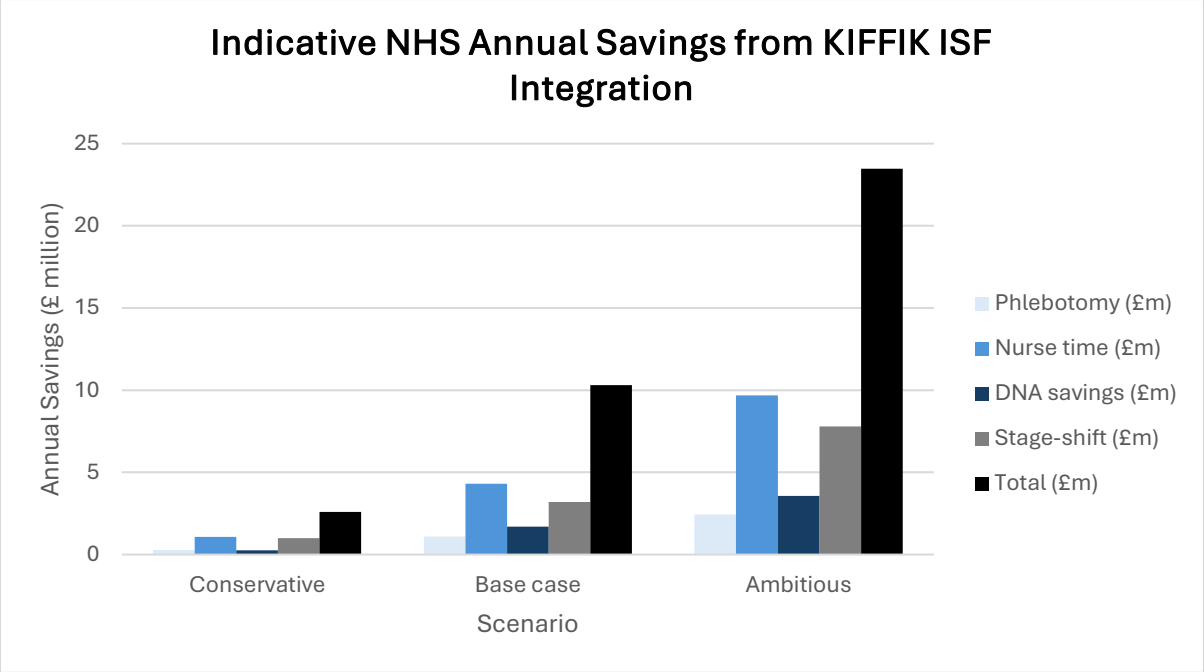

Figure 1. Indicative NHS Annual Savings from Integration of KIFFIK's ISF Electroporation Platform. Estimated annual savings under Conservative, Base Case, and Ambitious adoption scenarios, aggregated across phlebotomy avoidance, nurse time savings, reduced DNAs, and stage-shift effects from earlier diagnosis.

6. BUSINESS CASE FOR USING KIFFIK'S ISF ELECTROPORATION PLATFORM IN CLINICAL TRIALS

6.1 BACKGROUND AND RATIONALE

Phase II clinical trials often face high costs and participant burden due to frequent blood sampling, hospital visits, and complex pharmacokinetic (PK) assessments. According to the Association of Clinical Research Organisations (ACRO, 2022), biospecimen collection and processing can account for 20–30% of total Phase II costs, driven mainly by phlebotomy, sample logistics, and monitoring overhead.

KIFFIK Biomedical's non-invasive electroporation-based ISF collection platform enables near-continuous, needle-free monitoring of biomarkers, metabolites, and pharmacokinetic markers directly from ISF. The device's wearable compatibility enables remote sampling in ambulatory or home settings, significantly reducing the number of clinic visits, improving adherence, and allowing for richer temporal data capture.

This directly aligns with the ongoing shift toward Decentralised Clinical Trials (DCTs) promoted by the FDA, EMA, and MHRA (EMA 2021; FDA 2024).

6.2 CURRENT CHALLENGES IN PHASE II TRIALS

Phase II clinical trials are a critical inflexion point in drug development, where early signals of efficacy, dose–response relationships, and safety profiles are established. However, these studies are frequently constrained by operational and scientific challenges that limit data quality, increase costs, and slow decision-making. High sampling burden, complex bioanalytical workflows, limited temporal resolution of pharmacokinetic and pharmacodynamic measurements, and patient attrition collectively undermine trial efficiency and the robustness of dose-response modelling. Table 6 summarises the key challenges commonly encountered in Phase II trials and their downstream impacts on trial performance and outcomes.

Table 6. Key operational and scientific challenges in Phase II clinical trials. The table highlights significant barriers that impact trial efficiency and data quality, including high sampling burden, complex bioanalytical logistics, limited temporal resolution in pharmacokinetic (PK) sampling, and participant dropout. These challenges collectively increase costs, reduce participant retention, and undermine the robustness of dose–response modelling.

Challenge	**Impact**	**Reference**
High sampling burden (multiple venepuncture visits)	Increases cost, decreases participant retention	(Lingervelder et al. 2022)
Logistics of bioanalytical sample handling	Adds 10–15% to site operational costs	(Tufts CSDD 2021)
Limited temporal resolution of PK sampling	Reduces the accuracy of dose–response modelling	(Perera et al. 2022)
Patient dropout rates (15–25%)	Causes underpowered analyses, increases re-recruitment cost	(Bose et al. 2020; Skea et al. 2019)

6.2.1 VALUE PROPOSITION OF KIFFIK'S ISF PLATFORM

6.2.1.1 TECHNICAL ADVANTAGES

- Non-invasive ISF collection with no needles or catheters.
- Repeatable, low-burden sampling (up to multiple times per day).
- Compatible with remote monitoring, wearables, and digital endpoints.
- Suitable for real-time PK and PD assessment of small molecules and biologics.

6.2.1.2 OPERATIONAL BENEFITS

- Reduces clinic visits and staff workload.
- Improves patient adherence and retention.
- Minimises biohazard waste and cold-chain logistics.
- Enables hybrid or fully decentralised trial designs.

6.2.1.3 STRATEGIC BENEFITS

- Increases trial accessibility and diversity by enabling at-home participation.
- Generates richer, longitudinal datasets.
- Aligns with regulatory encouragement for digital and patient-centric trials. (FDA 2024)

6.3 QUANTITATIVE COST–SAVINGS MODEL

This section presents a quantitative cost-savings analysis comparing conventional venous blood sampling with KIFFIK's electroporation-enabled ISF platform in a representative Phase II clinical trial setting. Using a 120-participant, 6-month trial as the base case, the model captures key cost drivers across sampling logistics, laboratory processing, participant reimbursement, and recruitment and retention. The analysis demonstrates that replacing repeated venepuncture with ISF-based sampling can substantially reduce operational burden

and trial costs, with overall sampling-related expenditures projected to decrease by approximately 50%, delivering meaningful savings while supporting improved trial efficiency and participant experience.

Table 7. Comparative cost analysis of conventional blood sampling versus KIFFIK's electroporation-enabled ISF platform in a typical Phase II clinical study. The model assumes a 120-patient, 6-month trial with 10 sampling visits and 2 ISF collections each week. Significant cost savings are expected across phlebotomy, sample transport, laboratory processing, and participant reimbursement, as well as enhanced recruitment and retention rates. Overall, the KIFFIK ISF platform is projected to cut total sampling-related costs by around 50%, resulting in annual savings of approximately £222,000.

Cost Element	**Conventional Blood Sampling**	**KIFFIK ISF Platform**	**Estimated Saving**
Phlebotomy visits (10 per subject × £120/site cost per visit)	£144,000	£28,800	£115,200
Sample transport & processing	£35,000	£10,000	£25,000
Lab analysis prep & QC time	£22,000	£15,000	£7,000
Participant reimbursement (£50/visit × 10 visits)	£60,000	£12,000	£48,000
Recruitment & retention (15% fewer dropouts)	£180,000	£153,000	£27,000
Total	£441,000	£218,800	≈ £222,000 saved (50%)

6.4 ADDITIONAL VALUE TO SPONSORS AND CROS

Beyond direct cost reductions, KIFFIK's electroporation-enables the ISF sampling platform to deliver additional strategic value to both study sponsors and contract research organisations (CROs). By enabling less invasive, higher-frequency biomarker collection and reducing reliance on in-clinic visits, the platform supports improved data quality, stronger participant retention, and more efficient trial execution. These benefits translate into faster recruitment, smoother regulatory pathways, and shorter study timelines, enhancing overall trial success and competitiveness. Table 8 summarises the key sources of added value generated through the adoption of ISF-based sampling in clinical development programmes.

Table 8. Additional value of KIFFIK's electroporation-enabled ISF sampling platform for sponsors and CROs. The table outlines key advantages beyond direct cost savings, including improved PK data quality, streamlined regulatory compliance, enhanced participant retention through reduced invasiveness, faster and more diverse recruitment, and shorter trial durations due to reduced site burden and fewer missed appointments.

Category	**Description**
Data quality	Continuous ISF collection improves the temporal resolution of PK curves and biomarker dynamics.
Regulatory compliance	Electroporation-based sampling is classified as a non-significant risk device under MHRA guidance.
Participant retention	Reduced invasiveness lowers dropout and improves completion rates.
Recruitment speed	Enables geographically diverse recruitment with fewer in-clinic visits.
Trial duration	Reduces active-site involvement and potential delays caused by missed appointments.

6.5 EXAMPLE USE CASES

- Oncology (early PK assessment of targeted therapies) – frequent sampling without central line insertion.
- Metabolic / Endocrine studies – glucose, cytokine, or peptide biomarker kinetics.
- Dermal/transdermal delivery studies – correlation of ISF and plasma concentrations.
- Vaccines/immunotherapy trials – local immune response biomarkers.

6.6 STRATEGIC ALIGNMENT

- Regulatory: compliant with FDA & EMA guidance on remote data collection.
- Operational: supports hybrid and DCT frameworks.
- Sustainability: reduction in travel, consumables, and staff time.
- Data richness: enables adaptive dose modelling and AI-driven PK prediction.

6.7 SUMMARY OF FINANCIAL IMPACT

This section synthesises the financial and operational impacts of adopting KIFFIK's electroporation-enabled ISF sampling platform in a representative Phase II clinical trial. By comparing conventional venepuncture-based workflows with an ISF-enabled approach, the analysis highlights substantial reductions in per-participant and total study costs, alongside improvements in participant retention and reduced site staff utilisation. Together, these effects translate into a more efficient, scalable trial model that delivers meaningful cost savings and

performance gains for sponsors and contract research organisations. Table 9 and Figure 2 summarise the consolidated financial outcomes under the base-case scenario.

Table 9. Summary of financial impact for a representative Phase II clinical study using KIFFIK's electroporation*-enabled ISF platform. The table compares conventional venepuncture-based sampling with ISF-based sampling, highlighting reductions in per-participant and total study costs, improved participant retention, and decreased site staff utilisation. Overall, the model predicts a 50% reduction in sampling-related costs, resulting in a total saving of approximately £222,000 for a 120-participant Phase II trial.*

Metric	**Conventional Phase II**	**KIFFIK-Enabled Phase II**	**Change**
Cost per participant	£3,675	£1,825	-50%
Participant retention	80%	95%	+15%
Site staff utilisation	100% baseline	60%	-40%
Total study cost (120 subjects)	£441k	£219k	£222k saved

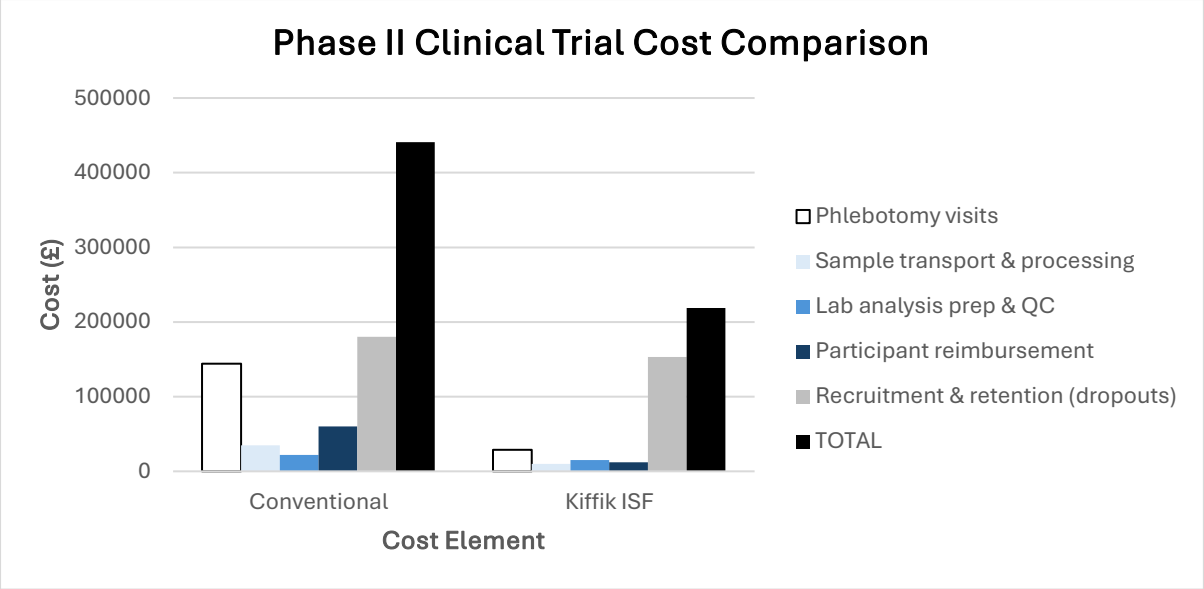

Figure 2. Phase II Clinical Trial Cost Comparison Using KIFFIK's ISF Platform. Bar chart comparing estimated costs associated with a 120-participant, 6-month Phase II clinical trial using conventional blood sampling versus KIFFIK Biomedical's ISF (ISF) electroporation platform. The model includes five major cost categories: phlebotomy visits, sample transport and processing, laboratory analysis and quality control, participant reimbursement, and recruitment and retention due to dropouts. The implementation of the KIFFIK ISF platform reduces overall trial costs by approximately 50%, primarily through lower phlebotomy and staff costs, reduced participant travel, and improved participant retention. The total estimated savings per trial are approximately £220,000, representing a substantial return on investment for sponsors and contract research organisations (CROs).

6.8 CLINICAL TRIALS CONCLUSION

Implementing KIFFIK's ISF electroporation platform in Phase II trials offers substantial cost savings, enhanced participant retention, and improved data resolution. By replacing conventional venepuncture with non-invasive ISF collection, sponsors can cut per-participant sampling costs by up to 50%, reduce logistical overhead, and accelerate timelines through improved adherence and decentralised operations. This aligns with both NHS and global regulatory priorities for patient-centric, data-rich, and cost-efficient clinical development.

7. CONCLUSION

Early and accessible disease detection remains one of the most critical challenges in modern healthcare. The traditional reliance on blood sampling limits diagnostic coverage and patient access, thereby increasing costs and delaying intervention. KIFFIK's electroporation-based ISF technology offers a practical, non-invasive solution, providing biomarker-rich data that reflects real-time physiological changes. By enabling remote, repeatable, and scalable sampling, it bridges a long-standing gap between laboratory insights and patient-centred care. For healthcare systems like the NHS, widespread adoption could lead to significant operational savings, improve early detection rates, and reduce workforce pressures. In the pharmaceutical sector, the same technology yields measurable efficiencies in clinical trials, resulting in lower costs, improved participant retention, and higher-resolution pharmacokinetic data. KIFFIK's platform represents more than an innovative sampling method; it is a technology that supports earlier diagnosis, decentralised clinical research, and a more efficient, equitable healthcare ecosystem.

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