ject funded under H2020-FTIPilot-2016

BreathSpec®

A rapid, non-invasive, cost-effective, analytical device for bacterial or viral infection diagnosis through ultra-high sensitivity breath analysis.

BREATHSPEC™

IMSPEX Diagnostics Ltd

Tender Ref: BSP001

August 2017

Invitation to Tender

Part Two –Goods and/or Services Requirement for Suppliers

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1. Introduction

IMSPEX Diagnostics Ltd (IMSPEX) has a requirement to subcontract services for the delivery of a multi-centered trial consisting of 6 NHS locations. In total, 2,000 patients must be recruited for the diagnosis of bacterial or viral infection through breath analysis. Presented below are details of the project and the requirements of the subcontracted services.

1.1 Project overview

Table 1 Project overview

Title:	**Title:** A multicentre prospective, observational, longitudinal cohort study in adult patients with suspected Upper or Lower Respiratory infection (URTI/LRTI) to identify a spectrum of biomarkers in exhaled breath to discriminate participants with bacterial RTI from participants without.
Objectives:	The primary objective of this study is to identify, quantify and compare the VOCs in the exhaled breath of a minimum of 2000 patients presenting with symptoms suggestive of respiratory tract infection (RTI) to confirm the signature of bacterial RTIs and to discriminate between bacterial RTI versus non-bacterial respiratory tract presentation. The secondary objectives of this Study are to assess the impact of other factors to optimise the sensitivity and selectivity of the VOC signature including environmental factors (locations) and patient factors.
Design:	This multicentre prospective, observational, longitudinal cohort study aims to obtain chemical information of exhaled breath biomarker data from adult patients with confirmed Upper and Lower Respiratory pathologies (URTI/LRTI) to support clinical decision making regarding the diagnosis and treatment of suspected RTI. Patients with suspected RTI who consent to participate in the study will be asked to provide two breath samples directly into two Breathspec instruments by exhaling into a disposable mouthpiece for 3-5 seconds. All patients will be asked to abstain from eating and drinking for 30 minutes prior to providing breath samples. Subjects will be asked to swill their mouth with water immediately before taking the test. An ambient air sample will be collected after each breath sample. Analysis of a sample (breath or ambient air) will take less than 10 minutes, the participant does not need to be present for this analysis. The results of the gas phase chemical analysis will be stored in the internal memory of each device for subsequent downloading and analysis. Patients will be assessed and treated at the study sites as per normal standard of care for the diagnosis and treatment of RTI.
Inclusion Criteria:	Male and female subjects aged 18 and above will be eligible for inclusion in this study if all of the following criteria apply: 1. Have symptoms consistent with a suspected Respiratory Tract Infection (RTI)

	2. Are willing to provide personal written informed consent
Exclusion Criteria:	A subject will not be eligible to participate in the study if they meet any of the following criteria: 1. Have antibiotic treatment started more than 6 hours before Breathspec administration 2. Have a diagnosis of lung cancer 3. Have received anti-cancer chemotherapy within last 30-days 4. Have a history/diagnosis of iatrogenic neutropaenia 5. Have a history/ diagnosis of bile acid mal-absorption 6. Have a history of inflammatory bowel disease 7. Any other condition which in the opinion of the Investigator no longer permits safe participation in the study
Number of Subjects:	The study aims to recruit a minimum of 2000 subjects with suspected RTI in 6 clinical sites in the United Kingdom (UK). 700 patients will be recruited from 2 primary care centers and a further 1300 patients from 4 secondary care sites. Recruitment is expected to take 8 months and will be conducted during the 2017/2018 influenza season (estimated October 2017 to May 2018). A further group of healthy volunteers (no more than 100 subjects) will be used to produce baseline information to ensure the efficacy of the instrument. It is not expected this data will be used as part of the main data analysis stages.
Number of Sites:	Up to 6 sites in the UK
Investigational Device:	The instrument used in the study will be a BreathSpec™ by Gesellschaft für analytische Sensorsysteme mbH (G.A.S.)
Reference Therapy:	Standard of Care for the treatments of RTIs at the participating sites
Duration of Participation:	The study will include a screening/eligibility phase followed by inclusion in the study and administration of the Breathspec test. The screening/eligibility and administration of Breathspec test will occur on the same day for participants who provide written informed consent. A 7-day follow-up will be performed on outpatients who did not receive antibiotics at the initial consultation.

1.2 Tender Options

This tender is for the sub-contraction of works to fulfill the requirements of the study outlined above. The project requires recruitment from multiple NHS locations and therefore the following tender options are available to potential suppliers:

1. Project coordinator and Sponsor with patient recruitment from secondary care setting – 1 NHS site required

2. Participating site with patient recruitment from secondary care setting – 3 NHS sites required
3. Participating site with patient recruitment from primary care setting – 2 NHS sites required

Suppliers are invited to submit a bid for more than option on the condition that the requirements for each option in Section 2 are met.

Please respond to each element below clearly stating the capabilities of your solution against the requirement of the specification, if exceeding the specification is deemed useful extra credit may be given. All items listed as essential that cannot be complied with must be listed on the **TECHNICAL NON COMPLIANCE STATEMENT**.

2. Goods / Service Requirement

2.1 Essential requirements at all sites

The following are **essential** requirements irrespective of which tender option is being bid for.

Table 2 outlines the general essential requirements of the study.

Table 3 shows the tests to be performed on all patients presenting with a suspected respiratory tract infection (RTI) in a primary or secondary care setting. A suspected RTI is defined as a new or worsening cough.

Table 2 General study requirements (essential)

Essential Requirement	Specification
Breath analysis clinical trial experience	Supplier must have experience in breath analysis and the use of a BreathSpec™ Device
A local Principal Investigator (PI) must be nominated	Full name and contact details must be submitted with tender
PI input into ethics process	Must provide all relevant information to the co-ordinator on request for contribution to ethics process for the Integrated Research Application System (IRAS) and Site Specific Information (SSI)
Number of recruited participants per site with suspected RTI	333
Site type	Patients must be recruited from a UK NHS site
Patient type	Adults aged 18+

Staff training	3 days (18th-20th September 2017)
Participant recruitment period	8 months (1st October 2017 – 31st May 2018)
Final participant data deadline	30th June 2018
Electronic Data Capture (EDC) system must be used	Provided by Statistica Medica
Provide laptop/computer with internet connection	For use with EDC
Local site clinician to attend remote monthly meeting for case definition requirements	Monthly 2 hour meeting
Daily check of 2 x BreathSpec devices	As per a standard operating procedure (provided at training)

Table 3 Essential tests required on all study participants

Participant Test	**Essential or if clinically indicated**
Chest radiograph	If clinically indicated
Sputum culture	If cough productive
Throat swab for bacterial culture	If clinically indicated
Nasal swab for viral and atypical bacterial polymerase chain reaction (PCR)	Yes
Urinary pneumococcal antigen	If test available within health board
Urinary legionella antigen	If clinically indicated
Venesection 1. Full blood count 2. Biochemistry panel (urea, electrolytes and creatinine, liver function tests and CRP)	Yes
Point of care lateral flow test 1. Procalcitonin (PCT) 2. CRP	Yes
7 day follow-up	Yes

All local Principal Investigators (PI) must agree to comply with the following these conditions:

1. The PI and persons authorised by the PI will be instructed by StatisticaMedica on how to complete the electronic Case Report Forms (eCRFs) in the EDC system. Entries in the eCRF must only be made by the PI or persons authorised by the PI.
2. The PI will keep a confidential list of names of all participants in the study, so that

the subjects' records can be identified if necessary.

3. The PI must abide by the principles of the GCP guidelines of the ICH, and of the current version of the World Medical Association Declaration of Helsinki. They must ensure the study also will be carried out in accordance with UK legal, regulatory and ethical requirements.
4. The study is to be conducted according to UK Guidance on the In Vitro Diagnostic Medical Devices Directive 98/79/EC, international standards of Good Clinical Practice (ISO 14155:2011) and International Conference on Harmonization guidelines), all applicable UK regulations and participating institutional research policies and procedures.

A study protocol will be available (in confidence) after tender award. The protocol and any amendments will be submitted to a properly constituted Independent Ethical Committees (IEC), in agreement with UK legal requirements, for formal approval of the study conduct. The decision of the IEC concerning the conduct of the study will be made in writing to the individual site PI and a copy of this decision will be provided to the Coordinator before commencement of this study.

A supplier or PI shall not publish any data (poster, abstract, paper, etc.) without having consulted with the study co-ordinator and IMSPEX in advance. A 28 day consultation period is required with study co-ordinator and IMSPEX after first notification of intent to publish.

2.2 Essential requirements by tender option

Tender Option 1

This option is for the study co-ordinator site and as such will be the lead NHS organisation of the project. This site will nominate a Chief Investigator and undertake the role of Study Sponsor. They will fulfil all ethical, legal and liability requirements for this study.

This site will recruit only from a **secondary** care setting.

Tender Option 2

This option is for a local participating NHS site and must declare a Principal Investigator.

This site will recruit only from a **secondary** care setting.

Tender Option 3

This option is for a local participating NHS site and must declare a Principal Investigator.

This site will recruit only from a **primary** care setting.

3. Payment Terms

IMSPEX will use the following payment schedule (Table 4). 30 days net from invoice date. Please confirm this payment schedule is acceptable. All payments will be made in Euros (and inclusive of VAT).

Table 4 Payment schedule

Payment	Date	Amount
Initial upfront payment	01st October 2017	30% of total tender award
Interim payment	31st July 2018	50% of total tender award
Final payment	31st August 2019	20% of total tender award

If under participant recruitment by any supplier, at any site has occurred by the recruitment period end outlined in Table 2, or data quality is poor, IMSPEX reserves the right to reduce the total tender award based on a percentage value of participant recruitment. This would be reflected in the interim payment. Over participant recruitment by any supplier at any site does not increase the tender award.

4. Delivery, Installation and Commissioning

G.A.S. (BreathSpec Project partner) will arrange delivery, instillation and commission of the BreathSpec devices prior to the recruitment start date.

The supplier is responsible for accepting delivery of the BreathSpec devices and providing sufficient space to house the devices whilst at NHS sites. The supplier is responsible for providing continuous connection of the devices to a power supply.

5. Training and Support

Staistica Medica (BreathSpec project partner) is responsible for all training and support to suppliers during the contracted period.

6. Warranty and Maintenance

G.A.S. assumes all responsibility for warranty and maintenance of the BreathSpec devices during the recruitment period.

The supplier is responsible for loss and damage to the BreathSpec devices whilst at NHS sites.

7. Consumables and Equipment

Consumables for the BreathSpec devices and associated breath tests will be provided by G.A.S. and delivered to the suppliers stated delivery address. Instrument return to G.A.S. Germany at study end is at suppliers own cost, approx. £200.

8. Tender Response

8.1 Tender Bid

Complete Table 5 with bid amount (add more lines if nessecary).

Table 5 Tender option and bid amount

Tender option	Number of sites	Price (Euros)
	Total Bid Price	Euro

8.2 Tender Questions

Provide written answers questions 1, 2 and 3. Maximum 500 word per question.

1. Please state previous clinical trials experience.

2. Please state previous breath analysis experience.

3. Please state previous experience of using a BreathSpec device.

8.3 Additional information

Please provide the additional information. Failure to provide this information may result in disqualification of tender bid.

Please confirm that the supplier is able to fulfil the essential requirements as outlined in Section 2.1	**Yes / No***
Please confirm that the supplier is able to fulfil the essential requirements as per the tender option specified in Table 5 as outlined in Section 2.2	**Yes / No***

*If No, complete the Technical Non-Compliance Statement

8.4 NHS organisation details

Information required for formal ethics application. Please duplicate table if more than one NHS organisation is to be used.

NHS organisation information	Response
NHS organisation to be used for recruitment	
Primary or Secondary setting	
Name of Principal Investigator nominated at organisation (all tender options)	
Name of Chief Investigator nominated (if tender option 1)	

8.5 Declaration

Supplier information	
Supplier Name:	
Supplier Address:	Contact Name: Contact Email: Contact Tel:
Signed:	Date:
Name:	Position:
Authorised to sign tenders for and on behalf of:	

9. Tender Evaluation

9.1 Evaluation criteria

IMSPEX will review all submissions utilising objective selection criteria and a formal evaluation model. IMSPEX will award the contract to the most economically advantageous tender based on the evaluation weightings detailed below.

IMSPEX reserves the right to seek clarification with the supplier(s) upon receipt of tender submissions.

Table 6 Evaluation criteria

Criteria (%)	Weighting (%)
Previous clinical trials experience	20
Previous breath analysis experience	30
Previous use of a BreathSpec device	35
Fulfils all essential criteria	10
Price	5

Responses will be scored on a scale 0 to 20, this scoring will then be weighted according to the above % to provide a total score out of 100.

Marks out of 20 will be awarded according to the following matrix with the exception of total cost which will be scored as per below:

Table 7 Marking matrix

15 marks	Excellent response: highly relevant and detailed. Meets expectations with significant added value
12 marks	Response is good. The response meets requirements and some additional value
10 marks	Average response. A score of 10 or above can only be achieved if the response meets minimum expectations
8 marks	Poor response. Below expectations / lacking detail and relevance
0 marks	No response provided

The lowest cost bid will be awarded the highest points, higher costed bids will receive a proportionate of the marks. However, this bid is ultimately based on quality.

Table 8 Proposed Timeline for this Invitation to Tender (ITT)

Process Stage	**Timescale**
Issue invitation to Tender	4th September 2017
Last date for Questions	13th September 2017
Deadline for Tender Submissions	Noon 14th September 2017
Tender Evaluation	19th September 2017
Contract Award	24th September 2017

Please note that this timeline is estimated only and may be subject to change.

10. Technical Non-Compliance Statement

Only if applicable, please detail below all technical matters in which your Tender response does not comply with the requirements laid down in this Part Two of the Invitation to Tender document. Sequentially number each point in the first column for ease of reference.

TENDERER: .....

Matter not complied with within Tender Requirements	Extent of Non-Compliance	Alternatives Offered	Effect on Tender

Signed .....Date.....

Name .....Position .....

Authorised to sign tenders for and on behalf of

.....