Tracer-QC Proposal

Tracer-QC™

Automated optical testing for PET-QC

TRACEABILITY INC

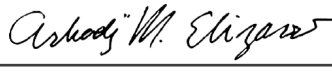
LabLogic

EXPERIENCE & EXPERTISE

Contents

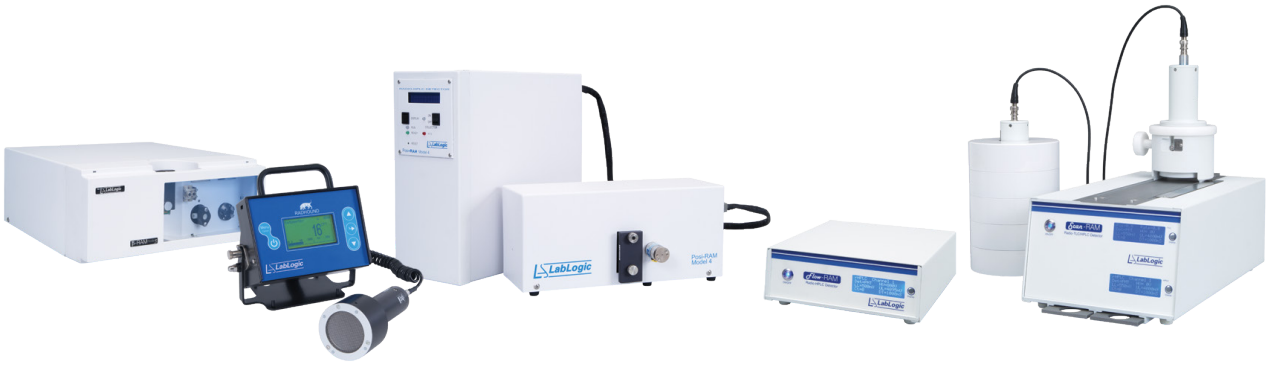
Authorisation

The following hereby agree to be bound by the terms, conditions and pricing of this proposal.

Name	Title	Signature	Date
Richard Brown	Managing Director, LabLogic Systems		07 April 2017
Elvir Zahirovic	Sales Director, LabLogic Systems		07 April 2017
Arkadij Elizarov	CEO, Trace-Ability Inc		07 April 2017

Author(s):	Richard Brown Elvir Zahirovic
Document type:	Tracer-QC Proposal
Document status:	Confidential
Version	1.0
Release date:	07 April 2017
Number of pages:	15
Document Ref:	C:\EZahirovic\Current Material\Lab-Logic\Proposals\Tracer-QC Proposal

LabLogic Company Profile



LabLogic Systems are a leading supplier and manufacturer of instrumentation and software to the life science, nuclear medicine / PET and radiation safety sectors.

We have over 35 years' experience and expertise in providing solutions within highly regulated environments.

Many of our solutions are the industry standard and can be found in over 50 countries around the world. Our customers range from 18 of the top 20 pharmaceutical companies to leading PET manufacturers and world-renowned universities.

LabLogic Systems are part of a wider group which includes:

- **LabLogic Systems Limited:** The head office of LabLogic Systems based in Sheffield, UK.
- **LabLogic Systems Inc:** Formally IN/US, now is the US branch of LabLogic Systems based in Brandon, Florida.
- **Southern Scientific Limited**: A supplier of radiation detection equipment to the medical, nuclear, security and defence sectors, based in the UK.
- **Knight Imaging**: A manufacturer of medical furniture based in Sheffield, UK.
- **Care Wise**: A manufacturer of gamma probes for sentinal node procedures.

What sets LabLogic apart from its competitors are five key values:

Focused Industry Specialists

We are focused industry specialists who aim to provide unrivalled experience and expertise within each sector we enter. Customers can be confident that they are dealing with a reputable and established vendor that specialise in these niche markets.

Commitment to Quality

Our commitment to quality is evident in the multiple awards we have won. We have had ISO and Investor in People accreditation for over 20 years.

High Service Standards

We recognise that providing the product alone is only one side of the story; successful implementation and continued trouble-free use of the product requires a comprehensive set of services. LabLogic pride ourselves on giving our customers nothing but the best service and support.

Innovation

At LabLogic, we are innovators. We are constantly trying to improve and develop new products in relation to our customers needs. User groups and regular customer feedback give us a unique insight. Recently significant investments have been made into the R&D team and a production facility alongside the likes of Boeing and Rolls Royce at the Advanced Manufacturing Park, Sheffield.

Customers for Life

We aim to build life long relationships with our customers that are mutually beneficial, helping achieve short, medium and long term goals.

Trace-Ability, Inc. Company Profile

Trace-Ability is a growing California-based company that answered the FDA call for modernization of testing technologies in radiopharmaceutical production. Years of experience in PET industry allowed the founders to recognize the opportunity to revolutionize and simplify PET-QC testing using optical techniques. The FDA funding and collaboration have enabled optimization and solid validation of Tracer-QC technology.

Trace-Ability's technical team is composed of well-recognized innovators with diverse skill-sets stemming from both industrial experience in companies like Siemens and scientific excellence developed under Nobel laureate mentors. Members of this team are known for their development of elegant and simple solutions to complex problems while relying on unconventional approaches. Their track record includes over 100 peer-reviewed publications and over 30 issued patents. Their work has been cited over 4000 times in scientific literature.

Trace-Ability has started as a private investor-funded venture also benefitting from proceeds of Innovation Fund America competition (as a 1st place awardee). Early results have demonstrating the power of the new technology and capabilities of the technical team. As a result continued development of Tracer-QC has been funded by the National Science Foundation (NSF), National Institutes of Health (NIH) and eventually the US Food and Drug Administration (FDA).

Over the course of its existence Trace-Ability has developed an extensive network of development and industrial partners, suppliers, regulators and KOL's that is critical for successful launch of Tracer-QC. Specifically, kit production has both primary and backup manufacturers to assure undisrupted supply. Additionally, partnership with Zevacor Pharma allowed us to validate Tracer-QC in a top-notch GMP facility known to produce the highest volume of FDG in the US. Finally, close relationship with the FDA has allowed us to develop a streamlined regulatory path that simplifies Tracer-QC adoption for our customers.

The LabLogic/Trace-Ability Partnership

LabLogic Systems have partnered with Trace-Ability Inc. to provide commercial and software development.

This relationship multiples the capabilities offered by each company individually. It allowed Trace-Ability to focus on the technical aspects of bringing Tracer-QC to market. They include development and validation of the core Tracer-QC technology and production of consumables. Meanwhile, LabLogic was able to leverage years of expertise in software development to develop the intuitive user interface backed up by 21 CFR Part 11 compliance. Finally, the hardware platform is uniquely enabled by balancing existing LabLogic and Trace-Ability relationships with analytical and robotic companies.

Commercialization of Tracer-QC is also a joint effort. On one hand, it benefits from the LabLogic's established global footprint and track record of successfully launching multiple products in the PET radiopharmaceutical field. On the other, it leverages Trace-Ability's direct ties with industry, KOL's and regulators. Participation of both companies in commercialization allows the joint product offering to be optimally tuned to each customer's technical and operational needs.

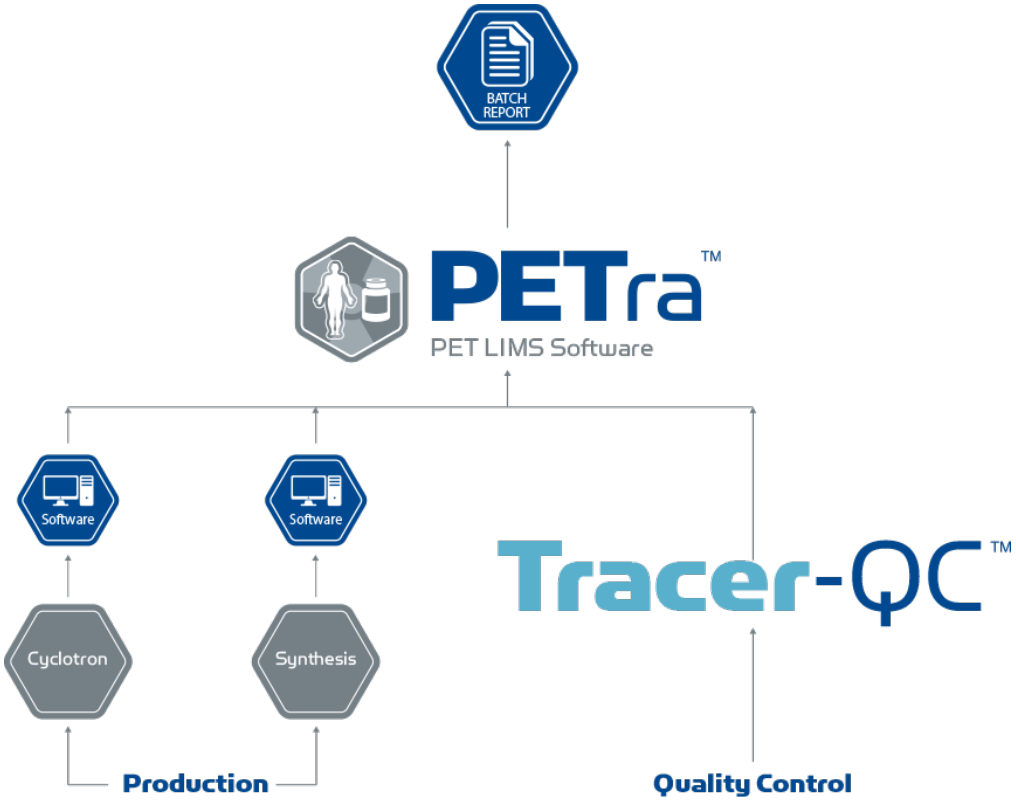
Tracer-QC Rationale

Industry Rationale – Ease of Compliance

An independent study by Proceutical, LTD analyzed a body of past Form 483 violations recorded by the FDA against 21 CFR Part 212 regulation. The report concluded that 85% of violations in Laboratory Controls stemmed from human error and could be avoided if Quality Control was completely automated. While this presents an opportunity to improve compliance, it is critical that the automated systems are simple, compact and reliable. Earlier attempts to automate PET tracer QC have resulted in complex mechanical systems that run the same tests as are done today. While providing a clear regulatory path by reliance on USP methods, such systems have proven to be complex, requiring constant maintenance, and cost prohibitive for both users and manufacturers. (The first such system has been built and patented by Trace-Ability founders during their earlier career enabling them to be the first to envision the next generation solution.) Tracer-QC takes an unconventional approach to QC automation. It provides the answers needed for QC of PET tracers, but it does not obtain them per USP. This allows all measurements to be made on one device, which makes the system very simple, compact and cost-effective. A truly simple solution for QC automation is set to offer unparalleled ease of compliance.

FDA Rationale – modernization of radiopharmaceutical production.

The agency sponsors development of technologies and regulatory science in areas where it sees a need for modernization and/or quality improvement (program # PAR-15-187). Trace-Ability's development of Tracer-QC (FDA Project number FD005517) addresses such a need in PET Tracer production. The metrics defined for Tracer-QC include measurable reduction in (a) quality risks, (b) radiation exposure, (c) number and complexity of SOP's and (d) future 483's. In a collaborative effort to facilitate the implementation of this solution, the agency has worked together with Trace-Ability to define a streamlined path for PET tracer manufacturers to transition to non-USP methods.

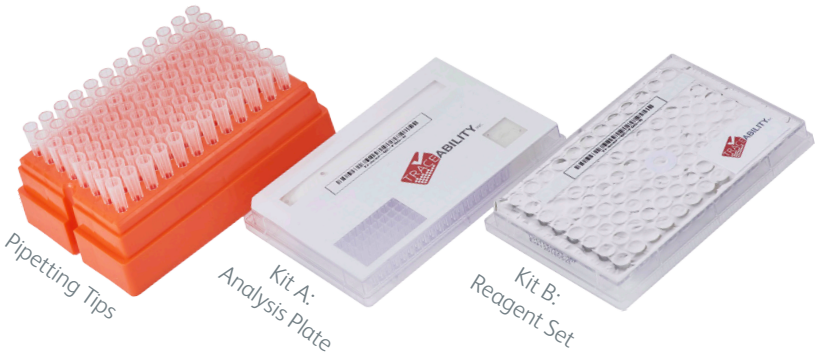


Tracer-QC Proposal

Tracer-QC Overview

A radical new solution for quality control of PET radiotracers.

The Tracer-QC revolutionizes testing operations within a Quality Control (QC) radiopharmacy. The system is completely automated whilst performing and reporting on 10 QC tests associated with PET and SPECT radiotracers, utilising only an optical plate reader, a pipetting robot and three simple-to-handle consumables.



Tracer-QC Software

Tracer-QC Pipetting Robot

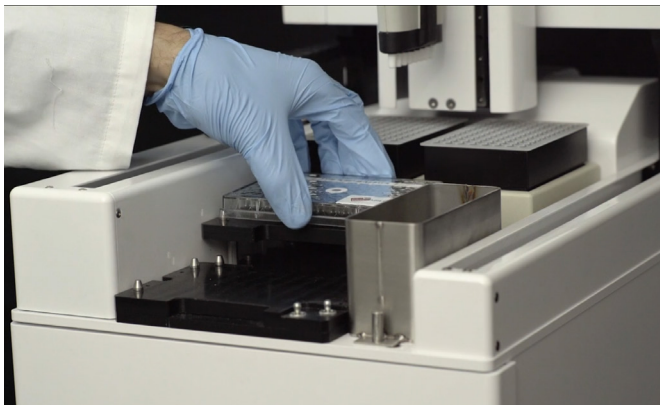
Tracer-QC Reader

The Process

Search Tracer-QC on YouTube to see the process in action

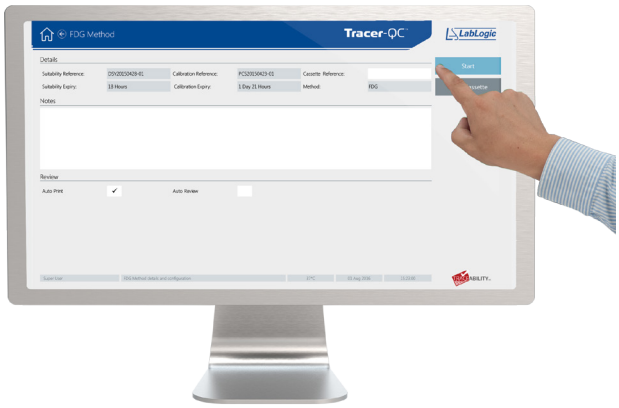
1. Add the sample and consumables

User installs three consumables and adds the product sample



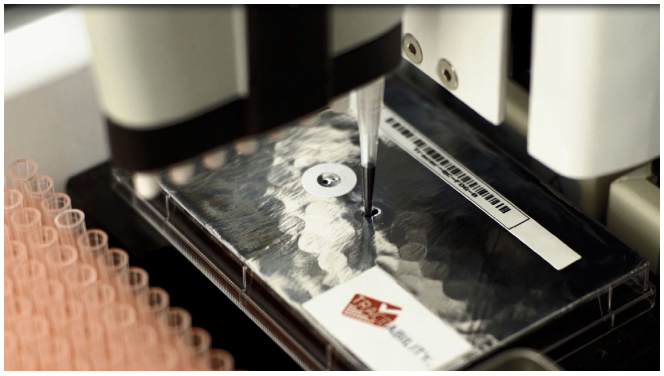
2. Initiates analysis

User initiates the analysis using the software



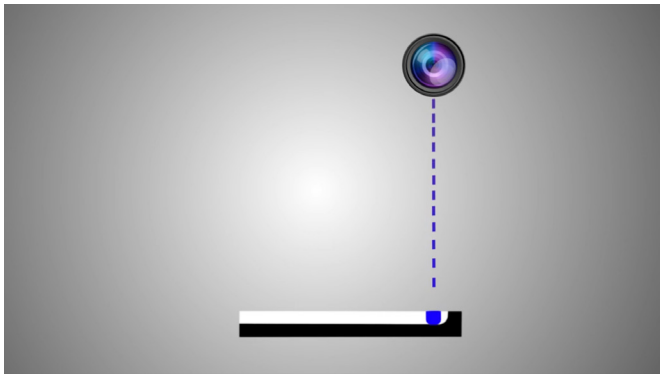
Tracer-QC Robot mixes and dispenses the sample

The pipetting robot mixes the sample with specific reagents and dispenses them to the analysis plate



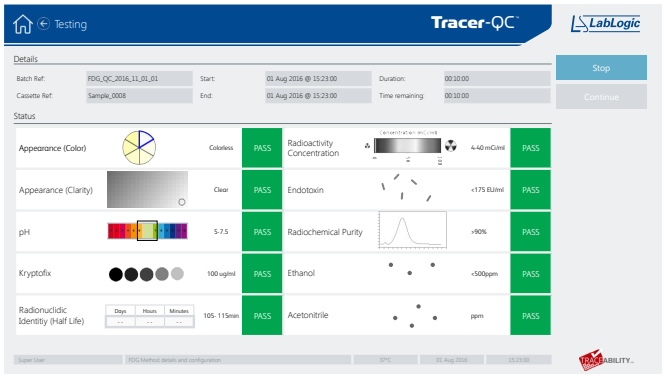
Tracer-QC Reader analyses the optical signals

The reader then analyses their optical characteristics against a set of predefined and validated reference specifications.



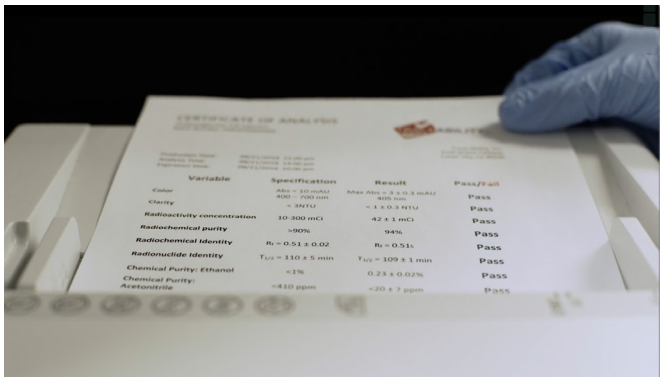
Analysis complete

After approximately 30 minutes a single page report on up to 10 QC parameters is delivered.



3. Collect the report

The pipetting robot mixes the sample with specific reagents and dispenses them to the analysis plate



Tracer-QC Proposal

Features & Benefits

Ease of Compliance

- No room for missing a process, record or signature
- Objective measurements with reference to standards and without any human interaction
- Data flow from measurement to batch record
  - Automated
  - Uncompromised
  - Completely traceable
- Regular automated suitability testing with permanent record
- 21 CFR 11 compliant software with access control
- No cross-contamination (samples never leave disposable kit)
- Ease of audit (internal or FDA) – instantaneous data retrieval

Efficiency and Safety

- 1 electronic report with all QC results, automatically generated
- Rapid QC results
- Increased throughput (to enable scale-up)
- Reduced risk of radioactive spills and contamination
- Reduced personnel exposure
- No cleaning or equilibration required (disposable kit)
- Inventory reduction (tracking individual expiry dates of multiple supplies/standards)
- Process standardization across sites and/or products

Cost Reduction

- Fewer and less skilled personnel
- Faster, cheaper training
- Faster, cheaper audits
- Remote record access/auditing
- Avoid cost of addressing 483's
- One machine to maintain
- Estimated net savings ~$26,000/year for FDG production (most common tracer)
- Estimated net savings of $56,000/year for each additional tracer beyond FDG

Size

- 34 cm (W), 98 cm (H), 67 cm (D)
- Takes up as much room as a typical GC

Scaleability

- Platform for easy addition of other tracers

One instrument

- Single mode of detection for all tests

Contactless Testing

- Sample never touches the instrument

Disposable Kits

- Single use, completely disposable path

Test Enabled by Tracer-QC

QC Test		Specification	Current Method	Tracer-QC method
1	Color	Colorless	Visual assessment	Absorbance measurements
2	Clarity	Clear	Visual assessment	
3	pH	5.5-7.5	Indicator + visual assessment	Colorigenic indicators
4	Kryptofix concentration	<50 ug/mL	Spot test + visual assessment	
5	Pyrogen concentration	<175 EU/dose	PTS reader	
6	Residual ethanol	NDA dependent	Gas Chromatograph	
7	Residual acetonitrile	<400 ppm	Gas Chromatograph	
8	Radionuclidic identity (T1/2)	105-115 min	Dose calibrator	Emission by scintillating material
9	Radioactivity concentration	4-40 mCi/mL	Dose calibrator	
10	Radiochemcial purity	>90%	TLC scanner	TLC + scintillating material
11	Sterility	>50 psi	Filter integrity (pre-injection)	Not included
12		Sterile	Culture test (post-injection)	

Radiotracers & Kits

Tracer-QC hardware and kits are designed to enable the tests listed in the above table across multiple tracers.

The most characterized process is that of QC of FDG. Most of the tests (1-9) developed for FDG are applicable to other tracers without changes.

Radiochemical purity test will require new composition of mobile phase (and possibly stationary phase) for non-FDG tracers.

The way we support your multi-tracer application is the following.

You can start by qualifying the system for QC of FDG, for which we offer the “FDG Kit” and FDG program.

Afterwards or in parallel you can develop the radiochemical purity test (with our support, if needed) for a non-FDG tracer using an “R&D Kit” and “R&D Tracer” program.

R&D Kits are less expensive while the R&D program allows more flexibility and yields QC reports watermarked “not for human use”.

Once you/we have developed/validated a process for your Tracer X, we will supply you with “Tracer X kits”.

Validation in partnership with the FDA
(U01FD005517)

Regulatory Considerations

As mentioned earlier, Tracer-QC methods do not follow Pharmacopoeial monographs. The streamlined path for anyone to start using them is the following. Once Tracer-QC is installed, qualified and validated on-site by LabLogic, the customer performs PQ for a given tracer. Then the customer files an amendment with the FDA to their respective NDA, ANDA or IND requesting addition of Tracer-QC method as an alternative method. This amendment includes a PQ report and cross-reference letter to Trace-Ability's Type V Drug Master File (DMF). That's all! The work necessary to prove Tracer-QC performance to the FDA has been done in context of extensive validation studies performed by the FDA Trace-Ability and Zevacor consortium with over 1000 pages of reports contained in the DMF. The validation studies have been designed in a manner that is not tracer-specific enabling application of Tracer-QC to a range of PET tracers.

Early Adopters. As an early adopter of Tracer-QC you get the benefit of additional support and discounts in exchange for starting to use Tracer-QC method before the DMF reference is available. The expectation is that validation for a method expected to work in your specific facility for your specific tracer will be much simpler than that being undertaken by the consortium (that validates methods across sites, tracers and even formulations).

FDA Funding Project

In context of FDA Project FD005517, the agency has dedicated internal resources and substantial funding with the goal of making Tracer-QC available to you and the rest of our industry as soon as possible with a clear regulatory mechanism for its adoption. Within the context of this project, Tracer-QC has been redesigned to: (a) achieve broad applicability across multiple manufacturers; (b) respond to validation requirements; (c) maximize performance across the pre-defined metrics discussed earlier.

Upon redesign, the system has been installed and qualified in Zevacor Pharma GMP facility, where it is currently undergoing validation. Additionally, in context of this project suitability testing procedures have been developed at University of California, San Francisco.

Scope of Supply

Tracer-QC offered herein is a complete solution for the performance of 10 tests required for QC of PET radio-pharmaceuticals. The offering includes the following components:

(a) Hardware. Tracer-QC instrument is composed of 2 subsystems – plate reader and liquid handling robot. The system will be assembled on-site and turned over as a single unit. The hardware provided withing this scope also includes a PC computer, monitor, keyboard and mouse.

(b) Kits. A single-use kit consists of Part A (analysis plate that is placed on the lower deck), Part B (set of reagents sealed in a plate placed on the upper deck), box of pipette tips (placed on upper deck), strip tubes placed in the heaters on the upper deck. All consumables needed for one run come as a package and are removed from the system after each run. Once the kit is removed, there is no radioactivity left within the stationary hardware and the system is ready for the next analysis run.

(c) Software. Validated software, FDA 21 CFR Part 11-compliant software allows execution of the complete QC process automatically. It offers an intuitive user interface that makes operation easy even for new employees with minimal training. It allows access control, data traceability and audit trails at the level needed for FDA 21 CFR 212 compliance.

(d) Installation and Validation. The system will be installed and qualified at the customer facility. IQ and OQ reports will be provided. Hardware and software will be validated on-site.

(e) Service. Tracer-QC solution comes with a 1 year warranty that covers all hardware and software. Customers have one contact point for all service needs.

(f) Support. Tracer-QC solution comes with a 1 year of application support that covers all inquiries related to the use of the system. Customers have one contact point for al service needs. As an early adopter, you will receive the maximum level of support that will allow you to quickly ramp up Tracer-QC for maximum use cases.

(g) Training. One training session for up to 5 users is included in the scope of this proposal. The level of automation offered by Tracer-QC leads to minimal time needed for the training and minimal pre-requisites.

Additional services that are not in the scope of this proposal but are available upon request include:

(a) Assistance with PQ in context of a specific PET tracer

(b) Assistance with regulatory filings

(c) SOP templates. These documents will provide content that can be easily pasted into existing customer templates as required by the local QMS.

Tracer-QC Proposal

Purchase Options

1) Outright capital purchase as detailed in the accompanying quotation

2) Option to take advantage of one of the extended payment plans

3) Option to take advantage of lease hire

Early adopter discounts

As an early adopter, we wish to reward your trust in us and by helping us bring Tracer-QC to the community in which we operate.

As reward, we propose to offer you the following;

1) 25% reduction of the package. This applies to outright purchase or any of the extended payment plans.

2) 25% reduction on aftersales support

3) 25% reduction of the purchase of FDG kits for as long as you use Tracer-QC in your facility

4) 25% reduction on the purchase of any future kits that we develop

Why we chose you

It is very simple, we see you as innovators. Additionally, we already have an established relationship that has been honed over the past few years; we each know how we operate.

Tracer-QC Proposal

Europe & Worldwide

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