Charles University, Faculty of Science
Place of business: Albertov 6, 128 00 Praha 2
IC: 00216208, DIC : CZ00216208,
Represented by: prof. RNDr. Jiří Zima, CSc., dean of the faculty
IBAN: CZ25 0100 0349 5609 2145 7021 hereinafter referred to as the Buyer

VZ/19/573

SELLER	CTL Europe GmbH		
Represented by		Position	COO with power of attorney
Place of business	Hans-Boeckler-Strasse 19-29	ID/	HRB 16468 Amtsgericht Bonn
Mailing address	53225 Bonn Germany	Tax N.	DE227818386
Registered in	Bonn Germany	Account number	

THE PURCHASE AGREEMENT

Seller's contract number..... Buyer's contract number[1].....

A. Special part

Department of Buyer	Department of Genetics and Microbiology		
Subject of the contract	**by the Seller** Transfer of ownership of the goods to the Buyer Delivery to the place of delivery Installation Providing necessary training with acquired goods to 2 persons (minimum six hours) Removal of packing material Handover of documents		
	by the Buyer Receipt of the goods at the point of delivery Payment of the purchase price		
Description of goods	New and unused -ImmunoSpot®Series 6 Ultimate UV Image Analyzer Further definition of the goods specified in the Annex 1 and 2.		
Delivery date	**Not later than 12 weeks**	**Place of delivery**	**BIOCEV, Průmyslová 595, 252 50 VESTEC, Czech Rep., room A2.024**
Price without VAT in Euros	**89 999,00**		
Payment of invoices	30 days after delivery	**Basic terms of payment**	- Advance is not provided - Payment after delivery / installation of goods - Number of this contract must be on the invoice
The warranty period	**30 months**	**removal of defects warranty**	On-site service at the latest in 72 hours and other defects within 25 working days from notification
Place of removal of defects	Prague – onsite- remote	**Contact for notification of warranty defects**	
Parts which wear out quickly (wear parts)	---	**Warranty on wear parts**	---
Terms of sanctions	- For delay with payment of financial performance. Interest on late payment 0,05 % of the owed amount for each day of delay - For delay in delivery of goods a penalty of 0.05% of the price for each day of delay - For delay in removing reported warranty defects 0.01% of the price for each failure to cure the defect and the warranty day delay		
Other arrangements	Seller's Authorized persons (contact): Buyer's Authorized persons (contact):		
Action name	**"Fluorescent ELISPOT reader"**		

[1]To be added manually by the buyer before signing the contract

B. General part

This part regulates detailed conditions of the purchase contract. The Part A defines basic conditions of Contract. In the event of any conflict between the Part A and the Part B of this Contract, the Part A has precedence.

I. Introductory provisions

1) The seller must deliver the new and unused goods and provide services associated with the delivered goods. If the Contract is concluded on the basis of a selection or an award procedure the goods must have product properties and parameters required by the buyer in the tender conditions. Goods must fulfil the stated purpose. If the purpose is not expressly stated, it must fulfil the purpose which is determined by the way the goods are generally used.
2) The goods delivered contrary to the paragraph 1 of this Article shall be deemed defective.

II. Invoicing and payment terms

1) The purchase price includes all costs and profit of the seller. The purchase price includes, in particular customs, taxation, banking and other fees, transport and installation of the goods, putting into a permanent operation, removal of packing material, an operator training and the buyer's costs for warranty service. The purchase price is fixed and complete and includes complete delivery.
2) The buyer shall pay the purchase price after receiving the goods and documents necessary for the operation of a device and the signature of the protocol of delivery and acceptance of goods, and possibly even the installation of signature of the Protocol, on the basis of an invoice (the "Invoice") with a maturity specified in the Part A of this Contract, which shall commence after the delivery of the invoice to the buyer.
3) The date of payment of the purchase price shall be considered the day on which the amount is debited from the account of the buyer to the seller's account stated on the invoice. The invoice must be in accordance with the generally binding legal regulations, it must contain the maturity date (in accordance with this Contract) and its annexes must contain a copy of the installation protocol signed by both parties. The invoice must contain a number of the Contract. If there is no obligation for the seller to install the goods, a copy of acceptance report signed by both parties shall be attached to the invoice. If the invoice is incorrect or incomplete, the buyer is entitled to return it to the seller for a revision or an amendment. In this case, a new maturity period runs from the date of receipt of the corrected invoice by the buyer.
4) If there is a risk that the buyer could be liable for an unpaid VAT within the meaning of § 109 of the VAT Act (č. 235/2004 Sb.), the buyer is entitled to pay the VAT on the deposit account pursuant to § 109a of the VAT Act.

III. Terms of delivery and transfer of title

1) The buyer reserves the right in a case of early or late delivery of the goods or incomplete deliveries, at its sole discretion either accept the goods or to reject them and by that withdraw from the Contract.
2) The seller delivers the goods with proper accessories. Accessories especially means (installation material, assembly jigs, connectors, jumper cables, user codes, passwords, etc..).
3) A protocol about delivery and acceptance of the goods (the "acceptance protocol") shall be drawn up and signed after the delivery and acceptance of the goods. The acceptance Protocol must include, among other things, information about the frequency and method of revisions. If there is a seller's responsibility to install the product, there shall be drawn up and signed an installation protocol by both parties about the installation of goods, commissioning and testing.
4) The buyer is obliged to accept the goods only if it is free of defects. The buyer is entitled to refuse defective goods.
5) The seller's and buyer's Authorized persons listed in the Part A of this Contract are entitled to collect the goods and pass and sign the acceptance protocol, and if the goods will be installed by the seller, Authorized persons are entitled to sign the installation protocol.
6) The seller agrees to deliver to the buyer the documents necessary for the proper use of the goods, for example appropriate approval certificates, declarations of conformity, instructions for usage and operation, assembly and installation instructions.
7) The buyer shall acquire right of ownership to the goods at the time of signing installation protocol by both parties. If there is not an obligation of the seller to install the goods, right of ownership to the goods passes to the buyer upon signing the acceptance protocol.
8) Risk of damage to the goods passes to the buyer upon signing the installation protocol. If there is not an obligation of the seller to install the goods, risk of damage passes to the buyer upon signing the acceptance protocol.
9) If the seller is required to install the product, the installation shall be completed immediately after the delivery of goods and without undue delay. The seller is obliged to perform the installation with professional care and warn the buyer about risks associated with the placement of goods. The seller is obliged to refuse an installation of the goods if the conditions specified by the manufacturer or by generally binding legal regulations for its implementation are not met.
10) If the seller is obliged to train operators, he must do so upon delivery, unless the parties agreed otherwise. The seller is obliged to provide the buyer with the necessary cooperation, in particular to determine the persons whom shall participate in the training and ensure their participation in the training.

IV. Guarantee of quality (warranty)

1) The seller provides the buyer a guarantee of quality (warranty) for the period specified in the Part A of this Contract. The guarantee (warranty) begins on the installation of the goods, unless the seller is obliged to perform, then it begins after the signing of acceptance protocol.
2) The seller guarantees that the product will have the usual characteristics or properties stated by the Contract during the guarantee period.
3) Warranty service is provided free of charge by the seller and includes all costs associated with the warranty service, especially the costs of spare parts, travel and labour services of a technician.

4) In the event that the goods are a medical device according to the law No. 268/2014 Sb., the seller is obliged to do free periodic safety technical inspections of goods in accordance with the law No. 268/2014 Sb. and its implementing regulations.
5) The buyer announces warranty defects to the Contact for notification of warranty defects or seller's Authorized person referred to in the Part A of this Contract. Seller shall start examining and working on the removal of the claimed defects after the receipt of the notice of defects without undue delay. If the seller will not be able to remove the defects within the period of time provided for removal of warranty defects set out in the Part A of this Contract, the seller will provide and deliver an adequate replacement device or devices that functionally replace the defective goods, until the defective goods are repaired and put into operation.
6) If the warranty defects are removed by the seller according to the Part A of this Contract, the buyer sends notice along with the goods.
7) The warranty period does not run as long as the buyer cannot use the goods for its defects, for which is the seller accountable for.
8) The warranty does not cover damage to the goods caused by an improper or incorrect installation or an incorrect operation contrary to the instructions given in the operating instructions, or an inadequate storage contrary to its technical characteristics.
9) The buyer is entitled to withdraw from the Contract if he cannot deliver the notice of defects to the seller.
10) If the seller is in default with the removal of warranty defects, the buyer has the right to withdraw from the Contract after providing an additional reasonable time for removal of defects.
11) In the event that the warranty defect is not repairable defect, the buyer is entitled to withdraw from the Contract or to request delivery of new goods.
12) In the case of an unjustified notice of defects the buyer pays the costs of removing defects.
13) The buyer has the right for the removal of defects even if the defects were knowable during the Contract closure.

V. Final negotiations

1) Contract's penalties are set out in the Part A of this Contract.
2) If the goods or its part meet the criteria of a copyrighted work, the seller transfer to the buyer even the non-exclusive license to all types of usage of such work without the restrictions of time or spatial constraints. The buyer is not obligated to use the work. The price of the license is included in the purchase price.
3) Individuals who enter into this Contract on behalf of each party signature the Contract claim that they are entitled to make a valid contract.
4) The seller is not entitled without the prior written consent of the buyer to assign any rights or duties arising from this Contract to a third party.
5) The seller agrees to cooperate with the control pursuant to §13 paragraph. 3 of Law no.320/2001 Sb., on financial control.
6) If the Contract follows the selection or procurement procedure, then this contractual relationship governed by these documents are of descending importance:
   a) Annexes to this Contract,
   b) the tender documentation,
   c) offer of the seller.
7) This Contract can only be modified by numbered amendments in writing signed by both parties.
8) The seller undertakes the risk of a change in circumstances within the meaning of § 1765 paragraph. 2 of the Civil Code of the Czech Republic
9) The buyer excludes the possibility of accepting new contract or variation to the contract or addition to the contract within the meaning of §1740 paragraph. 3 of the Civil Code of the Czech Republic.
10) The Contracting Parties agree that the rights and obligations of this agreement shall be governed by the Civil Code of the Czech Republic.
11) The seller acknowledges that the buyer is obliged to publish all contracts including its annexes and any amendments if the price of performance is greater than 50 000 CZK without VAT. The seller agrees that the buyer discloses the Contract pursuant to the Act No. 340/2015 Sb. or/and also according to the Act No. 134/2016 Sb. as a whole, because there is no information in the contract which disclosure would be an unlawful interference with the rights and obligations of the seller or its employees. The seller agrees that the contract will be disclosed, including manual signatures of representatives of the parties.
12) The Contracting Authority assumes that this Contract will be signed electronically. If this Contract is in paper form, it will be written in two counterparts. Each of the Contracting Parties shall receive one counterpart.
13) This Contract shall enter into force upon a signature by both parties. This Contract shall enter into effect upon publication of the Contract pursuant to the Act No. 340/2015 Sb.
14) The Contracting Parties declare that they have read this Agreement, and that it was made after mutual negotiation using their free, serious, determinate and comprehensible will, not in distress or grossly disadvantageous conditions.

In Prague .....

Buyer: prof. RNDr. Jiří Zima, CSc.
Digitálně podepsal prof. RNDr. Jiří Zima, CSc.
Datum: 2020.02.24 12:52:30 +01'00'

.....
prof. RNDr. Jiří Zima, CSc.
Dean of Faculty of Science,
Charles University

In Bonn on February 18th, 2020

COO with Power of Attorney
CTL Europe GmbH

CTL Europe GmbH
Hans-Boeckler-Str. 19-29
53225 Bonn, Germany
HRB 16468
Amtsgericht Bonn

Annex 1

Annex No. 3 to the Tender Documentation

Specification of the Subject Matter of the Performance and the Technical Requirement of the Contracting Authority

For the purposes of performing the public contract entitled "Fluorescent ELISPOT reader_repeating", the Contracting Authority has set forth the below absolute (minimum) technical requirements. For the basic device description, see Section 2.1 of the tender documentation.

If the Tenderer fails to comply with any of these absolute (minimum) technical requirements and fails to offer an equivalent or better solution, they will be excluded from the tender procedure. Compliance with these parameters will also be required by the Contracting Authority with the demonstration of functionality.

The Tenderer shall complete all the rows of the table below according to the solution on offer. If they fail to specify YES in either row (i.e. the information that the device fulfils the required parameter), they will be excluded from the tender procedure. The Contracting Authority shall take the similar approach if the Tenderer fails to complete any of the rows.

In addition to demonstrating the compliance with the minimum requirements, the Tenderer shall provide a detailed description of their solution proposal (i.e. the technical specifications of the performance and the specification of the device parameters) so that the subject matter of the tender bid is definite. The description of the solution will form Annex No. 2 to the draft contract.

In addition, the Contracting Authority also emphasises the tender procedure condition that the offered solution must have better or equivalent parameters as the parameters required below in the absolute (minimum) technical requirements.

The Contracting Authority sets the absolute (minimum) technical requirements as follows:

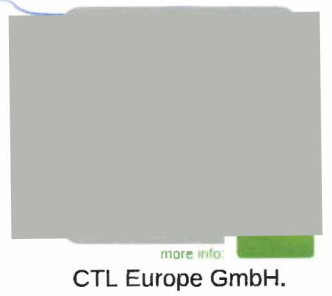
	Absolute (minimum) technical requirements **Fluorescent ELISPOT reader_repeating**		
	Name of the technical parameter including the required upper / lower limits	**Met by the Supplier YES/NO**	**Possible specification of the offered product[1]**
1.	Number of fluorescent excitation sources: at least 4	YES	The instrument will be supplied with 4 different Long Life, Ultra-High Power LEDs
2.	Number of emission filters: at least 7	YES	The instrument comes with 7 filters, with matching multi band cube enabling to visualize up to 14

[1] The Supplier will provide the parameter specification in a separate chapter of the tender bid.

			colors
3.	Computer controlled, motorized zoom lens with autofocus.	YES	Zoom and focus is motorized, computer controlled, for Multicolor FluoroSpot and Cell counting
4.	Camera resolution: at least 25 megapixels	YES	25 megapixel, with Planar backlight
5.	Barcode reader for sample encoding and verification	YES	Integrated bar code reader supplied for automated plate identification; in line with GLP
6.	Supported plate formats: at least 384 – 6 wells including 96, 48, 24, and 12 wells.	YES	The Instrument supports in addition to 6,12,24,48,96,384 well plates, Terasaki plates as well; Integrated bar code reader is supplied for automated plate identification; *Optionally* extendable to read Petri dishes; *Optionally* extendable to high-throughput with plate loader
7.	Counting of various cells (including splenocytes and tumor cells) in hemocytometer and in 96 well multiwell plates with black walls and a flat and clear coverslip bottom – distinguish between live, dead and apoptotic cells by fluorescent staining; supplying a reference plate for counting calibration.	YES	The requirement is fully met, inclusive the annually renewable reference plate, assuring that cells counted are appropriate.
8.	Analysis of histological slides	YES	Default adapter for 4 slides; Customized adapter can be manufactured and provided on special request
9.	Dedicated software for: • single color enzymatic ELISPOT assays • dual color enzymatic ELISPOT assays • single and multicolor FluoroSpot assays – with simultaneous detection, providing inclusive and exclusive spot counts and all co-expressors • bioassays counting plaques, colonies or spots with various size and shape: virus neutralization assay, serum neutralization assay, viral plaques assay,	YES	Dedicated SW are provided for all, i.e. : ImmunoSpot® SW for SCE; ImmunoSpot® for DCE, ImmunoSpot® for Scientifically validated, objective, single & multicolour FluoroSpot analysis; BioSpot® SW :Viral Plaque Assays • Microbial Colony Counting • Yeast Colony Counting • Serum Bactericidal Assay • Clonogenic Assays

	focus forming assay, bacterial colony counting • cell counting, providing calculation of cell concentration, including dilution of samples • measurement of cell-mediated cytotoxicity • statistical evaluation All above counting software has to have a Quality Control module for correcting any item (artefacts, damaged membrane area etc.) and stored annotations for each action or modifications made on counted wells		• Viral-ICA • Minimum Inhibitory Concentration (MIC) • Osteoclast • Most Probable Number (MPN) • Cytopathic Effect (CPE) • Mouse Lymphoma Assay (MLA) • Ames Test • Stem Cell Assays (CFU-EC, CFU-GM, etc.) • Serum Neutralization Assay • Plaque Reduction Neutralization Testing (PRNT) ☑ Virus neutralization assay (96&384 well plates) • Opsonophagocytic CellCounting SW for L/D/A, with comprehensive reports as requested Dedicated SW module for NK-TVA All SW and module comes with Quality Control, all action effected is annotated; audit trail for each action performed is documented SpotStat® provides statical data evaluation
10.	Personal computer: processor with PassMark > 9000, RAM > 16 GB, HDD > 1 TB, monitor at least 24" 1920 x 1200, operating system MS Windows	YES	Data processing unit: processor with PassMark > 9000, RAM 16 GB, HDD 1 TB, Monitor 24" Professional Widescreen, Please note bigger than 24" monitor can be supplied on demand, however it might be prohibited by Health and Safety regulation because the minimum working distance to the monitor cannot be granted; Operating system MS Windows 10 Pro x64, Microsoft Office 2019 Business

Bonn, December 18th, 2019



CTL Europe GmbH.

Annex 2

Scientifically validated, objective ELISPOT analysis

Scientifically validated objective ELISPOT counting to establish absolute numbers and frequencies of cytokines secreting T cells using CTL's proprietary SmartSpot/SmartCount. The primary scope of ELISPOT analysis is to establish the number of antigen-specific T cells within the entire pool of cells contained within PBMC.

As T cells have only one antigen specificity per cell, the number of antigen-specific T cells per PBMC is absolute, i.e. there is a set number of the antigen-specific T cells present in a well. From this notion it also follows that the variation of this number will follow normal distribution among replicate well. Accurate ELISPOT analysis establishes the absolute number of antigen-specific T cells within PBMC. The challenge hereby is that spot sizes produced by antigen-specific T cells vary tremendously between T cells specific for the same antigen. Our studies even of T cell clones showed this widespread of spot sizes produced by the individual cells contained within the.

Our experimental studies established however that the size variation of the spots follows predictably a log normal function thus using parametric statistics can be used to define what spots are produced by individual T cells vs. cell clusters of such or by other non-antigen specific T cells containing PBMC such as cytokine producing NK and dendritic cells that should be **gated out** and must not be counted as counting them would inflate the number of antigen specific T cells causing false positive results. Using this statistics-based counting approach we could establish that 100% of the cloned T cells plated per well are indeed detected and that this approach is indeed essential to accurately establish the absolute number/frequency of T cells per well.

Extensive follow up studies showed that what was shown for T cell clones also applied for polyclonal antigen specific T cells in PBMC.

The ImmunoSpot® SW **AutoGate** function operating within the SmartCount module sets automatically upper and lower size gates based on the above well-established principle. Of course this objectively set gates can be used as a mere "suggestion" for gating and can be overwritten by fine-tuning for those investigators who believe that their subjective assessment is more precise than the statistics-based generation of gates.

For such investigators we would like to draw the attention to nine experienced independent laboratories which were asked to set the size gates according to their best judgement while analyzing one and the same ELISPOT plate. Not surprisingly the counts established subjectively showed considerable inter-investigator variation. However the mean of the nine subjective counts precisely corresponded to the numbers established using the AutoGate function of ImmunoSpot® verifying its objectivity. The **VerifyGate** function within the ImmunoSpot® SW is an additional tool which permits to compare how much manually set gates deviate from those established from the range predicted by

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stringent statistical criteria. The ELISPOT reader is not a mere spot counter, but a scientific instrument that needs reliably establish the frequency of antigen specific T cells within PBMC.

While working with PBMC and primarily with different cytokines one needs to account for the background produced by the cells of the innate immune system that can also produce cytokine spot counts, which if not excluded as background spots, will produce essentially meaningless numbers.

An issue with ELISPOT analysis is also that the background coloration of the well is frequently uneven requiring the utilization of different counting parameters or accurate identification of corresponding (foreground or background) spot categories. The ImmunoSpot® SW **BackgroundBalance** feature embedded in the SmartCount module, automatically makes such adjustments as required for accurate counting. Cytokines are produced asynchronously by T cells peaking at 24 hrs for IFNg and IL2, 48 hrs for IL4 and 72 hrs for IL17. This differential cytokine secretion kinetics along with different quantities of cytokine secreted and different affinities of the capture antibodies for the respective cytokines result in different spot morphology for each cytokine that need to be accounted for in enumerating ELISPOT. Counting parameters therefore need to be adjusted and fine-tuned for each analyte to be detected. ImmunoSpot®'s **SmartSpot** feature along with its auto gating function permits to do so automatically and objectively to generate objective, accurate counting results. Artificial intelligence features embedded in the SW will permit you to come up with such parameters for any assay type. CTL is the only company that has firsthand in-house experience in T cell ELISPOT analysis. CTL's founding scientists have dedicated over 200 peer-reviewed publications to elevating T cell ELISPOT to an exact science.

The lessons learnt in the laboratory have been incorporated into the ImmunoSpot® SW through relentless refinement of analysis to meet the highest demand of academic and regulated scientists. The ImmunoSpot® SW has matured for over 20 years with bench scientists and programmers working hand-in-hand. We at CTL have all reasons to maintain that the professional ELISPOT reader must not be a subjective spot counter but an instrument that provides objective, user-independent, scientifically validate count results. The software and not the hardware makes all the difference. A side by side comparison will reveal the differences.

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Scientifically validated, objective, multicolour FluoroSpot analysis

- To simultaneously enumerate the number of antigen-specific T cells that produce several cytokines
- Even more importantly to precisely define the cytokine co-expression pattern by individual T cells as this permits to identify T cell subpopulations such as polyfunctional stem cells like effector memory and other population that differentially contribute to cell-mediated immunity

Until recently the latter was confined to flow cytometry analysis, but now can be done with much higher sensitivity with a fraction of the PBMC needed, with much higher throughput capability at a fraction of the cost by 4 colour FluoroSpot.

As to scope number 1 the accurate frequency determination for T cells producing analytes each of the analytes in a multi-colour FluoroSpot assay it is important to fine-tune a FluoroSpot reader such that each of the fluorochromes can be detected separately without cross-bleeding of colour. This can be accomplished by fine-tuning excitation and emission wave lengths corresponding filters. CTL analyzers permit 7 colour analysis in their standard configuration, but can be customized for more. Because all of this is accomplished without cross-bleeding of colours, the analysis of each colour can be done without the need for compensation following the same rules as described for single colour assay objectively fully automated in a scientifically validated manner. Accurately establishing cytokine co-expression patterns by individual antigen-specific T cell subpopulation is slightly more complex. Somewhat naively one might expect that simple centre of mass overlays for different analytes might suffice to identify co-expression by one individual cell, i.e. if a T cell produces X and Y analytes simultaneously then the spot in the X colour plane and the one in the Y colour plane would precisely overlap when the two colour planes are overlaid. Upon a closer look this notion does not hold up however. We argued the precise number of cytokine co-expressors should be linearly related to the number of T cell plated per well, thus if the frequency of the IFNg, IL2 and TNFa co-expressing polyfunctional T cells is e.g. 40 per 400,000 PBMC, then the number of such T cells should be half of that if half as many PBMC is plated 20 in 200,000 in this example, and 10 if 100,000 PBMC are plated per well; doubling the PBMCs to 800,000 would double the number of polyfunctional cells of 80 in this example. Any deviation from such a linear relationship between PBMC number plated and cytokine co-expression proves that the frequency of the polyfunctional cells is not measured accurately. Simple centre of mass overlays in such serial dilution experiments entirely failed to reveal a linear relationship between cell numbers plated and centre of mass based co-expressors. ^

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Scientifically validated, objective, multicolour FluoroSpot analysis

Introducing an analyte combination specific tolerance parameter for a tolerated centre of mass deviation however resulted in a close to perfectly linear relationship between PMBC numbers plated and cytokine co-expression seen. This observation follows the well-established notion that individual T cells secrete cytokines asynchronously one after the other while moving from APC to APC in the interim. Centre of mass tolerance adjustments are therefore essential for the accurate measurement of the frequency of antigen-specific T cell subpopulation based on the individual cells' of serial cytokine expression profile.

The ImmunoSpot® SW permits such measurement accurately. Simple centre of mass overlays are unsuited for such purpose. Contributing to this type of experimental studies to verify the requirements

for scientifically validated data analysis is a recent example of CTL's long-term commitment to elevating ELISPOT to an exact science

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