LAMBDA light Chains CISH kit

For *In vitro* Diagnostic Use

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CE IVD

LAMBDA light Chains CISH kit

1 AVAILABLE PRODUCT FORMATS

The LAMBDA light Chains CISH kit is designed for 20 tests and includes the following components:

Vitro Ref	Biocare Ref	Tests	Vitro Component Ref	Biocare Components Ref	Quantity x Volume
MAD-001894QHVSBC	EG023-VTR-CK-CE-NP	20	MAD-001894HSVS	EG023-VTR-CP-CE-NP	1 x 1.41mL
			MAD-001892QDVS	EG024-VTR-DIG-CE-NP	1 x 7mL
			MAD-011892QECVS	EG025-VTR-PK-CE-NP	1 x 14mL

Table 1. References and presentation

2 INTENDED PURPOSE OF THE PRODUCT

The LAMBDA light Chains CISH kit is a qualitative automated test designed for the detection of lambda (λ) light chain mRNA in formalin-fixed paraffin-embedded (FFPE) tissue specimens through chromogenic in situ hybridization (CISH).

3 SUMMARY AND EXPLANATION

Immunoglobulins (Igs) are composed of two heavy chains and two light chains, with each light chain containing a constant and a variable domain. During early B-cell development, gene rearrangements of the variable (V), diversity (D), and joining (J) regions result in the production of a functional immunoglobulin molecule. Heavy chain rearrangement occurs first (pro-B stage), followed by light chain rearrangement (pre-B stage).

Human B lymphocytes express one of two light chain isotypes: kappa (κ) or lambda (λ), but never both. The κ gene is located on chromosome 2 and the λ gene on chromosome 22. Under normal conditions, about 60% of B cells express κ, and 40% express λ light chains. This balanced distribution produces a polyclonal expression pattern in reactive lymphoid tissue.

Like all malignant neoplasms, B-cell lymphomas are clonal proliferations arising from a single transformed B lymphocyte. As a result, they produce immunoglobulins containing only one type of light chain, either kappa (κ) or lambda (λ), a feature known as monoclonal expression. Consequently, assessing the κ/λ light chain ratio within a given cell population is a key diagnostic tool for determining clonality, and for distinguishing malignant B-cell lymphomas or plasma cell neoplasms from reactive, polyclonal proliferations.

The LAMBDA light Chains CISH kit is designed for the *in situ* detection of lambda (λ) light chain mRNA in formalin-fixed, paraffin-embedded (FFPE) tissues using chromogenic in situ hybridization (CISH).

4 PRINCIPLE OF PROCEDURE

Chromogenic In Situ Hybridization (CISH) is a molecular technique used to detect specific nucleic acid sequences in formalin-fixed, paraffin-embedded (FFPE) tissue sections. The LAMBDA light Chains CISH kit is designed for the automatic qualitative detection of mRNA of Lambda light chains sequences in tissue specimens. The method is based on the hybridization of a labeled probe to complementary sequences within B-cells expressing mRNA Light chains. Following hybridization, the probe is visualized through an enzyme-conjugated detection system (peroxidase) and a chromogenic substrate (DAB). Enzymatic activation of the chromogen produces a visible reaction product at the hybridization site.

After chromogenic development, specimens may be counterstained and coverslipped. Results are interpreted using a standard light microscope.

5 RECONSTITUTION, MIXING, DILUTION

This product is provided in a ready-to-use format. It is not necessary to reconstitute, mix or dilute it.

6 ADDITIONAL REQUIRED MATERIAL NOT SUPPLIED

6.1 Reagents and materials

- Cover, Biocare Ref NPRI10002L2, Vitro Ref. MAD-003983VS
- Dewax Solution, Biocare Ref. NPRI10001T280, Vitro Ref. MAD-004080VS
- DAB Enhancer, Biocare Ref. NPRI10005L2, Vitro Ref. MAD-001560QV
- Contrast Hematoxylin HDH3, Biocare Ref. NPRI10006L2, Vitro Ref. MAD-HDH3-100VS
- TBS Tween 20 Buffer 10X, Biocare Ref. NPRI10007MM, Vitro Ref. MAD-004077R-10
- Cleaning Solution 10X, Biocare Ref. NPRI10008MM, Vitro Ref. MAD-003931CSVS
- Probe Cleaning Kit, Biocare Ref. NPRI10009KC10, Vitro Ref. MAD-PCLK
- Master Polymer Plus Detection System, Biocare Ref. NPRI10010T135, Vitro Ref. MAD-000237QKVSBC
- IHC Treated Slides, Biocare Ref. NPRI10011, Vitro Ref. MAD-15-188-55/100
- Mixing Tubes, Biocare Ref. NPP20001, Vitro Ref. MAD-60732-100

6.2 Equipment

- NeoPATH Pro
- Optical microscope and/or digital scanner of histological slides

7 STORAGE AND STABILITY CONDITIONS

Component:	Use conditions
Storage conditions	Store at 2°-8°C and keep away from sources of intense heat/cold until the expiration date of the product.
In-use stability	Once open, keep at 2°-8°C until the expiration date of the product.

Component:	Use conditions
Shipping conditions	Shipment should be performed at 2-8°C.

Table 2. Storage and stability conditions.

The product is stable to the expiration date printed on the label when stored at 15°-25°C. Do not use after expiration date.

8 SPECIMEN PREPARATION

Paraffin Sections: Tissues fixed in *formalin* are suitable for use prior to paraffin embedding.

9 WARNINGS AND PRECAUTIONS

- **Read the instructions for use before using this product.** In case of atypical or unexpected results, please contact your Authorized Supplier/Distributor.
- **Professional Use.** This product is only intended for professional laboratory purposes, and it is not intended for pharmacological, domestic or any other type of use. When the product is used as an aid to diagnosis it should only be handled by trained users and in authorized laboratories.
- Do not use reagent after the expiration date printed on the label.
- Rx Only **Physician prescribed test.** This product is for professional use only on prescription by a physician or other healthcare professional.
- **Use**:

- Specimens, before and after fixation, and all materials exposed to them, should be handled as if capable of transmitting infection and disposed of with proper precautions.
- Microbial contamination of reagents may result in an increase in nonspecific staining or/and erroneous results.
- Incubation times or temperatures other than those specified may give erroneous results. The user must validate any such change.
- Do not use reagent after the expiration date printed on the label.

- **Serious incident.** Any serious incident related to the use of this product that involves or may involve a serious deterioration, temporary or permanent, of the state of health of a patient, user or other person, or even death, or a serious threat to public health, must be reported as soon as possible to the manufacturer by e-mail at regulatory@vitro.bio and to the competent Health Authority of the EU member state where the user or patient is established. If the user is located in USA, report any serious incidents related to this device by contacting the local distributor (information identified on the product labelling) and the applicable competent authority of the Member State. Incidents caused by misuse of the product or by the use of the product beyond the useful life established on its labeling will be the responsibility of the user.
- **The safety and disposal precautions are described in the Safety Data Sheet of this product.** The current version of the Safety Data Sheet (SDS) of this product can be downloaded in the web page www.vitro.bio or requested at regulatory@vitro.bio.
- **Waste disposal:** The handling of wastes generated by the use of the products commercialized by Vitro S.A. must be performed according to the applicable law in the country in which these products are being used. As reference, the following table indicates the classification of wastes generated by this kit

according to the European Law, specifically according to the *European Commission Decision of December 18, 2014* amending decision 2000/532/CE on the list of waste pursuant to Directive 2008/98/EC of the European Parliament and of the Council:

POTENTIAL WASTE GENERATED AFTER USING THIS PRODUCT	ELW* CODE	TYPE OF WASTE ACCORDING TO ELW*
Container for reagents used classified as dangerous (according to the Safety Data Sheet).	150110	"Containers containing waste or contaminated by dangerous substances"
Aqueous liquid waste containing hazardous substances (not solvents).	161001	"Liquids generated from the use of automatic IHC/HIS instruments: - Waste deposit of immunostainers. - used PT-Module buffers"
Consumables (tubes, tips, etc.). Any element that has been in contact with tissue samples.	180103	"Waste whose collection and disposal is subject to special requirements in order to prevent infection"
Liquids containing solvents (xylol, haematoxylin, alcohol, eosin), generated from immunostaining techniques.	160506	"Laboratory chemicals consisting of or containing dangerous substances, including mixtures of laboratory chemicals".

Table 3. Classification of waste generated by the use of this kit according to the European Legislation. *ELW: *European Legislation of Waste.*

***Note: This classification is included as a general guideline of action, being under the final responsibility of the user the accomplishment of all the local, regional, and national regulations on the disposal of this type of materials**.

10 INSTRUCTIONS FOR USE

Place the reagent in the NeoPATH Pro before starting the CISH process in the instrument. Select the appropriate protocol from the instrument's menu and follow the on-screen instructions.

11 TROUBLESHOOTING

Follow the CISH recommendations according to NeoPATH Pro protocol. If atypical results occur, contact Vitro's Regulatory Department at regulatory@vitro.bio.

12 LIMITATIONS

- Results must be interpreted by qualified healthcare professional in the context of patient´s clinical history, symptoms, and other diagnostic findings.
- The correct performance of the test depends on the quality of the sample.
- NeoPATH Pro and the ancillary reagents should be used with formalin-fixed paraffin-embedded tissue sections. The use of any other type of sample may generate erroneous results and its performance must be verified beforehand.
- Tissue staining is dependent on the handling and processing of the tissue prior to staining. Improper

fixation, freezing, thawing, washing, drying, heating, sectioning or contamination with other tissues or fluids may produce artifacts, antibody trapping, or false negative results. Inconsistent results may be due to variations in fixation and embedding methods, or to inherent irregularities within the tissue.

- Excessive or incomplete counterstaining may compromise proper interpretation of results.
- The manufacturer provides this reagent for use following the instructions for CISH on prepared tissue sections. Any deviation from recommended test procedures may invalidate declared expected results; appropriate controls must be employed and documented. Users who deviate from recommended test procedures must accept responsibility for interpretation of patient results under these circumstances.
- Due to variations in specimen processing it may be necessary to either increase or decrease the protease treatment time. Such changes must be validated by the user. Users who deviate from recommended test procedures are responsible for interpretation of patient results under these circumstances.
- Tissues from individuals infected with hepatitis B virus and containing hepatitis B surface antigen (HBsAg) may exhibit nonspecific staining with horseradish peroxidase.

13 PERFORMANCE CHARASTERISTICS

The intra-run and inter-run reproducibility of the Lambda light Chains CISH Kit performance was evaluated by staining slides containing the same tissue on different instruments and operators. The staining results were consistent across all conditions, demonstrating 100% concordance in tissue samples and performing as expected.

14 BIBLIOGRAPHY

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- Levy R, Warnke R, Dorfman RF, Haimovich J. The monoclonality of human B-cell lymphomas. J Exp Med 1977;154:1014-1028.
- Marshall-Taylor CE, Cartun RW, Mandich D, DiGiuseppe JA.Immunohistochemical detection of immunoglobulin light chain expression in B-cell non-Hodgkin lymphomas using formalin-fixed, paraffin-embedded tissues and a heat-induced epitope retrieval technique. Appl Immunohistochem Mol Morphol. 2002;10:258-262.
- Leers MP, Theunissen PH, Ramaekers FC, Schutte B, Nap M.Clonality assessment of lymphoproliferative disorders by multiparameter flow cytometry of paraffin-embedded tissue: an additional diagnostic tool in surgical pathology. Hum Pathol. 2000;31:422-7.

15 LABEL AND BOX SYMBOLS

Explanation of the symbols of the product label and box:

IVD	*In vitro* diagnostic medical device		Expiration date
REF	Catalog number		Temperature limit
LOT	Lot code		Manufacturer
	Refer to the instructions for use	e-SDS	Safety data sheet
	Distributor		Importer

16 CHANGELOG

Date	Description
2025-08-08	Creation of the document.