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PROLACTIN

RABBIT ANTI-PROLACTIN MONOCLONAL ANTIBODY (Clone EP193)

1	CATALOG REFERENCES AND PRESENTATIONS	2
2	INTENDED PURPOSE OF THE PRODUCT	2
3	OTHER POSSIBLE APPLICATIONS OF THE PRODUCT	2
4	DESCRIPTION OF THE MOLECULE IDENTIFIED BY THE PRODUCT	2
5	EXPRESSION IN NORMAL TISSUES	3
6	DIAGNOSTIC, PROGNOSTIC AND PREDICTIVE AID APPLICATIONS	3
7	PRODUCT DESCRIPTION	5
8	CALBRATORS AND CONTROL MATERIALS RECOMMENDED FOR LABORATORY USE DURING IHC TEST	6
9	SAMPLE TYPES	7
10	ANTIGEN RETRIEVAL	7
11	ANALYTICAL PRINCIPLE OF THE METHOD AND PERFORMANCE CHARACTERISTICS	7
12	PRODUCT LIMITATIONS	9
13	EQUIPMENT AND PRODUCTS REQUIRED	9
14	WARNINGS AND PRECAUTIONS	10
15	BIBLIOGRAPHY	12
16	LABEL AND BOX SYMBOLS	13
17	CHANGE LOG	14



1 CATALOG REFERENCES AND PRESENTATIONS

The references and presentations available for this product are described in the following table:

Table 1. References and presentation

Reference		Presentation ¹
MAD-000706	Q	1 mL
	QD-3	3 mL
	QD-7	7 mL
	QD-12	12 mL
	QDS-1	7 mL
	QDS-2	14 mL
	QDS-3	28 mL

¹ All product presentations are in Ready-to-Use format, except for the reference ending in Q, which is supplied in Concentrate format. References ending in S are for use in the VitroStainer 42. The use of the product in other immunostainers must be validated locally according to the instrument and the existing conditions in each laboratory. Not to be used for western blotting and flow cytometry techniques.

2 INTENDED PURPOSE OF THE PRODUCT

Prolactin is a primary antiserum for immunohistology for professional use, for the qualitative determination of Prolactin antigen to *in vitro* diagnostics in the laboratory by automated and manual immunohistochemistry, on paraffin-embedded tissue in neoplasms and in all other clinicopathological and physiological situations where identification is required. The product is intended to be used as an aid for screening, diagnosis, staging or monitoring of cancer for people of any age with suspected neoplasms or other clinicopathological and physiological situations requiring the analysis of Prolactin molecule expression.

This antibody is essential for the identification of lactotroph (prolactinomas) and mixed mammosomatotroph pituitary adenomas and to identify prolactin secreting cells in normal or residual hypophysis. The clinical interpretation of any staining or lack thereof should be supplemented by morphologic studies using appropriate controls and should be evaluated by a qualified pathologist in the context of the patient's medical history and other appropriate diagnostic tests.

3 OTHER POSSIBLE APPLICATIONS OF THE PRODUCT

It has also been reported that Prolactin antibody is also of interest in the identification of hyperplastic or ectopic prolactin secreting cells in different lesion and non-sellar neoplasias. Nevertheless, this antibody has not been validated for its use in these pathologies.

4 DESCRIPTION OF THE MOLECULE IDENTIFIED BY THE PRODUCT

Prolactin, initially identified in 1933 for its role in lactation, has since been found to have over 300 functions, impacting reproductive, metabolic, fluid, and immune systems. It is encoded by a gene on chromosome 6 and the mature protein consists of 199 amino acids. Prolactin has several molecular forms, including monomeric prolactin (23 kDa), "big prolactin," and "big-big prolactin" (macroprolactin), though the larger forms have minimal biological activity. Various post-translational modifications give rise to prolactin variants, with smaller forms like the 16 kDa prolactin possessing antiangiogenic properties.

The prolactin receptor (PRLR) belongs to the cytokine receptor family, expressed on cell surfaces, and activated upon ligand binding, triggering intracellular signal transduction. This activation stimulates pathways including JAK-2 and MAPK, which regulate gene transcription for cell proliferation and differentiation.

Prolactin secretion is primarily inhibited by dopamine. Dopamine neurons from the hypothalamus regulate prolactin levels, with different factors either inhibiting or stimulating dopamine and thus prolactin secretion (1).

Gene summary: This gene encodes the anterior pituitary hormone prolactin. This secreted hormone is a growth regulator for many tissues, including cells of the immune system. It may also play a role in cell survival by suppressing apoptosis, and it is essential for lactation. Alternative splicing results in multiple transcript variants that encode the same protein¹.

Protein function: Prolactin acts primarily on the mammary gland by promoting lactation².

5 EXPRESSION IN NORMAL TISSUES

Prolactin (PRL) is primarily produced by lactotroph cells in the anterior pituitary gland, where it plays a crucial role in stimulating milk production during lactation. Outside the pituitary, prolactin is also expressed in various normal tissues, including the mammary glands, where it supports breast development and lactation. Additionally, prolactin can be found in immune cells, such as lymphocytes, indicating its role in modulating immune responses. Prolactin expression is also observed in other tissues, including the endometrium, where it contributes to reproductive function, and adipose tissue, where it may influence metabolic processes. The expression of prolactin in these tissues highlights its diverse physiological roles beyond lactation and underscores its importance in various biological systems (2,3).

6 DIAGNOSTIC, PROGNOSTIC AND PREDICTIVE AID APPLICATIONS

6.1 Diagnostic aid, monitoring and staging

6.1.1 Prolactin in lactotroph tumours

Lactotroph tumours are the most common PitNETs overall, accounting for up to half of cases in postmortem and prevalence series (4,5). By far the most common subtype, the incidence has diminished considerably in surgical series due to successful medical therapy with dopamine agonists, because typically account for less than 30% of all cases (6).

The majority of lactotroph tumours (prolactinomas) are intrasellar, but macrotumours are often invasive, extending to suprasellar and parasellar structures, including possible presentation as a nasal mass (7). Ectopic examples are rare, but have been reported in numerous cerebral, vascular, nasal and brain areas (6).

Lactotroph tumours frequently cause reproductive and sexual dysfunction, with clinical manifestations differing based on patient sex. The most common symptoms in women with lactotroph tumours are galactorrhoea, ovulatory disorders, and amenorrhoea. In men, when symptoms are present, such as erectile dysfunction and decreased libido, they can be subtle, often resulting in delayed diagnosis. Women are more likely to present at a younger age with microtumours, whereas men mostly present with macrotumours (> 10 mm in greatest dimension) (6).

¹ <https://www.proteinatlas.org/ENSG00000172179-PRL>

² <https://www.proteinatlas.org/ENSG00000172179-PRL>

Histologically lactotroph tumours are divided into 3 histologic subtypes: the common sparsely granulated lactotroph tumour and the rare densely granulated lactotroph and acidophilic stem cells tumour subtypes (less of 10% and 3% of cases, respectively), the last commonly as mixed mammosomatotroph aggressive adenoma (4).

For immunohistochemistry and analogous to normal lactotrophs cells, the more sparsely lactotroph adenoma type shows a characteristic paranuclear globular, Golgi-type staining pattern for prolactin (4,8). In the densely granulated lactotroph tumour subtype, cells show strong and diffuse cytoplasmic prolactin expression (4,8). In tumours with massive apoplexy with extensive haemorrhagic necrosis, and it may be difficult to find viable tumour to assess with immunostains. Nevertheless, even in necrotic areas, a reticulin histochemical stain highlights the typical loss of normal adenohypophyseal microacinar pattern that is characteristic of a PitNET, and in most examples there is sufficient viable tumour, at least focally, to establish lactotroph differentiation with immunostains (6). Frequently, lactotroph tumour have extrasellar overgrown, including rare giant forms. Although generally benign, giant prolactinomas are aggressive and invasive, extending into the suprasellar region and involving the cavernous sinuses and optic chiasm (9).

Rare examples of ectopic prolactin secretion have also described in ovarian teratomas (10,11) and other tumours as uterine low-grade malignant mesenchymal tumour (12), uterine tumour resembling ovarian sex cord tumours (UTROCST) (13), among others.

6.1.2 Prolactin in neoplasms of other organs

Not applicable.

6.1.3 Other applications

No other applications have been described for this antibody.

6.1.4 Possible indications of prognostic and predictive use

At younger ages, women tend to have microtumours that rarely grow, even in the absence of treatment, and the prognosis for lactotroph tumours is worse in men than women (because the tumours are typically larger at presentation, more invasive, and generally more aggressive) (6). In this sense, high-risk pituitary adenomas are aggressive. They show clinical and imaging features that includes infiltration of the surrounding brain structures in absence of lack cerebrospinal or systemic metastases (14). In addition, they display distinct behaviour, including tendency for fast growth and frequent recurrences and under the term "high risk" adenoma has been included sparsely granulated lactotroph adenoma and mixed mammosomatotroph tumours, that for definition are sparse in granules and poor in secreting prolactin (15).

6.2 Clinical specificity and sensitivity

In the pursuit of clinical validation, we deemed it appropriate to rely on a comparative analysis of the positive cases detected using our product against those documented in the literature for similar products. This approach is grounded in the following considerations:

The Prolactin (EP193) enjoys a well-established reputation as a diagnostic marker, bolstered by robust support in the existing literature.

The Prolactin (EP193) serves as a diagnostic tool that primarily leans on qualitative assessment rather than quantitative measures. It is largely contingent on the clinical judgment of pathologists, who, in conjunction with other histopathological data and additional markers, arrive at a diagnosis.

The Prolactin product is a monoclonal antibody with specific diagnostic potential and high specificity, and its immunohistochemical interpretation is not dependent of performed in the morphologic context of the lesion analyzed and in conjunction with other immunohistochemical markers. This way, the Prolactin antibody has proven its utility in the diagnosis and classification of lactotroph and mixed pituitary adenomas.

In relation to the use of the Prolactin antibody as a diagnostic support and considering that its high specificity is widely recognized in the literature (it can be positive in only a very small histological types of malignant neoplasms), with high sensitivity, to evaluate the metrological traceability of the antibody we show the comparative results between the literature and the Prolactin product from VITRO, S.A. in the short list of cases include in adnexal table where the Prolactin antibody shows sensitivity in 100% of cases as well as remarkable specificity with intense/moderate staining in the presence of a concordant histology.

The sensitivity of VITRO, S.A. data has been compared to the sensitivity value found in the literature.

Table 2. Comparison of VITRO, S.A.'s sensitivity value with data obtained in literature.

Prolactin	Sensitivity Literature	Specificity Literature	Sensitivity clinical series of VITRO, S.A
<i>Lactotroph adenomas and mixed mammosomatotroph adenomas (16)</i>	100%	High (100%) in the proper histological and immunohistochemical context	100% (9 cases out of 9)
<i>Lactotroph adenomas (15)</i>	100%	High (100%) in the proper histological and immunohistochemical context	100% (9 cases out of 9)

Test results should be evaluated in conjunction with other diagnostic technologies, patient's medical history and other findings.

Since the performance characteristics may vary with pre analytical conditions, sample handling and storage, reagents, it is recommended that each laboratory establish its own verification of the results.

7 PRODUCT DESCRIPTION

7.1 Composition

Ready-to-use rabbit anti-prolactin monoclonal antibody supplied in liquid format in an pH7.6 buffer containing the stabilizing protein. Although it is not a sterile product, microbiological contamination is controlled, although not monitored since the solution contains sodium azide as a bacteriostatic and bactericidal agent. This additive improves device performance without affecting measurement results. The amount of active antibody in the sample is 1,28 µg/ml.

The antibody is also available in concentrated format supplied in liquid form in a pH7.6 buffer containing stabilizing protein with added sodium azide as a bacteriostatic and bactericidal agent.

7.2 Clone

EP193 (identified in the batch field of the product label)

7.3 Immunostaining pattern (samples and controls)

Cytoplasm

7.4 Immunogen

A synthetic peptide corresponding to residues of human Prolactin protein.

7.5 Immunoglobulin source and isotype

Rabbit IgG.

7.6 Intended Use

Professional laboratory use. In vitro diagnosis in humans.

7.7 Application

Immunohistochemical determinations on paraffin-embedded tissue.

7.8 Storage conditions

Fridge or cold store between 2 and 8 °C. Do not freeze.

7.9 Validity period

The product, if preserved in the established storage conditions, can be used up to the expiration date indicated on the label. If the reagent has been stored in different conditions than the ones specified, the user must make sure that it works correctly, being aware that the product warranty is no longer valid.

The reagent, once opened and in use, is stable up to 19 months and at most up to the expiration date indicated on the label if stored and used according to the manufacturer's recommendations.

7.10 Special instructions for manipulation

This reagent is specially designed for its use in the immunostainer VitroStainer 42, although the use of other automated immunostainers and manual procedures is possible as long as the reagent is validated locally according to the conditions existing in each laboratory.

For a concentrated format, the recommended dilution is 1:100 (it has been validated with the immunodetection system Master Polymer Plus Detection System-Peroxidase ref. MAD-000237QK). The recommended buffer for this product is MAD-004048R Antibody diluent from VITRO, S.A.

8 CALIBRATORS AND CONTROL MATERIALS RECOMMENDED FOR LABORATORY USE DURING IHC TEST

8.1 Internal positive control

Any of the normal cells described in section 5 when present in the test sample.

8.2 External positive control

Tissue section from normal pituitary gland with previous expression of this marker, ideally placed on the same slide as the test specimen.

8.3 Negative control

Preparation homologous to the test sample incubated with a non-specific isotype antibody for prolactin.

8.4 External quality controls

It is highly recommended that each laboratory establishes an external quality assurance control system for its immunohistochemical procedures through recognized intercomparison programs.

9 SAMPLE TYPES

Paraffin-embedded tissue sections 2 to 4 microns thickness and mounted on special slides for immunohistochemistry. These sections do not require any special conditions for sample collection, handling and preparation other than the standards established in each laboratory, except in the case of suspected prion infection where appropriate preventive measures should be taken (see also section 14 Warnings and Precautions). In buffered formalin-fixed samples the determination is direct and universal. If the sample has been processed in other fixatives or if it is frozen material, a local validation of the procedure must be carried out beforehand. Product intended for people of any age range requiring the analysis of prolactin molecule expression levels by immunohistochemistry techniques on formalin-fixed and paraffin-embedded tissue.

10 ANTIGEN RETRIEVAL

The sections must be subjected to heat-induced antigen retrieval according to the standard procedure of each laboratory. In short, the process includes deparaffining of the sections, heat-induced antigen retrieval and subsequent washes in buffer. It is highly recommended that the samples used for immunostaining have been freshly sectioned on the microtome (freshly cut or cut the day before the test is performed).

In order to know the technical conditions of this antibody on VitroStainer 42, contact your authorized Supplier/Distributor.

Although this antibody clone has been successfully used in antigen retrieval systems and other immunostainers than those mentioned above, its use in them requires prior validation.

11 ANALYTICAL PRINCIPLE OF THE METHOD AND PERFORMANCE CHARACTERISTICS

Antigen detection on tissues and cells using a multistep immunohistochemical procedure that at least includes incubation with the primary antibody, incubation with an enzymatically labeled bridging immune reagent (ideally multispecies and polymeric in structure), revealing of such activity by a colorimetric reaction, contrast staining with hematoxylin and corresponding washes between steps.

11.1 Analytical sensitivity and specificity

This antibody is specific for the human Prolactin and does not cross-react with other molecules. Likewise, the concentration at which it is supplied, determined by dilution of the culture supernatant, is suitable for immunohistochemical determination by kits using peroxidase or alkaline phosphatase polymers.

11.1.1 Analytical sensitivity

Analytical sensitivity was carried out with both manual and automated procedures on VitroStainer 42 instrument, to confirm the optimal dilution and time of incubation of the Prolactin Antibody assuring the good results under the final selected conditions. Results showed that optimal results on target cells without nonspecific labeling or background noise were obtained.

11.1.2 Analytical Specificity (Interference / Cross-reactivity)

Analytical specificity testing was performed in order to find interference substances or cross reactivity results.

- **Interference analysis:** Analysis substances used during the process which demonstrated a loss of staining activity and thus should not be used in conjunction with the processing of samples to be stained using Prolactin Antibody. The only known interference comes from alcohol containing fixatives, which demonstrated a loss of staining activity and thus should not be used in conjunction with the processing of samples to be stained using this product (17)

- **Cross reactivity:** The results obtained under the optimum conditions defined for the test are as follows:

Table 3. Cross reactivity results. Positive controls containing internal negative controls

Tissue	Positive	Negative
Pituitary Gland	Cytoplasmic staining in lactotrophs; strong staining in the paranuclear region in monohormonal adenomas; diffuse staining in multihormonal adenomas.	Absence of staining in non-lactotroph cells.
Result	Optimal	Optimal

All the results were analyzed by a pathologist.

Final optimal results were accorded with the acceptance criteria.

11.2 Precision

The determination of Prolactin by this monoclonal antibody is reproducible if the developing kits recommended in the instructions for use are used.

11.2.1 Repeatability

The repeatability of the method was analyzed using positive pituitary controls previously tested with positive results. The tests were performed by the same operator, at a single location and with the same instrument, and using the same batches of reagents on three consecutive days. All results were analyzed by a pathologist. It is concluded that the technique is 100% repeatable on all 3 days.

11.2.2 Reproducibility

The reproducibility of the method was analyzed using the automated method and optimized conditions for this marker by processing the same positive pituitary controls but performing the tests with different lots of reagents, operators and equipment. It is concluded that the technique is 100% reproducible.

11.3 Limits of detection

As there are currently used no routinely applicable quantitative procedures to ensure limits of detection on these qualitative non-linear products, as an alternative to these methods and to ensure dilution of the antibody, the following three internal procedures have been used:

1. Progressive dilution of the antibody in VitroStainer 42, on control tissues, confirming for experience the dilution located in the median between excessive staining not acceptable for diagnosis and weakly positive, which does not ensure the exclusion of false negatives.
2. Review of the dilution used in the scientific literature for this same type of clone and/or antibody evaluated. Through an extensive review of available literature and academic databases, no specific studies or papers were identified that address the topic of dilution in the context required for this work. Multiple search algorithms and keywords were used in the search process, yet relevant information was not found. Therefore, in light of this gap in the existing literature, the approach outlined here is based on established related methodologies and informed by best practices suitable for our study's objectives.

11.4 Measurement range

Not Applicable. The immunohistochemical process is not a quantitative method, it is a qualitative one where the marking obtained is interpreted as positive or negative complemented with the corresponding morphological and histological studies of each lesion and the appropriate controls.

12 PRODUCT LIMITATIONS

1. Not recommended for Western-blotting and flow cytometry techniques.
2. The use on frozen tissue has not been evaluated.
3. This antibody is intended for in vitro diagnostic (IVD) use by qualified laboratories only.
4. Test results should be evaluated in conjunction with other diagnostic technologies, patient's medical history and other findings.
5. Since the performance characteristics may vary with pre analytical conditions, sample handling and storage, reagents, it is recommended that each laboratory establish its own verification of the results.
6. Each laboratory must define its own use ratings for the product following the manufacturer's instructions and calibrate the equipment where they are to be used.
7. Due to inevitable variability in immunohistochemical procedures and variables, appropriate positive and negative controls must be used and documented, and the results are to be interpreted by a qualified pathologist.
8. Prediluted antibodies, which are provided in a ready- to-use optimally diluted format, must be used explicitly as instructed. Improper handling and processing of tissue samples and reagents, and any deviation from the recommended procedures outlined herein, may compromise the validity and/or analysis of the results.
9. If concentrated antibodies are provided in a format that requires dilution in the optimized buffer, in the context of appropriate validation by the user, any diluent different than that specified in the package insert must also be validated by the user to ensure proper compatibility with the antibody. Once diluted, any deviation from the recommended procedures outlined herein may compromise the validity and/or analysis of the results.
10. The potential for unexpected results in patient tissue specimens cannot be discarded due to inherent biological variability in the expression of certain antigens.
11. The potential for false positive results in patient tissue specimens cannot be discarded due to the possibility of non-immunological binding of substrate reaction products or proteins. False positive results may also occur subject to the type of immunostaining technique used, or due to the activity of pseudoperoxidase, endogenous peroxidase, or endogenous biotin.
12. Due to the effect of autoantibodies or natural antibodies, normal sera from an animal source the same as the secondary antisera may result in false negative or false positive results when used in blocking steps.

13 EQUIPMENT AND PRODUCTS REQUIRED

13.1 Supplied with the reagent

Besides the antibody the product does not include any additional reagents needed.

13.2 Not supplied with the reagent

Reagents, materials and equipment necessary for the immunohistochemistry technique are available in the VITRO, S.A. product catalog, but not supplied with the device:

- VitroStainer 42
- Pretreatment Kit
- Detection system
- Silane-treated slide
- TBS buffer – Tween 20
- Optical microscope and/or a digital scanner of histological slides

All the immunostaining process of the sections and the codes of the system (which allows the online recognition of the reagent and the slides undergoing a study) are programmed in the immunostainer's software. Therefore, when a laboratory implements this analysis procedure for the first time, it is essential to ensure that the information accumulated in the instrument is correctly programmed. Contact your Authorized Supplier / Distributor if required.

Keep in mind that the optimal working conditions can vary depending on the type of tissue and that, in any case, they must be individually established for each laboratory. In general, and to optimize the process, it is recommended to use the different amplification, development and counterstaining products in form of kits manufactured by VITRO, S.A., in the immunostainer, as well as the specific buffers and consumables for these instruments.

This antibody has been optimized and validated with the detection system commercialized by VITRO, S.A. (MAD-000237QK, QP, QKVS) in the automated VitroStainer 42 although the product can work well with any other polymer-based detection system and with other automated systems or manual immunostaining procedures. If the product is to be used with detection systems and systems other than those recommended above, it is necessary to carry out a prior validation process in each laboratory.

14 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.** When the product is used as an aid to diagnosis, or to establish parameters of prognostic or predictive value about neoplasms, it should only be handled by trained users and in authorized laboratories and strictly following the instructions contained in this brochure.
- **Optimization and interpretation.** It should be borne in mind that the ultimate responsibility for the optimization and interpretation of the immunostaining performed lies with the physician and technicians who use it and that, likewise, this reagent is only a tool for the interpretation of the morphological findings of each case in conjunction with other diagnostic and prognostic tests and the pertinent clinical data of the patient.
- **Use:**
 - For its handling in research, the presentation as a concentrated antibody is more suitable, which allows investigating the most appropriate antibody dilution and conditions of use in each case.
 - The reagent only works properly with a reagent chain suitable for amplification and development, so

its use with other systems than the recommended one should be subject to close review and/or eventual validation in each laboratory.

- Except for the requirement that the special slides on which the sections to be treated with this reagent are mounted (which are electrostatically charged) must be kept away from sources of radiation, and those relating to exposure to high temperatures or excessive light, there are no other external or environmental influences on the reagent or interference of the reagent with other investigations or treatments to be performed on the patient.
- **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. 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.** This product is only intended for professional laboratory purposes, and it is not intended for pharmacological, home or any other type of use. The current version of the Safety Data Sheet of this product can be downloaded in the web page www.vitro.bio or requested at regulatory@vitro.bio.
- **Summary of Safety and Performance (SSP):** The Summary of Safety and Performance (SSP) of this product will be available on EUDAMED database (subject to EUDAMED availability). This summary is also available on request by e-mail at regulatory@vitro.bio.
- **Recommendations for the Safe Handling of Samples Suspected of Containing Prions:**
The following protective measures are recommended for professional personnel handling immunohistochemistry (IHC) samples suspected of containing prions:
 - Personal protective equipment (PPE): full PPE should be worn, including a mask (preferably FFP2 or higher), protective goggles or face shield, head cover, and shoe covers.
 - Precautions during microtome sectioning: use disposable blades and avoid the use of aerosols or compressed air to clean the microtome area.
 - Surface and equipment decontamination: disinfect with sodium hydroxide (NaOH) 1N or sodium hypochlorite at 2%.
 - Waste management: all disposable materials must be discarded as special biological risk waste, in accordance with the applicable national regulations on hazardous healthcare waste.
- **Waste disposal:** The handling of waste 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 waste 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:

Table 4. Classification of waste generated by this kit according to the European Legislation. *ELW: European Legislation of Waste

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 material (tubes, tips, aluminum foil, 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, hematoxylin, alcohol, eosin), generated from immunostaining techniques.	160506	"Laboratory chemicals consisting of or containing dangerous substances, including mixtures of laboratory chemicals"

***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.**

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16 LABEL AND BOX SYMBOLS

Explanation of the symbols of the product label and box:

	In vitro diagnostic medical device		Expiration date
	Catalog number		Temperature limit
	Lot code		Manufacturer
	Refer to the instructions for use		Sufficient content for <n> assays
	Safety data sheet		Distributor
	Importer		

17 CHANGE LOG

Date	Description
31/10/2024	Initial elaboration of the document
03/03/2025	The document is updated to the new version of the template
08/09/2025	Section 7.9 is updated to include conditions in use of the product. Section 7.10 is updated to include the recommended buffer for the concentrated format. Section 9 is updated to include correct reference to Section 14 Section 14 is updated to include "Recommendations for the Safe Handling of Samples Suspected of Containing Prions"