BIOGNOST®

4% NB FORMALDEHYDE

IVD In vitro diagnostic medical device CE

10% neutral buffered and stabilized formalin solution, pH 7.0

INSTRUCTIONS FOR USE

REF Product code: FNB4-1L (1000 mL) FNB4-5L (5000 mL) FNB4-10L (10000 mL) FNB4C-10L (10000 mL) FNB4-20L (20000 mL)

Introduction

An impeccable sample fixation is a prerequisite for a correct histological diagnosis. Tissue samples must be immersed in an optimally chosen fixative immediately after sampling, because a timely fixation will prevent autolysis, putrefaction and other unwanted cellular changes. Although there are hundreds of histological fixatives and at least tens of formaldehyde-based fixatives, neutral buffered formaldehyde solutions with a concentration range from 4% to 10% are the most commonly used fixatives, primarily because of their simple and universal application. Tissue fixation using a buffered formaldehyde solution results in forming cross-links, i. e. it forms methylene bridges between proteins, that is, it results in keeping tissue components in their *in vivo* relation. If fixated properly, the tissue sample can withstand additional histological tissue processing and staining. The NB 4% formaldehyde solution is 10% buffered formalin, which is the most commonly used fixative. It is suitable for fixating bioptic materials, smaller tissue samples and long-term fixated samples storing. It is a colorless solution with a characteristic odor, ready for applying. Phosphate buffer with optimal molarity secures a constant pH range between 6.8 and 7.2 at 25 °C, and with additional methyl alcohol formation of formaldehyde polymers is prevented. It is a primary tissue fixative. Tissue samples can be fixated and/or stored for a longer period of time without severe hardening of tissue or formalin pigment forming in tissues, which then leads to process of removing the so-called acid hematein. It is suitable for usage in all automated devices for tissue processing, as well as for manual histological techniques. It is conveniently packaged in 1 liter bottles, 5, 10 and 20 liter canisters.

Product description

- **4% NB FORMALDEHYDE** - neutral buffered 10% stabilized formalin solution, pH 7.0. Suitable for fixating smaller tissue samples and biopsy samples. Synonyms: neutral buffered formalin 10%, NBF 10%
  Note: Formaldehyde NB 4% (Neutral Buffered) is a formaldehyde solution stabilized with methyl alcohol and buffered with phosphate buffer 7.0 ± 0.2. BioGnost's NB formaldehyde solutions are produced in accordance with all the EU regulations regarding *in vitro* diagnostic devices and bear the CE marking.

Fixating guidelines

If the tissue was not properly stored or stabilized during the fixation process, or if an unsuitable fixative was used, all the subsequent procedures in tissue processing and diagnostics will be of mediocre quality or useless. If the fixative is of inferior quality, pH value over its physiological bounds, or if the volume ratios between tissue and active substance in the fixative are not suitable, improper fixation can occur as well as tissue degradation and misdiagnosis. For that reason the fixative must be produced in accordance with the *in vitro* diagnostic devices norms and must bear the CE marking of conformity, and the processes of fixating, processing and staining must be carried out by a qualified person (histotechnician). In order to avoid mistakes during the procedure, a suitable fixative must be applied in accordance with the standard norms of histotechnology. If there is uncertainty regarding the choice of the fixative and possibility that the tissue would not be stored in a satisfactory manner, consultation with an experienced histotechnician is required.

Fixating instructions

- Always wear protective gloves while handling formaldehyde and fixated tissue samples. The rooms in which the buffered formaldehyde is being used should be well aerated by using an exhaust fan or a digester in order to remove toxic evaporation. Additional security information can be found in the Material Safety Data Sheet of this product
- Before the process a fixative should be chosen in accordance with the subsequent histological, histochemical or immunohistochemical diagnostic methods. If a neutral buffered formaldehyde was chosen as an optimal fixative, the tissue sample should be immediately immersed in the solution container
- The sample should be fixated as soon as possible in order to prevent autolysis, putrefaction, and other changes. If it is not possible to put the sample in the fixative immediately, it is advised to maintain it moist and keep it in a cold place. The sample should not be bent or folded in the fixation container. Samples should be 3 to 6 mm in width for a proper fixation. All the samples should be clearly marked
- During the fixation the sample should be immersed in an adequate amount of fixative. An optimal ratio should be 20 to 40 parts of fixative to 1 part of tissue. That in particular applies to Formaldehyde NB 4%, while that ratio may be lower in case of Formaldehyde NB 10%. The fixative to tissue sample ratio should never be lower than 10 parts of fixative to 1 part of tissue
- If an entire organ is being fixated, the fixative should be injected into the organ or it can be cut into thin slices so that the solution can permeate the tissue thoroughly
- The fixative can also be poured into hollow organs, and before immersing into the fixative container they can be filled with gauze soaked with the fixative. Certain organs, such as the colon, can be opened and pinned on a board before immersing in the fixative. Encapsulated tissue should be processed by an expert in order for the fixation to be successful
- Fixation time can vary from a few hours to a few weeks. That depends on the type of tissue and sample thickness, fixation temperature, tissue and fixative volume ratio, as well as the concentration of formaldehyde in the fixative
- Selection of concentration of formaldehyde and fixation time must be determined in accordance with the norms of histotechnology and professional experience. In case of fixation of a larger tissue sample or an organ, fixation can last up to 24 hours or even more. The process can be shortened by fixating the sample in an incubator or a microwave oven
  If the tissue has not been dimensioned for processing prior to fixation, after the fixation it should be processed down to thickness of 3-5 mm. The first solution to come into contact with the tissue should be 70% alcohol solution in order to avoid the subsidence of phosphate salts used to neutrally buffer the formaldehyde solution. Fixation can be conducted using formalin fixatives containing buffers soluble in alcohol

Preparing the sample and diagnostics

Use only appropriate instruments for collecting and preparing the samples. Process the samples with modern technology and mark them clearly. Follow the manufacturer's instructions for use. In order to avoid mistakes, the covering or mounting and staining procedure as well as diagnostics should only be conducted by authorized and qualified personnel. Use only microscope according to standards of the medical diagnostic laboratory. In order to avoid an erroneous result, a positive and negative check is advised before application.

Safety at work and environmental protection

Handle the product in accordance with safety at work and environmental protection guidelines. Used medical products and out of date products should be taken care of as a special waste in accordance with national guidelines. Chemicals used in this procedure could pose danger to human health. Tested tissue specimens are potentially infectious. Necessary safety measures for protecting human health should be taken in accordance with good laboratory practice. Act in accordance with signs and warnings notices printed on the product's label, as well as in BioGnost's material safety data sheet.

Storing, stability and expiry date

Keep 4% NB Formaldehyde in a tightly sealed original packaging at temperature between +15°C and +25°C. Do not freeze and avoid exposing to direct sunlight. Date of manufacture and expiry date are printed on the product's label.

References

1. Carson, F. L., Hladik, C. (2009): *Histotechnology: A Self-Instructional Text*, 3rd ed., Chicago: ASCP Press
2. Cook, D. J. (2006): *Cellular Pathology*, 2nd ed., Banbury: Scion Publishing Ltd.
3. Kiernan, J.A. (2008): *Histological and Histochemical Methods, Theory and Practice*, 4th ed., Scion Publishing Ltd, Banbury.

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	Refer to the supplied documentation	°C	Storage temperature range	Σ	Number of tests in package	REF	Product code	CE	European Conformity		BIOGNOST Ltd. Medjugorska 59 10040 Zagreb CROATIA www.biognost.com
	Refer to supplied instructions		Keep away from heat and sunlight		Valid until	LOT	Lot number		Manufacturer		
IVD	For *in vitro* diagnostic use only		Keep in dry place		Caution - fragile						

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