



Histology Goes Green

Milestone products for a safer, environmental-friendly histology laboratory

Our challenge

Milestone is striving to improve the laboratory work environment by developing safer and greener reagents and accessories. Through to our line of products important steps in the histological specimens preparation, such as fixation, decalcification and processing, can be dramatically shortened in time by improving the instrumentation power-saving features. Great attention is also given to the development of reagents, with the goal to eliminate operators exposure to toxic reagents such as xylene and formaldehyde, for a safer laboratory environment.

I FIXATION

FineFIX, FormSAFE

I PROCESSING

MileONE & MileTWO, JFC, MileGREEN

I TRANSPORTATION AND STORAGE

Vacuum Bags, Synergy KIT

I DECALCIFICATION

MoL-DECALCIFIER

I FROZEN SECTION

MCC

FineFIX. THE FORMALIN SUBSTITUTE

The ideal fixative should present a low level of toxicity, produce optimal H&E, IHC and histochemical staining and allow recovery of DNA, RNA, and protein for molecular analysis. FineFIX is a patented formalin-free, water-based concentrate. When diluted with ethanol, its formulation of low toxicity additives overcomes the drawbacks commonly associated with the use of pure ethanol or ethanol based fixatives, e.g., significant tissue shrinkage, vacuolization and pyknotic nuclei. FineFIX also provides optimal preservation of tissue antigens, nuclear and cytoplasmic morphology and reduced lysis of red blood cells with preservation of the cytoplasmic membranes. FineFIX working solution is prepared by mixing 1 part of FineFIX concentrated to 3 parts of ethanol (99%). The ethanol concentration in the working solution of FineFIX is approximately 70%. This concentration was found to produce good



histology and to allow optimal recovery of DNA/RNA and proteins, sufficient for several downstream molecular analyses (1) (2).

The benefits of FineFIX in the grossing room

- Simultaneous specimen fixation, dehydration and fat extraction while immersed in FineFIX.
- Macro firming of specimens allows pathologists to easily palpate, dissect and cut thinner representative blocks.
- Elimination of the slimy feel and consistency of fatty specimens for a rapid, easy clean up.
- More "real-life" color compared to "grayish" appearance of formalin fixed specimens.
- Easy detection of lymph nodes: an easy gray-white contrast following FineFIX fixation.



⁽¹⁾ Gillespie JW, Best CJM, et al. Evaluation of non-formalin tissue for fixation for molecular profiling studies. Am J Pathol 2002; 160: 449-457.

⁽²⁾ A Novel fixative improves opportunities of nucleic acids and proteomic analysis in human archive's tissues. (Giorgio Stanta et all. - Diagn. Mol. Pathol. 2006 June 15(2): 115-23.

FormSAFE. HIGH SAFETY FORMALIN PREFILLED BIOPSIES CONTAINER

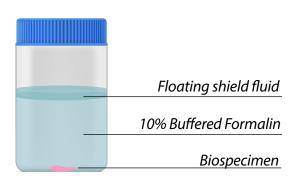
Today's reality

In December 2013 the EU-REACH (Registration, Evaluation, Authorization and Restriction of Chemicals) adopted a decision to reclassify formaldehyde as a Category 1B carcinogen and Category 2 mutagen under the EU CLP (Classification, Labeling and Packaging) Regulation. As a Category 1 carcinogen, formaldehyde use will be regulated by the restrictive Carcinogens Directive in EU workplaces from January 1st 2016. This will mandate the replacement of formaldehyde with less dangerous alternatives and, when that is not possible, restricting exposure using engineering and other controls. Mandatory prevention and protection obligations are among others.



The challenge

FormSAFE provides an excellent alternative to traditional prefilled containers when personnel are concerned with formalin exposure during collection, transport and storage. A second stratified fluid component floats above the formalin and acts as a protective shield preventing fixative fumes from escaping the container. This concept of a multi-layered liquids container allows safe handling both to the endoscopist at sampling and to the histologist when preparing the cassette. The endoscopist can easly detach the specimen from the tweezer by immersing them in the liquid without being exposed to formalin vapours. The histologist can open the container, and pick up the specimen without being exposed to fumes.





FormSAFE containers in its carton box

Technical specifications

- 60 ml container
- 30 ml 10% neutral buffered formalin
- · Floating shield fluid

MileONE - MileTWo. FORGET UNDER-PROCESSED FATTY TISSUE

Tissue Processing with no compromise to quality, even for fatty tissues

Fatty tissues are known to be the most tedious tissues Pathology Laboratories have to deal with. Processing breast, skin, brain and fatty colon specimens often leads to either suboptimal morphological quality or inconsistent results No compromise to quality for any tissues of any size; fatty tissues included. MileONE and MileTWO were designed by Milestone to grant consistent processing of normal fat content tissues with no compromise to high-fat content tissues like breast, brain, fatty colon and skin.

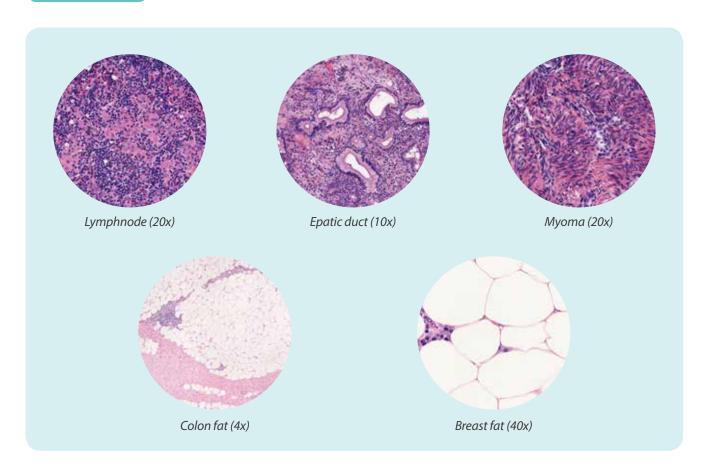


MileONE and MileTWO values

- NO Xylene, NO Toluene
- NO Limonene
- NO Aromatic Compounds
- NO Acetone

Fatty tissues need better treatment and your team deserves quality which will lead to a prompt and reliable diagnosis, at any time for any tissue. Give your laboratory a gift with MileONE and MileTWO! Convenient 5 Litre tanks of quality reagents, developed for more efficient processing in Milestone units, with 2D identification barcodes for documentation and reagent tracking.





JFC. THE HIGH PERFORMANCE XYLENE-FREE PROCESSING SOLUTION

The JFC Solution is an innovative patented solution composed of a mixture of ethanol, isopropanol and a long-chain hydrocarbon. Under the influence of microwaves this solution becomes highly effective in the extraction of water and lipids from biological tissue, in a single step, without the need for further dehydration or clearing. The miscibility of the three components of the JFC Solution lets the performance of dehydration and clearing to take place in a single step, dehydration and clearing, thus representing a significant advantage over the conventional processing method. The action of the mixture can be explained by the polarity of the molecules. In general, for an optimal extraction, the polarity of the solvent should be similar to that of the impurity you want to remove. In histoprocessing such impurities are generally water and lipids. The isopropanol, a polar molecule, contributes to



dehydration and also improves the extraction of non polar fatty. Ethanol, also a polar molecule, primarily serves to dehydrate. The action of both alcohols will be highly efficient under the stimulation of microwaves. The third component of the JFC Solution, an organic solvent, is chemically inert, and not polar. Although it has relatively low affinity with fats in normal conditions, its clearing activity is highly reinforced by the action of the microwaves on ethanol and isopropanol.



MileGREEN. THE XYLENE SUBSTITUTE

MileGREEN is a solvent, consisting of iso-paraffins and replaces xylene both in the clearing and mounting process. Moreover, it can be used for cleaning paraffin contaminated items, for example in the Milestone HistosMATE module. When heated this solution becomes highly effective in extracting lipids from biological tissue. MileGREEN is an almost odorless, non-carcinogenic solvent and has fat and paraffin dissolving properties. MileGREEN formulation of low toxicity overcomes the drawbacks commonly associated with xylene, a hazardous product for the human nervous system. MileGREEN also provides optimal preservation of fat cell; structure, nuclear, and cytoplasmic morphology.





VACUUM BAGS, VACUUM BAGS FOR FORMALIN-FREE SURGERY SUITES

Standup vacuum bags for both TissueSAFE and SealSAFE specimen management systems provide an innovative barrier against infective agents, undesired smells and toxic formalin fumes! Milestone bags make tissue transportation and storage effective and safe, at a fraction of the space compared to standard containers.

- Dual thermal sealing, ensures secure containment of specimens and fixative
- Pleated base adds stability to filled bags
- Re-sealable up to four times, economic reuse for additional specimen access
- · Made of dioxine-free plastic, Milestone bags make their disposal environmental friendly
- Provides visibility to archived case/patient information, making retrieval quick and easy



Features

- Double layered PA/PE, 135 microns in thickness guarantees greater mechanical flexibility and resistance to perforation. Available in five different dimensions, suitable for all kind of specimens.
- Three sealing areas and cutting lines marked for multiple reuse
- Sealable document pouch provides security for patient information
- Automatically printed adhesive label contains: ID, date, time, specimen and fixative weight
- Self standing expanding base

Available in **different sizes** to suit individual requirements

Synergy KIT. KITS FOR PROCESSING PLUS EMBEDDING IN ONE STEP

The joint effort of Milestone and Klinipath created Synergy, a revolutionary method (patent n. EP 2 439 510 A1) to automatically embed tissues as part of the processing protocols. This method is applied to Milestone's rapid tissue processors Pathos DELTA and LOGOS. Through dedicated rack and consumables, the same tissue processor unit can simultaneously achieve processing and automatic embedding. All range of tissues and dimensions can be processed and embedded with this method.



DELTA Synergy rack



LOGOS Synergy rack



Molds and Pads



Consumables Package (1360 Molds, 1400 Pads)

MoL-DECALCIFIER. EDTA BASED DECALCIFYING SOLUTION

For faster decalcification time, the process with EDTA is best carried out at a pH value of 7.2-7.4. Milestone has developed an innovative, pure EDTA solution, based on a stoichiometric mixture of bibasic or tribasic EDTA to reach this pH value without the addition of an acid/base buffer. The combination of increased temperature, stirring and the MoL-DECALCIFIER, during the decalcificacion phase allows fixation, decalcification and processing of bone marrows within 48 hours.

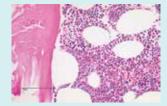
Optimized molecular results

A presentation* during the "First Symposium on Pre-analytic of Pathological Specimens - Berlin March 2013" reported the first results on H&E, IHC, FISH and molecular using the Milestone decalcifying solution MoL-DECALCIFIER on bone marrow trephine biopsies.

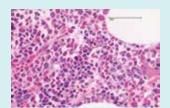




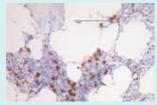
H&E and IHC CD 138



H&E MoL-DECALCIFIER



H&E MoL-DECALCIFIER



CD138 MoL-DECALCIFIER

► FISH (BCL6 Break Apart Probe, Abbott)



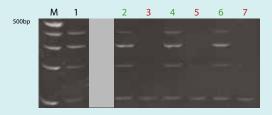
Conventional



MoL-DECALCIFIER

▶ Quality control-PCR

Control multiplex-PCR: amplification of different-sized genomic segments (100, 200, 300, 400 bp) harboring single-copy genes (Biomed-2).



M: size standard 1: Tonsil conventional 2, 4, 6: MoL-DECALCIFIER 3, 5, 7: Conventional

*Bone marrow work-up, loannis Anagnostopoulos Institute for Pathology Charité – Campus Mitte, Berlin Germany.

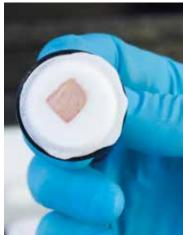
MCC. OPTIMIZED CRYOEMBEDDING COMPOUND

The perfect cryoembedding composition for the PrestoCHILL system

- MCC is a proprietary formulation of glycols and resins specifically developed for optimal support during cryotomy of dissected tissues down to -40°C.
- Being water soluble, MCC doesn't leave residue on slides, eliminating non specific background staining. Additionally, MCC will not dull microtome knives.

Available in **125 ml squeeze bottles**, box of **12 bottles**







About Milestone

Milestone was founded in 1988 as a company specialized in advanced microwave instrumentation for analytical and organic chemistry labs. We are an industry leader in this field, with a worldwide installation base of over 20,000 systems in large and small research institutions, universities and industrial laboratories. Milestone offers different solutions to simplify all processes; starting from the specimens' arrival to the lab, dealing with accessioning and documentation, passing through frozen sections for urgent biopsies, decalcification of bone marrow, tissue processing and finally, storage.

With the Milestone's Lean Approach you will be able to:

- · Maximize the value of your procedure
- · Minimize the necessary steps
- · Eliminate unnecessary processes

Headquarters

MILESTONE Srl Via Fatebenefratelli, 1/5 24010 Sorisole (BG) - Italy Tel: +39 035 4128264 Fax: +39 035 575498

US Operations

MILESTONE MEDICAL TECHNOLOGIES, INC. 6475 Technology Avenue Suite F, Kalamazoo, MI 49009 - USA Tel: 269-488-4950 - Toll-free: 866-995-5300 Fax: 269-488-4949