



Innovation in Anatomic Pathology for the Management of Chemical and Clinical Risk in Healthcare Institutions: SafeCapsule

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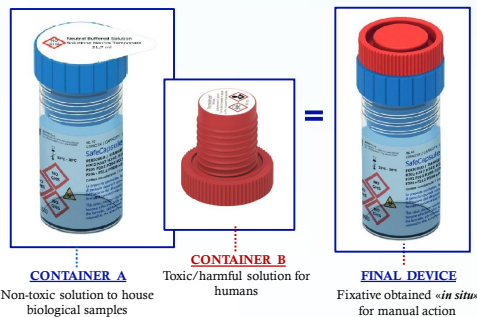
INTRODUCTION

Formaldehyde, a colourless gas with a pungent and irritating odour, is produced and marketed as an aqueous solution called Formalin. It is the fixative par excellence because it is easy to find it, it has a low cost, it leaves cell morphology and tissue architecture intact and it guarantees standardized protocols for histochemistry and molecular testing. Formaldehyde has recently been reclassified as a carcinogenic (category 1B) and mutagenic (category 2)¹ substance. Since there are no valuable alternatives to formaldehyde as tissue fixating agent in healthcare institutions, it was necessary to update the **Risk Evaluation Document**² and implement technical-organizational and procedural measures according to the guidelines issued by the Ministry of Health³ and the recommendation document drawn up by the Italian Association of Anatomical Pathology (SIAPEC)⁴.

To minimize the risk of exposure to Formalin and its vapours for operators in a free environment, the industry has offered several solutions with “vacuum” containers releasing Formalin when closed, which however have the following drawbacks:

- Increase in the size of containers, with resulting logistic and stocking issues;
- Instability of the container due to the weight concentrated in the upper part;
- Absence of liquid for clamps/needle wash and release of the biological sample;
- Impossibility to collect multiple samples in just one container before or after Formalin release;
- Exsiccation of the biological sample due to the absence of Formalin release;
- Difficulties in visualizing the sample in devices containing oily gels.

Therefore, a new CE-IVD marked device for the collection, storage and/or transportation of biologic samples called “**SafeCapsule**” has been presented: it has been patented by the Biomedical Campus of the University of Rome and the company Diapath and launched on the market in October 2018.



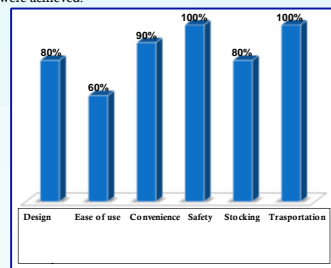
¹EU Regulation N. 609/2014
²EU Directive N. 12 of the Legislative Power 81/68
³Ministry of Health C.S.S. May 2015: Transmissibility, collection, transportation, recording and storage of cells and tissues for Anatomical Pathology diagnostics tests
⁴Notes about the usage of Formalin, reclassified as 'carcinogenic' - Guidelines from the Italian Association of SIAPEC-IAP February 2016.

PURPOSE OF THE WORK

- Collection and processing of the data obtained through a dedicated questionnaire distributed in the different wards and returned after the usage of the **SafeCapsule** device during routine work.
- Evaluation of the preservation of the cell morphology and the biochemical and molecular properties of tissues (collected from several organs and systems) fixed with **SafeCapsule**.

METHODS & RESULTS

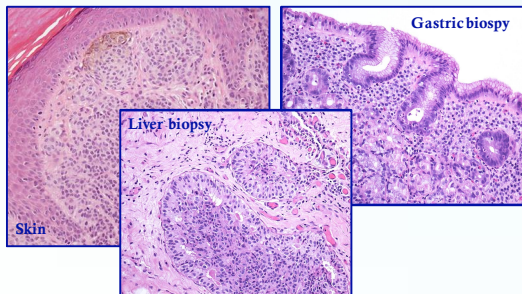
In agreement with the Biomedical Campus' SSPP, some samples of **SafeCapsule** were provided to operators to allow their usage in clinical practice. Following the completion of an evaluation card on the device quality and data processing, the results presented in the graph were achieved.



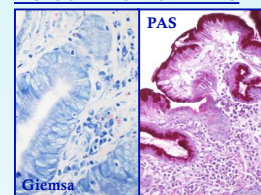
The validation of SafeCapsule's functionality in terms of storage and optimal fixation of the biological sample was performed through a series of lab test:

H&E STAINING (Hematoxylin & Eosin)

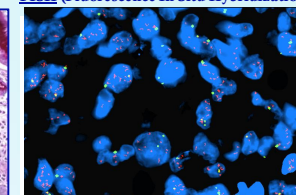
Microscopic test of cell morphology and tissue architecture



HISTOCHEMICAL STAINING

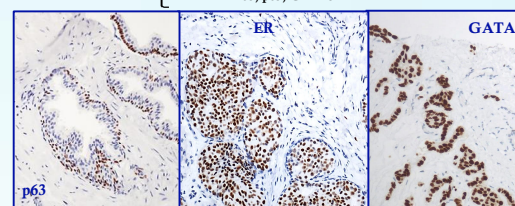


FISH (Fluorescence In Situ Hybridization)

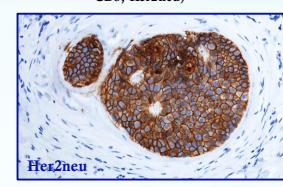


IMMUNOHISTOCHEMISTRY REACTIONS

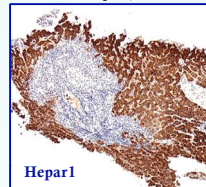
- **Nuclear antigens** { Oestrogen or ER receptor, Progesterone Receptor or PGR, Ki67, p63, GATA3



- **Membrane antigens** (Epithelial Membrane Antigen, or EMA, CD3, Her2neu)



- **Cytoplasmic antigens** (Cytokeratin or CK, Racemase, Hepar1)



FISH : Testing for **ALK** and **ROS1** and **HER2** gene amplification.

DNA EXTRACTION AND MOLECULAR TESTS

- Assessment of the extracted DNA's concentration and purity
- Testing for the main **EGFR** gene mutations

CONCLUSIONS

The **SafeCapsule** device was found to be ergonomic, convenient and easy to use during work activities.

It has shown 100% integrity and perfect hold during transportation. No Formalin spills, dispersion of vapours or loss of biological material occurred.

It usage was 100% safe and it was greatly appreciated by healthcare institutions operators.

Lab tests on samples storage and fixation with SafeCapsule have shown that:

- **Cell morphology** is of a high quality with preservation of the staining properties of cell components (basophilic and acidophilic);
- The **histochemical staining** prepared were perfectly executable and provided consistent results;
- **Immunohistochemistry** tests have demonstrated the antigen's perfect storage and accessibility and high signal enhancement without non-specific background staining;
- **FISH** test could be performed with excellent preservation of the probes' binding specificity;
- The **extracted DNA** has a good concentration and A260/280 ratio and subsequent mutational tests have confirmed that the samples fixed with **SafeCapsule** can be perfectly used for molecular testing.

Finally, it can be confirmed that **SafeCapsule** allows:

- To overcome the issues related to conventional devices thanks to its characterizing qualities and functionality.
- Excellent storage and fixation of biological samples, key conditions for a correct diagnosis.