

# MEMO

**TO:** FDA's Hematology and Pathology Devices Panel

**FROM:** Juan Rosai, M.D.

**RE:** October 22-23<sup>rd</sup> 2009 FDA Meeting on the regulatory future for the advancement of Digital Pathology devices to be used to be used as diagnostic instruments to assist pathologists in the evaluation of histopathology tissue samples, in a manner equivalent to the traditional light microscope.

**DATE OF THIS MEMO:** September 18, 2009

Dear Sirs:

My name is Juan Rosai. I am an M.D. and a senior surgical pathologist with a long experience in American academic (and lately private) medicine. This includes pathology training under Dr. Lauren Ackerman at Washington University in St Louis, Director of Anatomic Pathology at the University of Minnesota in Minneapolis (10 years), Director of Anatomic Pathology at Yale University in New Haven (6 years), Chairman of the Pathology Department at Memorial Sloan-Kettering Cancer Center in New York (10 years), Chairman of the Pathology Department of the National Cancer Institute in Milàn, Italy (5 years), and currently holding the dual position of Senior Diagnostic Pathologist at Genzyme-Genetics, New York, and the directorship of the International Center for Pathology Consultations at the Centro Diagnostico Italiano (Italian Diagnostic Center) in Milàn, Italy. I am the author of the textbook "Rosai and Ackerman's Surgical Pathology" now in its ninth edition, and widely regarded the premier publication in the field. I have also been the Editor-in-Chief of the Third Series A.F.I.P. Atlas of Tumor Pathology and senior author of two of the fascicles of that Series (Tumors of Thymus-2<sup>nd</sup> series; Tumors of Thyroid gland-Third Series). I am currently collaborating with Aperio in a series of didactic projects, one of them co-sponsored by the United States and Canadian Academy of Pathology (USCAP), the largest pathology organization in the country. I am not a shareholder or consultant for Aperio, and I have no other official ties with them.

For the past 25 years my diagnostic work has been limited almost exclusively to the examination of consult pathology material submitted to me by pathologists, clinicians and (increasingly) the patients themselves. In nearly all of these cases I receive a set of glass slides and a brief summary of the clinical history, supplemented if indicated by paraffin blocks, x-rays, CT scans, MRI's and other

pertinent material. I have explored many years ago, in collaboration with Dr. Stephen Erde, at Cornell University, and Prof. Vincenzo Eusebi, from the University of Bologna (Italy), the possibility of performing part and eventually most of my consultation work (especially the one originating from overseas) using what at the time was a rather primitive technology, and reported on our early encouraging efforts (Hum Pathol 28: 13-16, 1997). I have followed with increasing enthusiasm the technology impressive advances that the technology has undergone in recent times, until reaching a level such that I believe it matches and to some extent surpasses the capabilities of the traditional examination of glass slides under the microscope. With the best digital instruments currently available, the image resolution (the absolute key feature in a microscopic evaluation) is just as good if not better, and the capability of manipulating the image (moving to different fields, changing magnifications, changing focus in some of the models, etc.) is certainly easier. There are actually some aspects of the procedure that are better carried out with digital images than with traditional slides, such as examination of the material at very low (panoramic) magnification, the simultaneous examination of the low-and high-power appearances of the same field, the side-by-side comparison in the same screen on the images of the problem case with known standards, and the capability of quantifying the findings, a procedure that according to some authors will finally elevate microscopy to an objective and reproducible technique. This includes the precise measurement of cells, nuclei, nucleoli, depth of invasion, etc., and the quantification of positive cells in special preparations such as immunohistochemistry, as opposed to the time-honored but highly imprecise “eye-balling” done currently by most pathologists, their occasional denials notwithstanding.

Along these lines, I concluded recently a pilot study with three prominent pathologists practicing in Lima (Perù), Buenos Aires (Argentina) and Sao Paulo (Brazil), respectively, in the course of which these pathologists scanned the slides they had selected for my consultative evaluation, sent them to me, received my diagnostic opinions, and concluded that my diagnostic accuracy was essentially the same as when, in a second step, I examined under the microscope the glass slides of the corresponding cases.

Being that I receive consultations from many parts of the world, I particularly appreciate what I regard as a big plus of the technique, i.e., the speed of the consultation process (measured in minutes rather than in days or sometimes weeks) and the elimination of hazards such as loss or breakage of the material in transit, or significant delays at the Customs office of some countries (which we are experiencing with increasing frequency) on the grounds that the slide represents “biologic material” and is therefore incorrectly classified as “potentially hazardous” material, with all the logistic problems, delays and added costs that this decision implies.

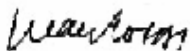
Further advantages of the digital technique are the fact that there are no limitation to the number of consultants that one may wish to engage, and the capability of viewing simultaneously the same field and to discuss the findings from several independent stations scattered in a large geographic area.

Whereas my work, as above stated, is almost entirely devoted to consultation material, it should be obvious that the technique is just as well suited for primary diagnosis, the assumption being that “routine cases” are, on the whole and by their very nature, easier to interpret than cases selected for consultation because of their complexity. Also not to be underestimated in the fact that the images on which the diagnoses are based can be stored indefinitely in secure servers without deterioration, and are not subject to the perils of glass slides, such as misfiling, drying out and breakage. Needless to say, there are legal and logistic issues that need to be worked out by the properly qualified individuals before approving this procedure. I would simply conclude by saying than from a technical and scientific standpoint I am thoroughly convinced that a diagnosis made on the basis of a well-prepared digital image of a representative whole section is just as informative and accurate as that performed by using the time-honored examination of a glass slide under the binocular microscope.

I hope you will find these comments of mine useful for your discussion and decision. It goes without saying that I would be gladly available for any further discussion of this matter through any venue you might like to choose.

I would like to conclude this letter by expressing my appreciation to the FDA for considering my opinions and views on such an important matter, which I have no doubts will revolutionize the field of pathology, if it is not doing that already.

Sincerely yours,



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