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November 26, 2002

Dockets Management Branch (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane  
Room 1061  
Rockville, Maryland 20852

Re: Docket No. 02N-0456  
Determining Hospital Procedures for Opened-But-Unused,  
Single-Use Medical Devices

Dear Sir or Madam:

On behalf of Johnson & Johnson, we respectfully submit the attached documents to the Food and Drug Administration's (FDA's) notice (the Notice) requesting comments about current practices with respect to opened-but-unused, single-use medical devices. 67 Fed. Reg. 55269.

Attachment A contains an October 2000 letter from Ethicon, Inc. to FDA regarding the safety issues associated with reprocessing open-but-unused absorbable sutures. While the regulatory and legal landscape for reprocessors has changed in the subsequent two years, the appended data are still applicable to the potential degradation of these devices as a result of reprocessing. Attachment B contains a more recent peer-reviewed publication authored by FDA's Office of Science & Technology regarding the adverse impact of reprocessing on sutures.

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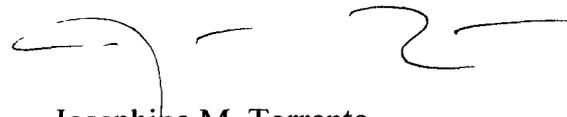
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HYMAN, PHELPS & MCNAMARA, P.C.

While both these studies are on file elsewhere at FDA, we believe that they are important in the context of the referenced docket and are therefore resubmitting them here for your consideration. We encourage FDA to consider these data in developing a reprocessing policy on opened-but-unused single-use devices.

We appreciate the opportunity to comment on this issue.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Josephine M. Torrente". The signature is fluid and cursive, with a long horizontal stroke at the end.

Josephine M. Torrente

JMT/dmh  
Enclosure

**ETHICON, INC.**  
a *Johnson & Johnson* company

P.O. BOX 151  
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October 5, 2000

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cc: CPCCF  
RDCF

**Reprocessing of Sutures**

There are several companies who are involved in the business of medical device reprocessing. The companies claim to clean, package and resterilize sutures in a safe and scientific manner. They offer substantial savings to medical facilities since the sutures can be reused. The companies are registered with the FDA but Ethicon has learned that many of these companies do not follow strict guidelines to control humidity, temperature and oxygen content during packaging and resterilization. This is especially critical for absorbable sutures and moisture sensitive non-absorbables such as nylon. This can lead to impaired suture performance such as decreased tensile strength, shelf life, and modulus leading to premature suture breakage or absorption.

Several historical studies were evaluated for a range of suture products in order to examine the effect of moisture, temperature, defects and liquid sterilizers on the performance of the sutures.

**PDS II\* (Polydioxanone) Suture**

PDS II specifications require a very low oxygen level during the packaging because of the interaction between oxygen and the undyed PDS II sutures in the presence of light. Several stability studies demonstrated that packages with a very low oxygen content contain product which is stable for five years (reference 1, 2 and 3). Years stable is defined as the number of years the product has a tensile strength above the Ethicon minimum specification. However, packages with high oxygen levels contain sutures with a significant loss of in-vivo tensile strength retention over time. Figure 1 shows that the shelf life of undyed PDS II sutures is reduced dramatically as the package oxygen content is increased from a controlled Ethicon standard level (X) to 28 times the Ethicon standard level (28X).

### MONOCRYL\* (Poliglecaprone 25) Suture

Hydrolysis is the degradation pathway for absorbable sutures, MONOCRYL and VICRYL. Two major factors, **moisture** and **temperature**, cause suture hydrolysis. The high moisture content in the package can significantly reduce product shelf life. A MONOCRYL suture shipping pouch study (reference 4) shows that when the moisture content in a sealed foil pouch is increased from a controlled Ethicon standard level (X) to 25 times the Ethicon standard level (25X), the product shelf life decreased from 7 years to about 3 years (see Figure 2).

### VICRYL\* (Polyglactin 910) Suture

A study of size 6-0 undyed VICRYL was performed at multiple moisture levels in the package. The packages were part of an accelerated stability study (reference 5). The relative 21 day in-vivo tensile strength was calculated in comparison to the control sample which had an Ethicon standard package moisture level. As shown in Figure 3, the in-vivo tensile strength at 21 days is significantly decreased when moisture level in the package is raised. A moisture level of 6x (x = Ethicon specification level) decreases the tensile strength by 42% and a moisture level of 8x decreases tensile strength by 58%.

Another study shows the strong impact of temperature during the sterilization process on suture in-vitro strength (reference 6). The effect of temperature during post-sterilization degassing on suture in-vitro performance was studied. The temperature was varied from the specification level (x) by 10°C and 18°C. After degassing, the packages were sealed and stored at 50°C/85% relative humidity for three months. Sutures were removed and placed in an in-vitro bath for 12 days. The relative 12 day in-vitro tensile strength was calculated in comparison to the control sample which had an Ethicon standard degassing temperature. As shown in Figure 4, increasing the degassing temperature by 10°C and 18°C decreases the tensile strength by 54% and 88% respectively.

### ETHILON\* Nylon Suture

Ethicon prehumidifies some sizes of nylon fiber to decrease the modulus for optimized handling properties, reduce package memory and improve pliability (reference 7). Prehumidification parameters are carefully controlled in order to optimize both tensile strength and modulus. As shown in Figure 5, failure to adequately control this step can lead to compromised suture properties.

Nylon fiber is also very sensitive to the number of cycles of cobalt sterilization. Size 10-0 ETHILON was subjected to up to three cycles of Cobalt-60 sterilization to study the effect on knot tensile strength (reference 8). From Figure 6, it can be shown that subjecting

nylon sutures to repeated sterilization cycles decreases the tensile strength by as much as 34% for three cycles.

### PROLENE\* Polypropylene Suture (reference 9)

The practice of repackaging hospital used or opened sutures into commercial product has raised serious issues that may jeopardize the patient safety and reduce the efficacy of the suture significantly. Among several safety issues, there are two which impact polypropylene suture mostly: instrument/handling-generated defects and re-sterilization using radiation such as cobalt.

#### **1. Effect of Instrument/Handling Generated Defects on Strength of Polypropylene Suture**

Due to the intrinsic nature of isotactic polypropylene, polypropylene suture is notch or defect sensitive. Any instrument or handling generated defect will significantly reduce the strength of polypropylene suture. The experimental tests were conducted using simulated defects (the defects were intentionally generated using several common surgical tools) to demonstrate the effect of type of defect on tensile strength of polypropylene suture. The typical micrograph of three different defects on size 2/0 polypropylene suture as well as control sample (no defect) is illustrated in Figure 7, which are surface cut, surface dent, surface teeth dent and no defect. The tensile strength of the suture samples was tested using an Instron 4201 tensiometer at room temperature. The relative strength of the suture samples with different type of defects was calculated in comparison to the control sample without defect (assigned as 100% strength), and the results are shown in Figure 8. As presented in Figure 8, the surface defects on polypropylene suture reduce the tensile strength. The surface cut has the most negative impact on the strength of the suture (48% reduction). The teeth like defect decreases the tensile strength by 21%, and the flat dent defect reduces the tensile strength by 23%. Furthermore, the experimental study shows the effect of a single surface defect on the suture strength. If multiple defects exist on the suture strand, the tensile strength of the suture will be reduced even further.

Opened polypropylene suture packages left from surgery have the possibility of being handled by the hospital staff or other personnel who have not received training on using suture material. This may cause surface defects on the suture material. Recycling those suture materials into product by repackaging and re-sterilization without defect inspection will likely produce defective sutures that may impose serious surgical risk to the patient.

#### **2. Effect of Incorrect Sterilization Method on Strength of Polypropylene Suture**

It is well known that polypropylene will undergo a significant degradation by cobalt radiation (reference 10). Such irradiation will cause major strength loss of polypropylene material. One of our controlled study has confirmed the negative impact

of cobalt sterilization on polypropylene suture: the tensile and knot strength of size 2/0 polypropylene suture were reduced by 32% and 18%, respectively, after 2.5 Mrad cobalt sterilization (Figure 9 and 10). If polypropylene suture were resterilized using cobalt radiation (common sterilization method for most of medical devices due to its low cost and efficient operation), the catastrophic failure of those suture materials during surgery would be expected, which may cause serious complication or even death.

### Conclusion

Several studies conducted at Ethicon demonstrated that failure to control critical parameters in the packaging and sterilization of sutures can result in compromised mechanical and in-vivo performance of the product.

### References

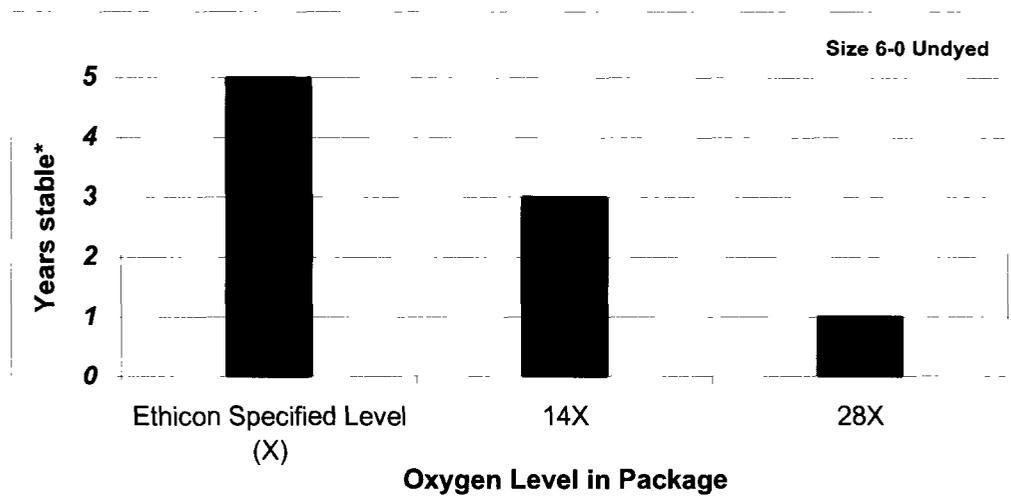
1. Ethicon Stability Study Number 1048-2
2. Ethicon Stability Study Number 1098
3. Ethicon Stability Study Number 1113
4. Ethicon Stability Study Number 1022
5. Ethicon Stability Study Number 526-6
6. R&D Central File 97-00718
7. R&D Central File 93-0573
8. R&D Central File 93-0483
9. Memo from Jack Zhou, PhD - Major Concerns of Practice of Repackaging Polypropylene Suture
10. "Stabilization and Degradation of Polymers", R.F. Gould, Editor, American Chemical Society (1978).

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Elizabeth Vailhe  
Scientist  
Corporate Product Characterization

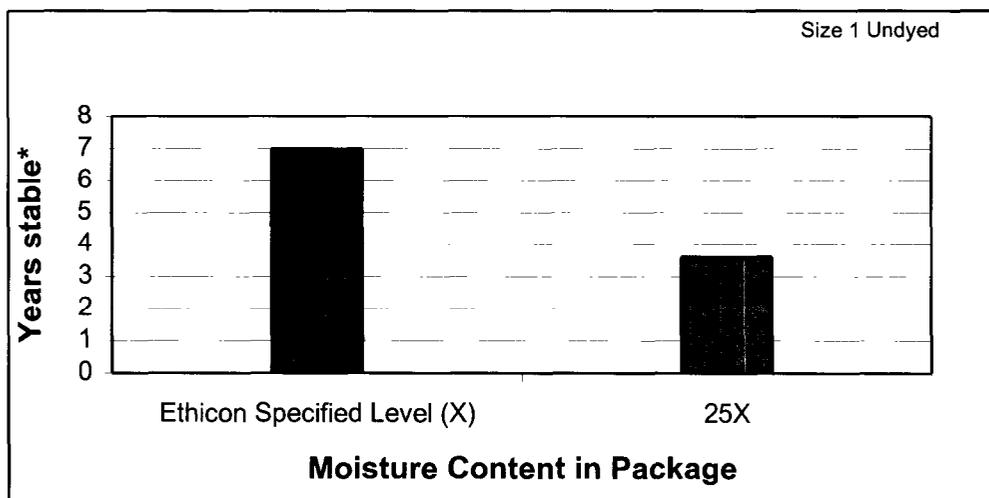
\* Trademark of Ethicon, Inc.

Figure 1- Effect of increasing oxygen level in package on ability of PDS II suture to meet minimum in-vivo BSR requirements (i.e. shelf life stability)



\* Years stable = Number of years meeting Ethicon minimum in-vivo BSR specification

Figure 2 -Effect of increasing moisture content in package on ability of MONOCRYL suture to meet minimum in-vivo BSR requirements (i.e. shelf life stability)



\*Years stable = Number of years meeting Ethicon minimum in-vivo BSR specification

Figure 3 -Effect of increasing moisture content in package on in-vivo strength of VICRYL suture following three months exposure at accelerated conditions (50°C/ambient humidity)

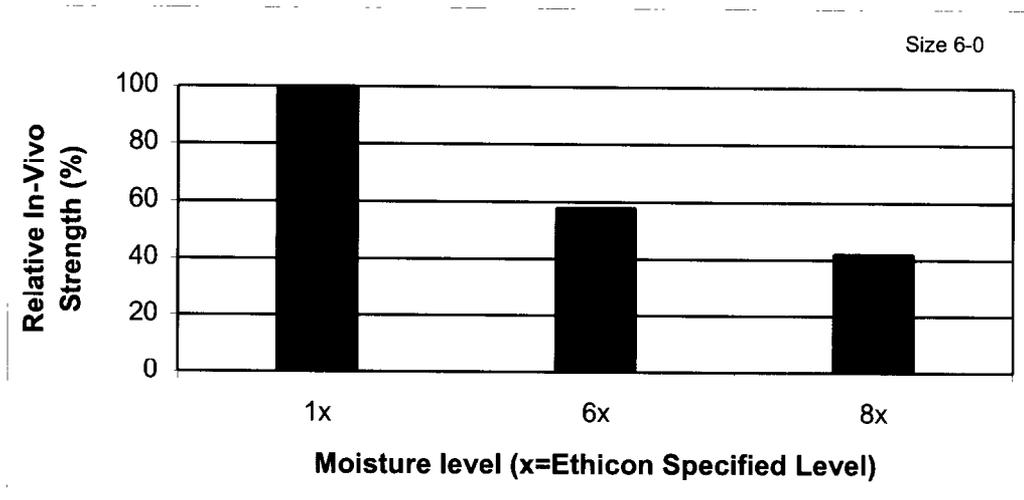


Figure 4 – Effect of increasing post sterilization degassing temperature on in-vitro strength of VICRYL suture following three months exposure at accelerated conditions (50°C/85% relative humidity)

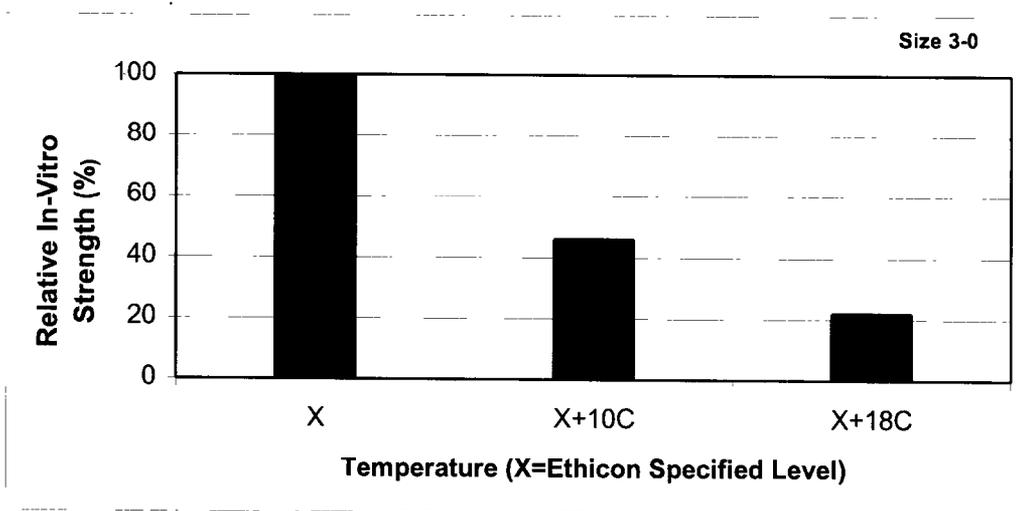


Figure 5 – Effect of prehumidification time on knot tensile strength and modulus (pliability) of ETHILON suture

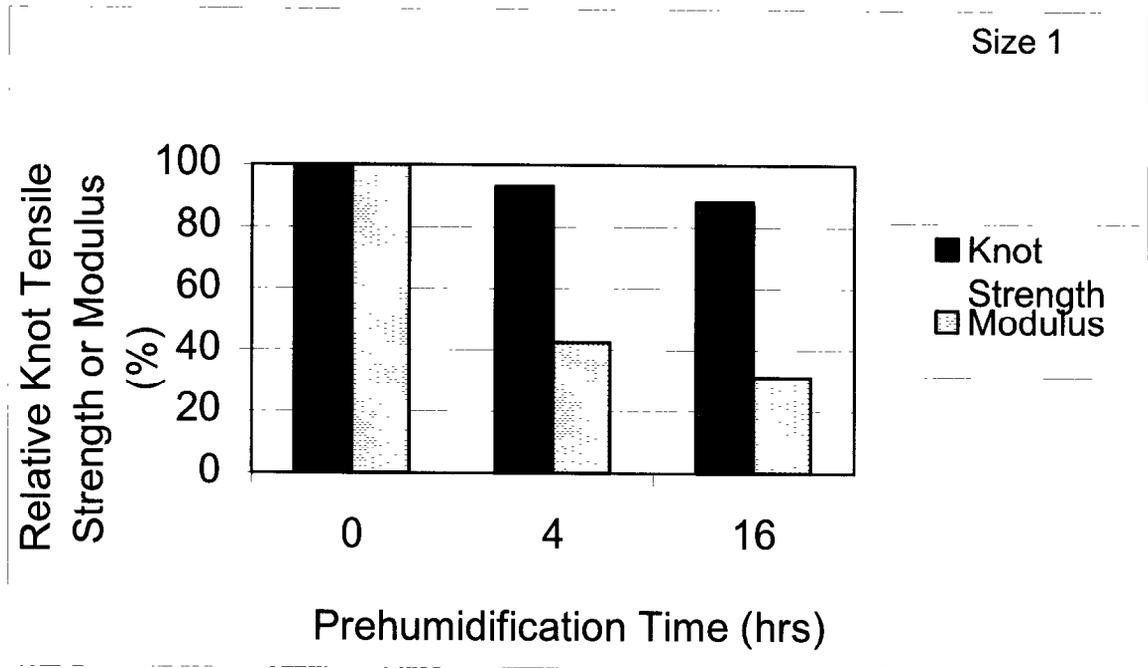


Figure 6 – Effect of cobalt sterilization on knot tensile strength of ETHILON suture

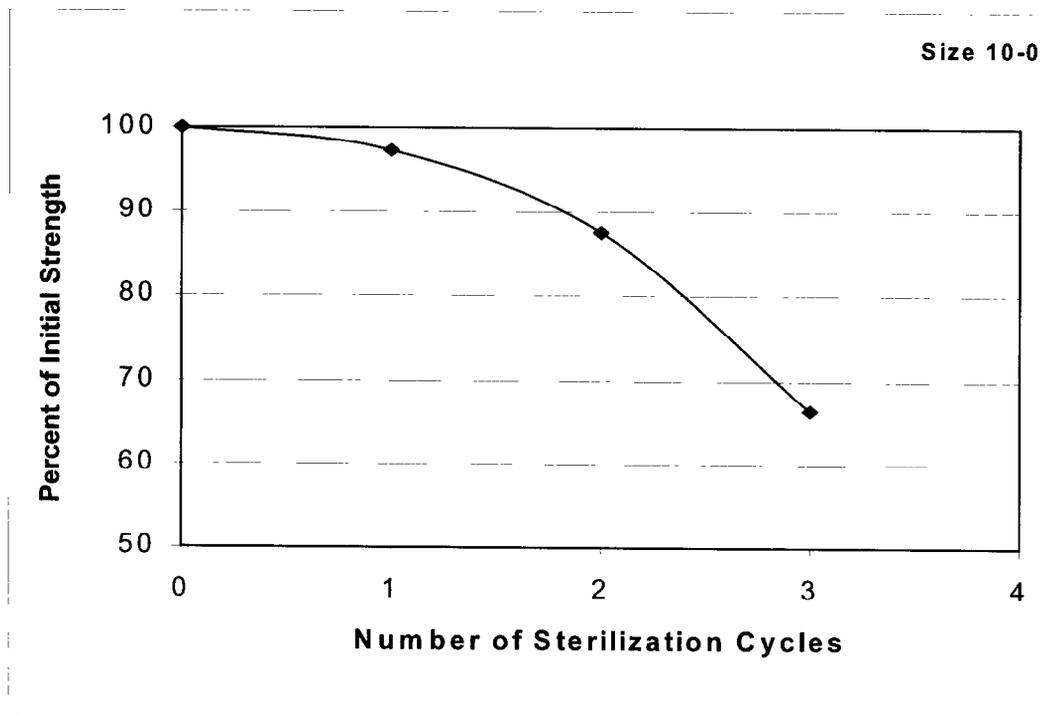


Figure 7. Possible types of surface defects for polypropylene sutures, (a) Surface Cut, (b) Teeth like Dent, (c) Flat Dent, (d) No Defect.

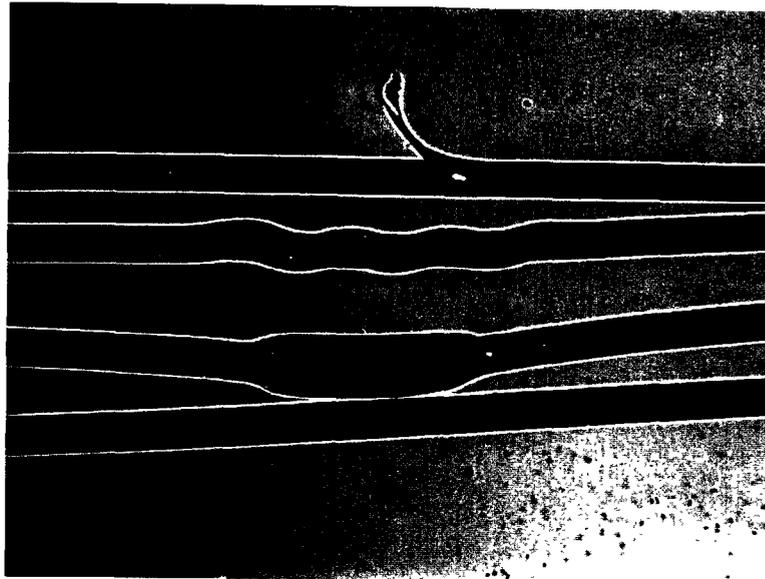


Figure 8. Effect of surface defects on tensile strength of polypropylene suture

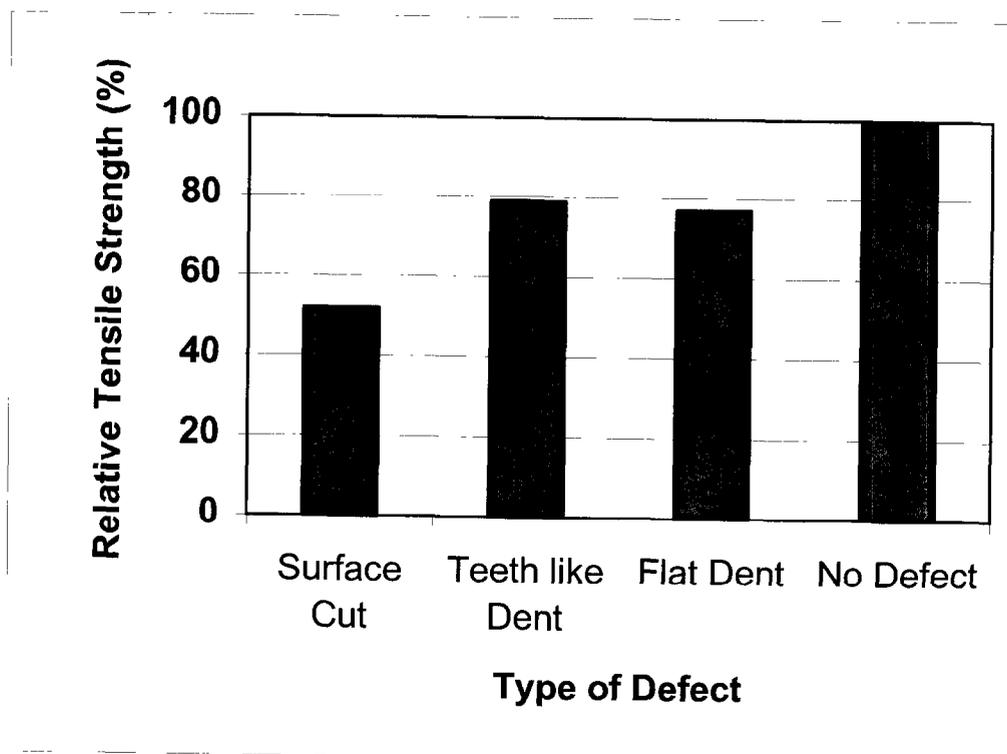


Figure 9 – Effect of sterilization method on tensile strength of polypropylene suture

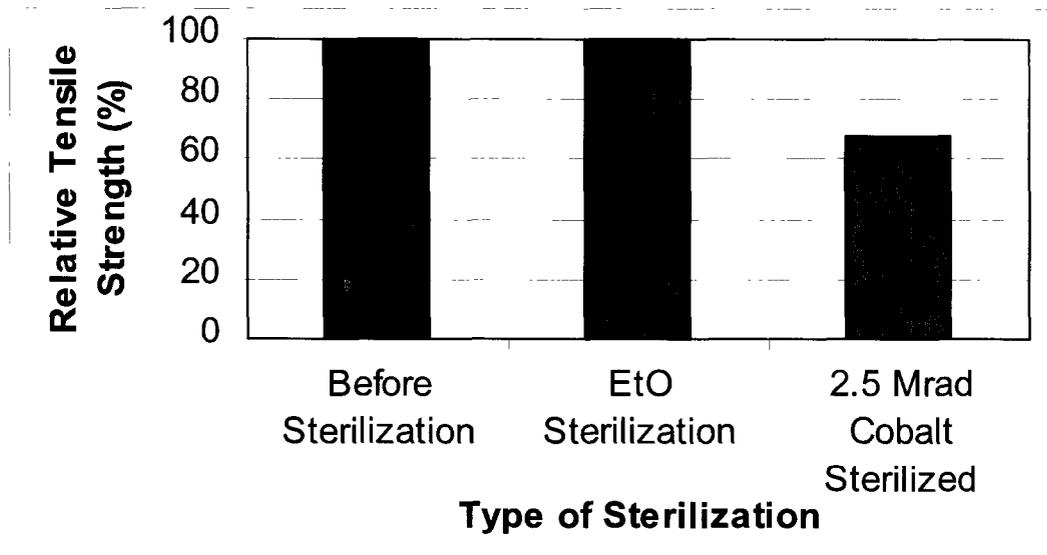


Figure 10 Effect of sterilization method on knot strength of polypropylene suture

