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I. PURPOSE

This analysis of explanted devices in the records of Mentor Texas' Product Evaluation Department (Irving, TX) was performed to better understand the rates of rupture failure of Mentor's Low Bleed Gel-filled Mammary Prostheses based upon examination of returned devices. Rates of failure (calculated based upon the number of returned ruptured domestically distributed devices and domestic sales of gel-filled devices) and numbers of returned ruptured devices per individual device lot were determined to understand whether failure rates differed due to device size, surface type, or product line. Numbers of device failures within device manufacturing lots or by year manufactured were used to examine whether manufacturing changes could have affected failure rates over time.

II. INTRODUCTION

This Low Bleed Gel-filled Mammary Prosthesis failure rate analysis due to ruptures was performed in order to better understand how and why gel-filled mammary devices can fail after implantation in patients. Mentor's Texas Product Evaluation (PE) Department database and returned devices (covering the period of time from about 1985 through 2003) were used for this analysis because of the numbers of available Mentor gel-filled devices with explantation data and post-explantation examination for failure mode verification. While Mentor understands that the PE devices which were returned are only a portion of the total devices which may have ruptured, and therefore has a limited value in what can be interpreted as a result of these analyses, this group of devices affords Mentor the best chance to examine failed devices and draw preliminary conclusions as to why and how gel-filled mammary devices rupture.

While the PE database contained information on all available device complaints, many complaints had no devices returned or those devices which were returned were a part of Mentor's class action mammary prosthesis lawsuit settlement which prevents testing or physical alteration of those devices. Complaints such as these were excluded from the analysis because the failure modes of these devices were not verifiable by PE Department examination. In addition, complaints not related to device rupture (e.g., packaging, cosmetics, etc.) were also excluded. The remaining devices for analysis were listed under the "Failure" column of the PE database as iatrogenic damage, "Rent - Unknown Cause," (RUC) and "Not Apparent - Etiology Unknown" (NA-EU). The latter two categories have been combined in this report as non-iatrogenic rupture failures.

This analysis investigated factors which could affect the rate of device rupture failures, such as the surface of the device (smooth or textured), the product configuration (e.g., low, moderate, and high profile), the product size, when the device was manufactured, and whether any particular device lot(s) contained many more failed devices than the other lots. The domestic sales data used for this analysis came from the sales data base used for Mentor's complaint analysis contained in the December 2003 Gel-filled

Mammary PMA Clinical Module submission. That data base was further sorted to provide sales numbers for sub-group analysis such as by product lines and surface type.

III. METHODS

In order to help understand the rupture rate of Mentor's gel-filled mammary prostheses, and what device related factors could affect those rupture rates, an analysis of returned ruptured device rates was performed. Only devices in which the reported complaint could be verified by examination of the returned device were used for the analysis. Only returned devices from domestic sales were examined because the gel-filled devices in Mentor's Low Bleed Gel-filled Mammary Prosthesis PMA are for domestic distribution only.

The factors of interest which might affect the rupture rate were device size, product line shape (e.g., low, moderate, or high profile), or device surface style (smooth or textured). The product lot and the year the device was produced were also analyzed. In addition to factors which may affect the rate of ruptures, the type of rupture (iatrogenic or non-iatrogenic shell, patch or wear related) and their rates of occurrence were also of interest. Any large differences in the rupture rates among these sub-categories of devices could lead to an understanding as to what factors might cause ruptures and the exact mechanisms of device failure.

Each sub-category of gel-filled mammary rupture failure to be compared was sorted from the complaint database (i.e., device line by size, device line by smooth or textured device surface, iatrogenic and non-iatrogenic failures by device line, etc). Non-iatrogenic ruptures included the database "Failure" column classifications of "Rent - Unknown Cause" and "Not Apparent - Etiology Unknown." The latter was included when it's "Observation 1" notation in the data base contained a shell, patch, or wear notation (devices with iatrogenic damage notations for these devices were not included in the non-iatrogenic category). The term RUC has been mostly used since about the mid 1990's to denote non-iatrogenic failures of unknown cause. The term NA-EU was mostly used in the data base prior to about the mid-1990's to denote the same type of failure description.

Domestic sales data were obtained from the sales data base used for the complaint analysis in Mentor's Low Bleed Gel-filled Mammary Prosthesis PMA. In order to get sales information for sub-categories of gel-filled devices, the sales data base was further sorted by device size of individual product lines. The sorted sales data can be found in Appendix D.

Iatrogenic failure rates by device sub-category were also investigated to see whether the factors of interest which might affect the non-iatrogenic failure rates might also affect the iatrogenic rates. Iatrogenic failures included all devices with "iatrogenic" noted in comments in the "Failure" column of the data base as well as "iatrogenic" noted in the

“Observation 1” column of the data base for those devices with “Not Apparent - Etiology Unknown.”

To determine whether any individual manufacturing lots or year of manufacture was associated with a large number of ruptured returned devices, the TX PE data base was sorted for iatrogenic and non-iatrogenic ruptured devices by lot number. The total number of each type of ruptured device reported per device lot number was reviewed. A rough timeline was also determined by correlating lot numbers at appropriate intervals to their year of production.

IV. RESULTS

Iatrogenic ruptured and non-iatrogenic ruptured (RUC plus NA-EU) gel-filled devices were sorted into the following product lines:

- Siltex Moderate Profile
- Siltex Old High Profile (last sold in 1996)
- Siltex New High Profile (first sold in 2001)
- Smooth Low Profile
- Smooth Moderate Profile
- Smooth Old High Profile (last sold in 1995)
- Smooth Oval (last sold in 1994)

The overall rupture rates for each product line (smooth and textured) can be seen in Table 1. Siltex and Smooth Moderate Profile Gel-filled devices, being the primary product lines which has been sold since 1985, had by far the largest number of returned ruptured devices. The other product lines had comparatively fewer ruptured returned devices. In general, the total rupture rates for the device lines returned to the Mentor Texas PE Department and included in this study were small, much less than one percent of the devices sold.

Each product line was further sorted by device size to see whether the size appeared to influence its rupture rate. The iatrogenic rupture rates by size in each smooth gel product line can be seen in Figure 1 (and Appendix A.1.) and each Siltex gel product line in Figure 2 (and Appendix A.2.). For most of the smooth product lines, no particular product size seems to have a noticeably higher iatrogenic failure rate [with the exception of 125cc Moderate Profile devices which may be due to the much lower number of devices sold ----- compared to all other sizes of that product line, thus allowing large changes in rate due to only a few explants]. Siltex product lines also show no obvious pattern of iatrogenic failures. There are two noticeably increased failure rates, 175cc New High Profile and 20-----t these are associated with very low numbers of devices sold -----

Iatrogenic ruptures were also sorted by device lot number (Figure 3). Although one would not expect to see a sizable number of iatrogenic ruptures concentrated within a device lot (since iatrogenic ruptures are usually thought of as random events), the

analysis was performed for the sake of completeness. No lot had more than two (2) iatrogenic ruptures with the vast majority of the explant lot numbers only having one iatrogenic rupture.

Non-iatrogenic rupture rates were sorted by device size within each product line. Figure 4 shows the distribution of RUC + NA-EU rates for smooth device sizes. Moderate Profile devices appear to possibly have a somewhat higher rate for smaller devices. On the other hand, Old High Profile devices appear to have a higher rate in the middle range of their sizes. Ovals and Low Profiles do not appear to have any consistent pattern in their failure rates. Figure 5 shows the distribution of RUC + NA-EU rates for Siltex device sizes. Siltex Moderate Profile devices may have a small increase in rate centered on the 175cc device. Old Siltex and Smooth High Profile devices may have a somewhat increased rate centered on or about the 275cc device, but there is much inconsistency in the gradual increase and decrease of the Siltex device rate with sizes smaller and larger than 275cc, respectively. There is no pattern related to New High Profile devices because so few have been explanted and returned to date.

Finally, non-iatrogenic ruptures (RUC and NA-EU ruptured devices combined) were sorted by lot number (Figure 6). No one lot had more than three (3) non-iatrogenic ruptures, with the vast majority of the lots listed having just one (1) or two (2) ruptures.

When lot numbers were correlated to their year of production (see Figures 3 and 4), it became possible to generally analyze the rupture data based upon the history of Mentor's manufacturing changes (including plant relocation, use of silicone raw materials made by different vendors, changes to the manufacturing processes, etc.). No concentration of lots with noticeably high numbers of ruptures was seen for either the iatrogenic or non-iatrogenic rupture distributions over time from about the mid 1980's.

V. DISCUSSION

A. Iatrogenic Ruptures

The seven gel-filled mammary product lines which Mentor has historically sold vary widely in the numbers of devices sold and returned. Siltex Moderate Profile devices have been sold during the entire 1985 through 2003 time period covered by this explant analysis. Smooth Moderate Profile Devices have been sold for most of this time period. The other product lines have only been available for sale for three to ten years during this time period. As a result of the difference in the numbers of sales years, there are vastly different numbers of sold and returned devices for each product line. This is reflected in the device sales numbers (see Appendix D) and the rupture rate data (see Appendices A and B). Relatively few Smooth Oval, Siltex Old High Profile, and Siltex New High Profile devices have been implanted; as a result, the calculated rupture rates can be greatly affected by as little as one returned device, especially when

the failure rates of product lines are examined with respect to individual device sizes.

Table 1 presents the overall gel-filled device iatrogenic and non-iatrogenic rupture rates by device surface, by product line, and by individual sizes within each product line. When comparing iatrogenic failure rates, textured and smooth surface devices have about the same rates, 0.18 and 0.21 respectively; however, no conclusions can be drawn from this overall comparison because so many complaint devices could not be evaluated for their rupture cause due to not being returned or being a part of Mentor's class action lawsuit settlement which prevented Mentor from performing testing on those devices.

By product line, New High Profile and Smooth Oval devices have noticeably lower iatrogenic rates of failure (0.02 – 0.08%) while Old Smooth High Profile devices have a noticeably higher failure level (0.50%) when compared to all other product lines (whose rates range from 0.18 – 0.24%). The low iatrogenic failure rates for New High Profiles and Ovals may in some way be related to the few numbers of years that each was or has been sold. On the other hand, if iatrogenic failures are random occurrences, one would probably expect the different product lines to have about the same rate of iatrogenic failures. Finally, it should be noted that all of the devices with iatrogenic ruptures contained in this analysis constitute only about ----- of all gel-filled devices sold by Mentor domestically from 1985 through 2003.

When looking at all iatrogenic failures sorted by product lot number and in relation to year of production (Figure 3), there is clearly no concentration of iatrogenic failures by lot number or by year of production. In addition, there are only minimal numbers of devices with iatrogenic failures in any given lot (two devices per lot at most) and even this occurrence is relatively rare during the period of interest. (Historically, Mentor has allowed between fifty and two hundred devices in a finished device lot.) As would be expected, iatrogenic failures are not associated with any particular product lots or manufacturing history changes (e.g., raw material changes, process changes, manufacturing plant location changes, etc.)

B. Non-iatrogenic Ruptures

Non-iatrogenic failures consisted of failures classified in TX's PE data base as "rent unknown cause" (RUC) and "not apparent - etiology unknown" (NA-EU). The former terminology is currently used while the latter term was used up until about the mid-1990's. When comparing all smooth to all textured gel-filled ----- s, the RUC + NA-EU rate of failure is very similar, ----- for Siltex and ----- for smooth devices. As with the iatrogenic failure rates, no conclusions ----- drawn regarding these rates because so many complaint devices could not be evaluated for their rupture cause due to not being returned or being a part of Mentor's class action lawsuit settlement which prevented Mentor from

performing testing and certain evaluations on those devices. When looking at individual product lines, however, some noticeable differences were observed.

Both smooth and textured New High Profile device RUC + NA-EU rates are very low (zero and 0.04%, respectively). Siltex Moderate Profile, Old Low Profile, Siltex Moderate Profile, and Smooth Oval devices have rates in the 0.23 – 0.39% range. Old Siltex High Profile and Old Smooth High Profile devices have rates of 0.67 and 0.61%, respectively. Compared to the more popular Moderate Profile product line, there appears to be a difference in the rates of non-iatrogenic failures. It should be noted that for the time that the Old High Profile device lines were being made, the same raw materials and manufacturing procedures were being used to make the Moderate Profile device lines. Due to all implanted Old High Profile devices being a part of Mentor's breast implant class action lawsuit settlement, any attempt to verify that the explanted Old High Profile devices do or do not have similar physical properties compared to explanted Moderate Profile devices cannot be undertaken. One other possibility for a difference in the failure rates between these product lines could be related to some difference in how the devices are used and/or inserted. Analysis of this issue is outside the scope of this report.

The Old High Profile product lines have not been sold since about 1995, and the total numbers of devices sold were relatively small compared to other product lines. Since that time, Mentor has used ----- vendors for the device gel and a new vendor for the device shell raw materials. The current shell raw -----t improved physical properties and an increased ----- specification. These improvements may help to ----- file device non-iatrogenic rupture rate from exceeding the Moderate Profile rates.

Non-iatrogenic rupture failures sorted by product lot number and in relation to year of production showed no obvious concentration of failures in any particular lot(s) or any time period of production. Only three lots had three failures per lot during the time period of interest. All other lots had only one or two failures per lot. This lot analysis for failures per lot can also be compared to a design and manufacturing change matrix for Mentor's Gel-filled Mammary Prostheses (see Table 2). The matrix lists all major changes to Mentor's gel-filled devices since Mentor's 1991 Gel-filled PMA submission to FDA. Given the listed effective date for each change, it is clear that the TX PE data base shows that there was no noticeable change in the number of device failures per lot after the implementation of any listed change. Since almost all explant device lots had two or less non-iatrogenic failures per lot, no manufacturing history changes appear to be related to the occurrence of non-iatrogenic failures when the explant data is analyzed in this manner.

VI. CONCLUSIONS

Using Mentor's Texas PE data base of complaints and verified failure data from those complaints, the overall rupture failure rate for gel-filled devices is much less than one percent of the devices sold. No difference was seen in the iatrogenic or non-iatrogenic failure rates of Mentor's Smooth and Siltex Gel-filled devices. This conclusion, and others that follow, are tentative because of the large number of explanted devices which could not be examined in a detailed manner due to being part of Mentor's class action lawsuit settlement or were not returned.

Iatrogenic failure rates are low for all product lines (mostly ----- of products sold). As one might expect, these rates do not appear to be influenced by product size, do not appear to be associated with any historical manufacturing changes, and appear to be a random occurrence in individual product lots.

Non-iatrogenic rupture rates are low for gel-filled product lines (usually ----- however, there is a noticeable increase in Smooth and Siltex Old High Profile device rates to 0.61% and 0.67%, respectively (but the latter two product lines sold relatively few devices compared to other product lines). Mentor is not able to further investigate these old high profile devices for potential root causes because all of these devices are part of Mentor's class action lawsuit settlement. Device size may have some effect on the non-iatrogenic failure rates of some product lines, but the effect is not consistent within a product line sizes and involves different sizes in different product lines. Non-iatrogenic ruptures do not appear to be related to any historical manufacturing changes and are not noticeably concentrated in any product lot(s).

Table 1: MENTOR GEL-FILLED MAMMARY PE DATABASE FAILURE ANALYSIS SUMMARY (DOMESTIC SALES)

| FAILURE RATE* | SILTEX | | | | SMOOTH | | | | | |
|---------------|--------|--------|--------|---------|--------|------|--------|--------|------|---------|
| | MP | Old HP | New HP | Overall | Old LP | MP | Old HP | New HP | Oval | Overall |
| ----- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- |
| ----- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | - | ---- | ---- |

(* - based upon verified failures and total domestic sales per device line)

Table 2: DESIGN AND MANUFACTURING CHANGE MATRIX*

| Change | Effective Date | Justification |
|--|----------------|---|
| ----- | ----- | <p>Material Substitution: Dow Corning announced in January 1993 that it would withdraw Silastic silicone elastomer materials from the market as well as silicone materials associated with applications related to reproduction, contraception, obstetrics, or cosmetic surgery procedures. Following Dow Corning's withdrawal of implant grade silicone from the market, FDA developed a strategy to provide an orderly transition to new suppliers that would minimize the impact on medical device availability while assuring the safety and effectiveness of the medical devices. FDA announced the availability of a guidance entitled "Guidance for Manufacturers of Silicone Medical Devices Affected by Withdrawal of Dow Corning Silastic Materials" in the Federal Register on July 6, 1993 (58 FR 36207). The guidance described the procedures for manufacturers to follow in order to document that the alternate material is "not substantially different" from the materials described in an original ----- -----s and finished devices confirm that the material is "not substantially different" from the original material.</p> |
| ----- | 3/3/1995 | <p>Material Substitution: Please refer to explanation above. As a result of Dow Corning's withdrawal from the ma-----</p> |
| Transferred manufacturing facility from Goleta, CA. to Irving, TX. | 3/8/1995 | <p>Manufacturing Location Change: Device manufacturing transferred from Goleta, CA to Irving, TX. The methods, equipment and controls used in the manufacturing, processing, packaging and storage at both plant sites are basically the same.</p> |
| Expanding In-Process Specifications and Testing to ----- | 10/9/1997 | <p>Manufacturing Process Change: The purpose of developing a product specification is to describe the characteristics of Mentor's finished product gel filled breast prostheses, as well as their critical parts during the manufacturing process. Use of these specifications will be one way to assure that the gel filled breast implants produced at Mentor's Irving, TX. facility consistently meet an acceptable level of quality and that they continue to meet their device design specification. Manufacturing and Quality improvements were implemented, including more defined specifications and test procedures to assure more consistent in-process -----</p> |
| Mentor Low Bleed gel implant ----- | 12/11/1998 | <p>Design Change: To ensure a more consistent shell thickness and facilitate----- ----- process qualification (HS33.980112.02C).</p> |
| ----- Mentor Low Bleed Gel implant. | 12/11/1998 | <p>Design Change: ----- implemented (HS33.980112.02C)</p> |

* - From Mentor's response to FDA's April 14, 2004 Gel-filled Mammary Prosthesis PMA deficiency letter

Table 2: DESIGN AND MANUFACTURING CHANGE MATRIX (cont.)*

| Change | Effective Date | Justification |
|---|----------------|---|
| ----- ----- approved. | 8/30/1999 | Manufacturing Process Change: ----- alified which allows for the reesterilization of product, when necessary. This change showed no impact on the product. |
| ----- introduced | 12/17/1999 | Material Substitution: ----- |
| Gel fill amount changes to meet ASTM requirements | 8/31/2001 | Manufacturing Process Change: These changes are being made to comply with both the ASTM-F703 and ISO-12180 requirements for gel device fill volumes. |
| Mentor High Profile gel implant re-introduced. | 11/28/2001 | New Product Introduction: To meet marketing demands a higher profile device is required. A High Profile was previously manufactured in Mentor's Goleta, CA facility. Qualifications were successfully completed. |
| Changed the tensile strength for cured HTV dispersions as follows: ----- ----- ----- | 6/3/2003 | Design Change: Report HS72.021216.01 documents testing of unfilled and gel filled moderate and high profile gel shells varying the material with incoming material tensile strength values ----- -----gh Profile HTV shells will have break force values greater |
| ----- ----- high profile gel shells from ----- | 6/20/2003 | Note: There was never any actual failures associated with this change. It was prompted by the fact that, if both materials were delivered within the then-current incoming material specification but at the lower limit of the modulus specification, a failure could theoretically result. This was a precautionary change to prevent this eventuality. |
| Moderate Plus Profile device introduction | 8/18/2003 | New Product Introduction: To meet marketing demands for a more comprehensive product offering the Moderate Plus Profile was added to the product family. Qualifications were successfully completed. |

* - From Mentor's response to FDA's April 14, 2004 Gel-filled Mammary Prosthesis PMA deficiency letter

Figure 1. Smooth Gel-filled Iatrogenic Rate Versus Size

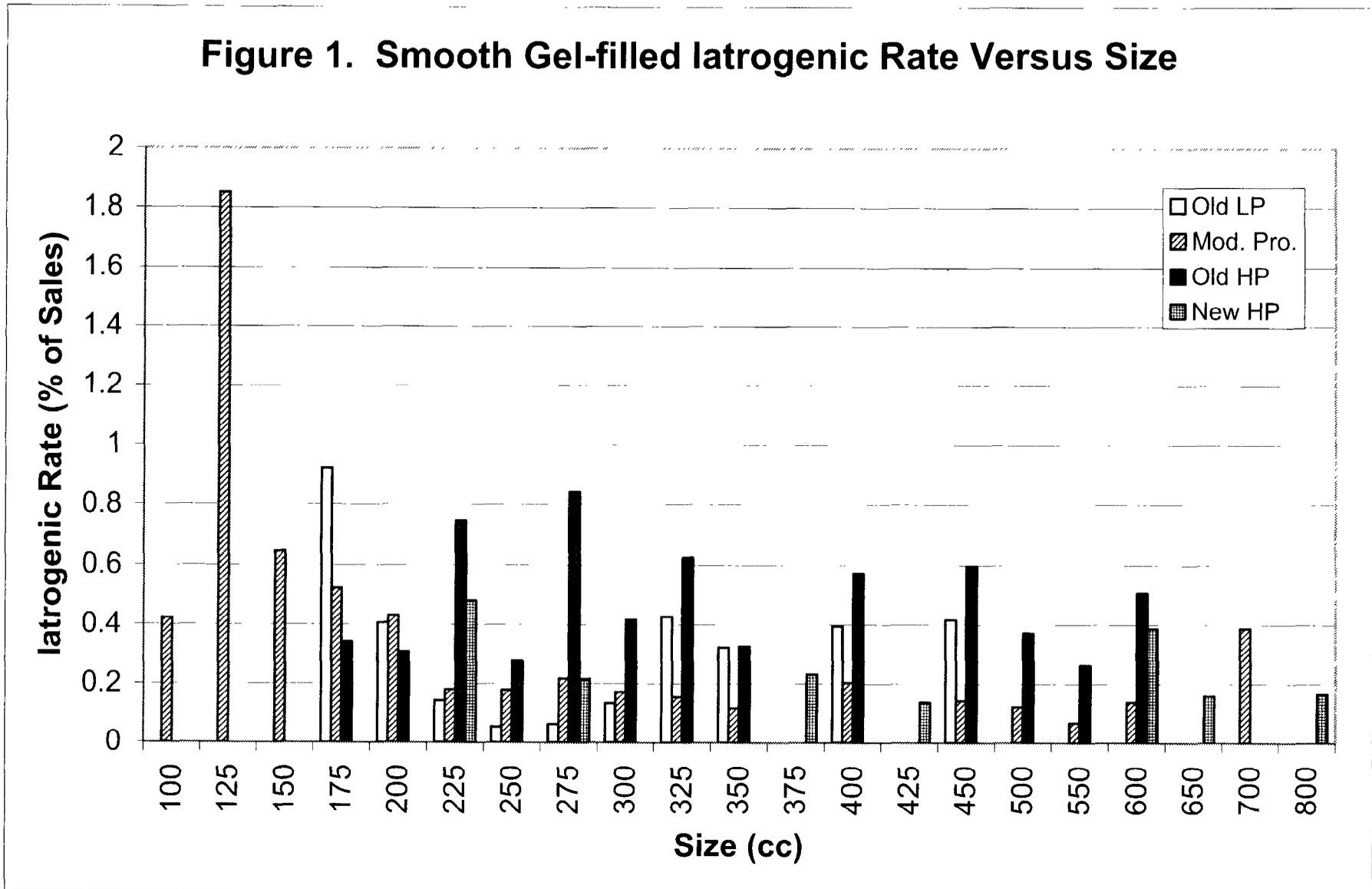


Figure 2. Siltex Gel-filled Iatrogenic Rate Versus Size

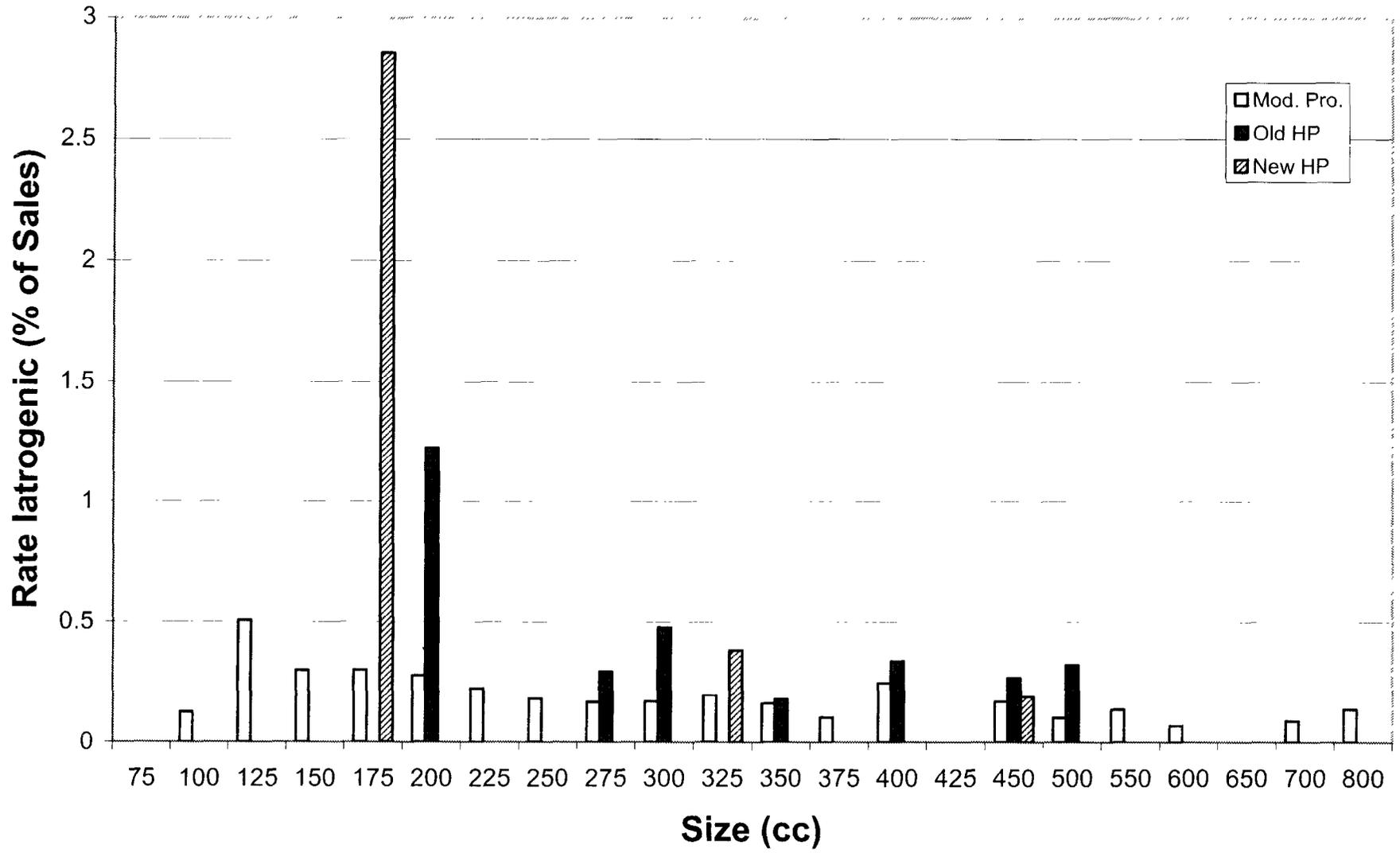


Figure 3. Iatrogenic Ruptures by Lot Number

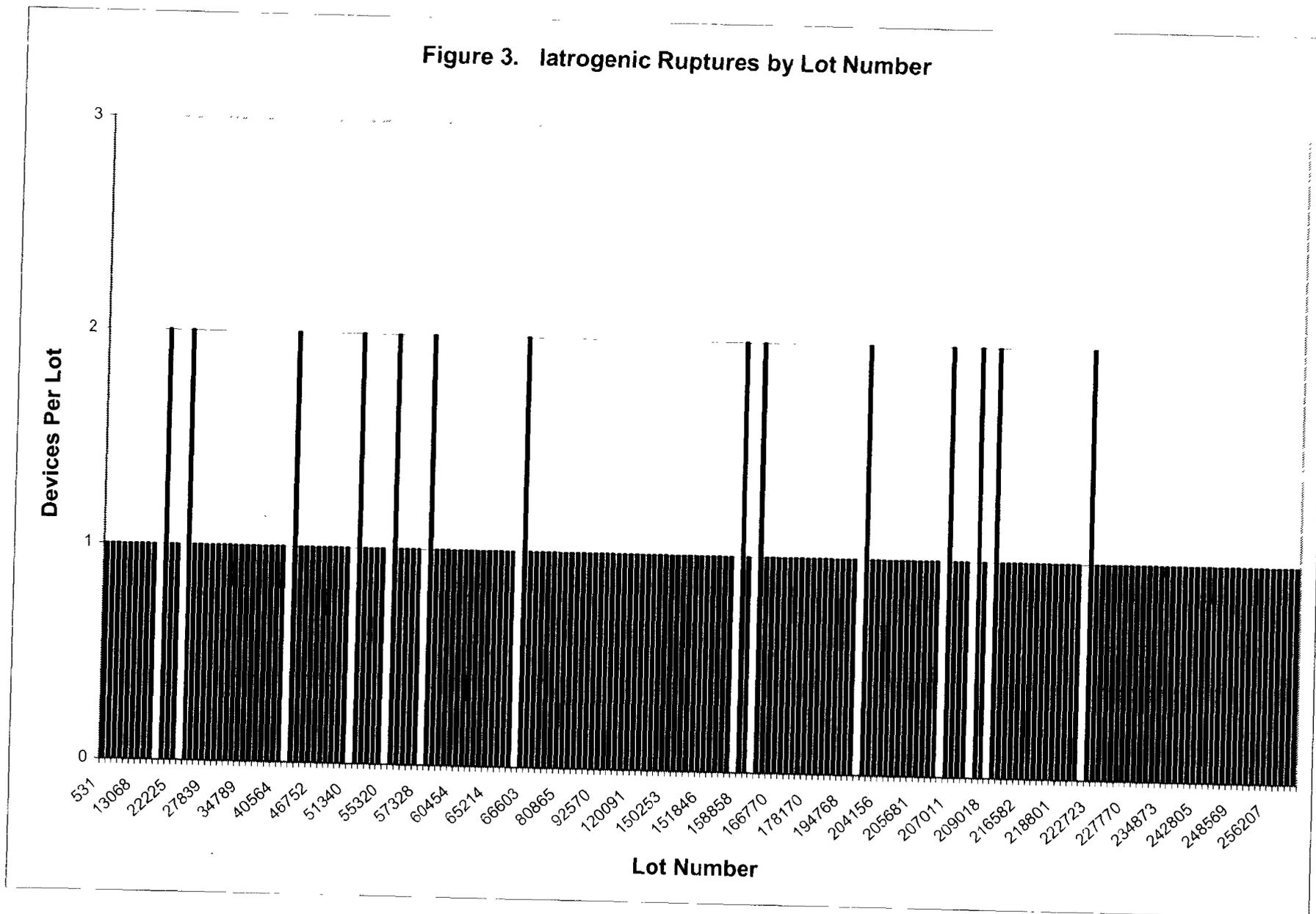


Figure 4. Smooth Gel-filled "RUC" + NA-EU Rate Versus Size

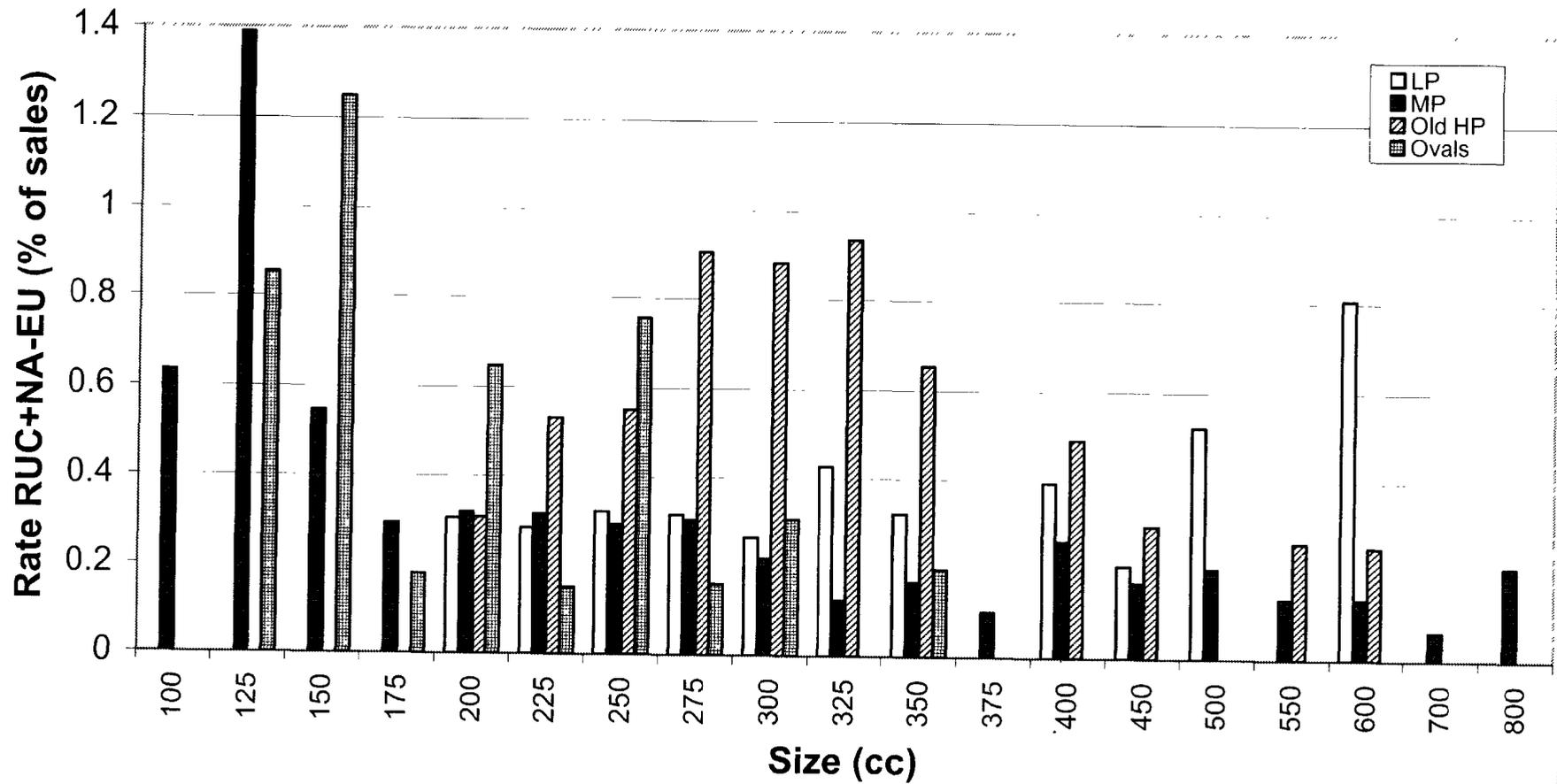


Figure 5. Siltex Gel-filled "RUC" + NA-EU Rate Versus Size

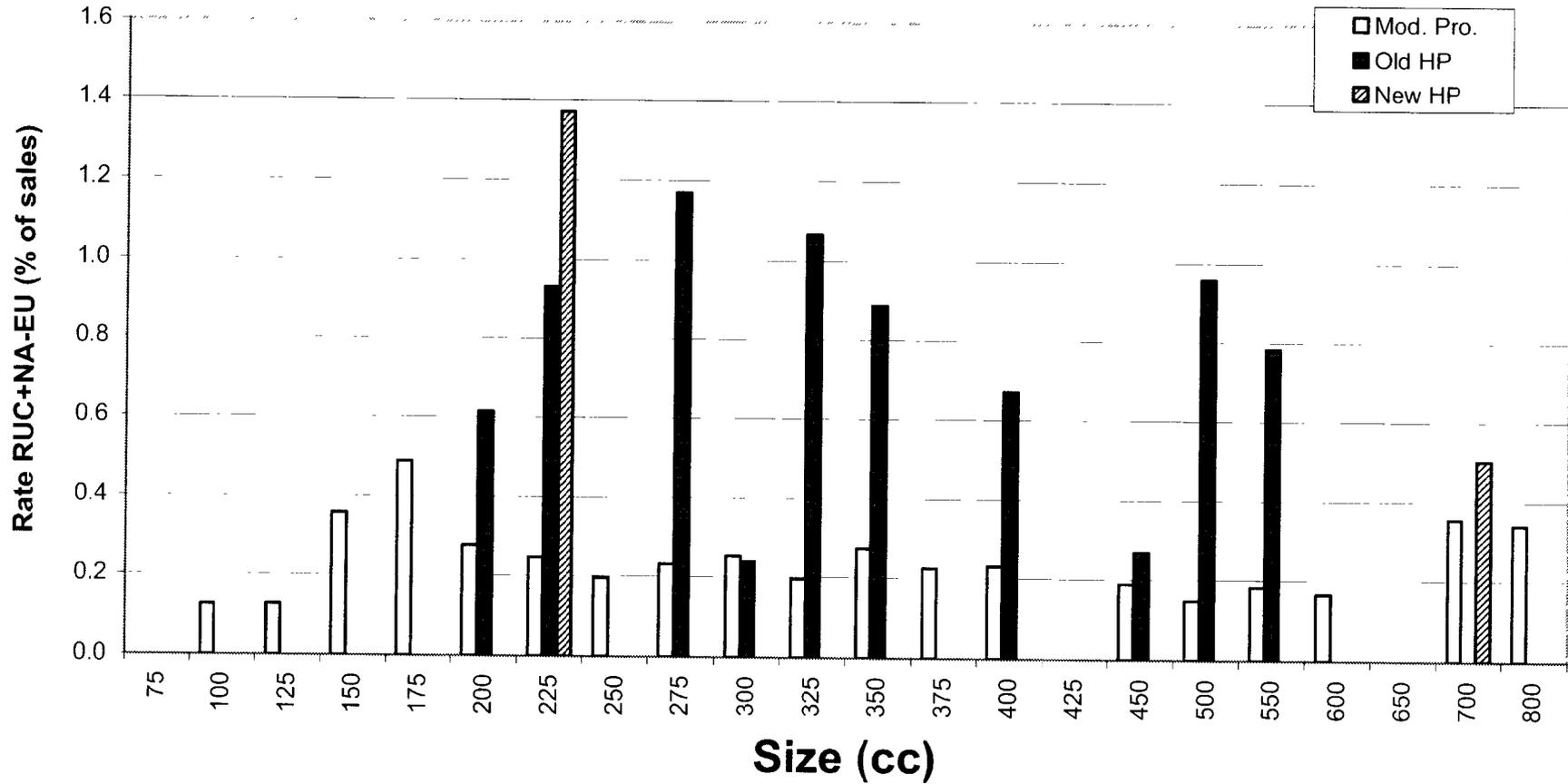


Figure 6. "RUC + NA-EU (Shell) By Lot Number

