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Thomas Golinski

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By

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Certificate of Approval

M.S. DEGREE THESIS

The M.S. Degree thesis of Thomas R. Golinski has been examined and approved by the thesis committee as satisfactory for the thesis requirements for the Master of Science Degree.

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October 2002

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ABSTRACT

The rapid growth of use of single use packages by medical device industry has had a great impact on the packaging industry. Materials used in these pacakages must be able to protect the product, withstand sterilization cycles, aid in easy opening, and be easy to identify. One such material used in this industry is Tyvek. This study will evaluate the effect of Tyvek porosity variations on burst test results. Two lots of Tyvek, a low porosity and a high porosity, were chosen and tested for porosity using a gurley densometer. This material was then constructed into pouches and burst tested. The data was analyzed statistically, and conclusions relating to the impact of porosity variation on the burst test results were drawn based on this data.

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Introduction to Medical Device Package Testing

1.1 The Need for Porous Materials in a Medical Device Package

As consumer healthcare demands rise, so will the need for disposable medical device packages. Since their emergence in the 1960s, single-use sterile medical products have seen rapid growth. The increased use of these products has helped reduce both risk and cost in hospitals. Costs have been reduced since the hospitals are no longer responsible for the sterilization of these now one-use medical devices. In addition to the cost benefit, the risk of contamination from a previously used product is reduced. However, these single-use sterile medical products present their own set of demands that a protective package must meet.

Maintaining a sterile barrier around the product (product protection) is the most important demand of a medical device package. This sterile barrier is often accomplished through the use of a low-cost flexible package or blister design. Allowing for sterilization is the next important demand of a medical device package. The package must be able to survive the chosen sterilization method. Since most sterilization is completed after the device is packaged, the package will encounter some stresses. The third demand is that the package must aid in the aseptic removal of the product. Medical personnel must be able to access the device easily so that it does not become contaminated. Additionally, the package should not add airborne contaminants. When the package is opened, all materials should remain intact so that the sterile environment is not compromised. Another demand is that the package should aid in product identification. Such identification is especially important in the case of products with many variations, and can be accomplished through the use of clear packaging or color-coded units. The last demand of a medical device package is that it should have evident

opening features. Once a package has been opened, there should be no way to reclose it, eliminating the possibility that a device package could be opened, contaminated, and resealed (Yambrach, 1997).

These factors are interdependent, and performance testing plays a key role in weighing the factors that lead to material selection. The primary focus of this research will fall in the area of product protection and sterilization, most notably the materials used to provide a sterile package.

In the medical device industry, there are three main types of sterilization: steam (autoclave), gas (Ethylene Oxide (EtO)), and radiation. Steam and EtO sterilizations are similar, and both sterilization processes require a porous package design. Both methods use a mechanical system to deliver a sterilant to the product. With steam the sterilant is hot moist air; and with EtO it is a warm chemical gas. Both systems rely on the pressure differences created by a vacuum vessel to allow for the sterilants to move through the package and come in contact with the product. Packages are first placed in a sealed chamber and a vacuum is pulled. The sterilant is then introduced into the chamber, and due to the pressure differences the sterilant replaces the low-pressure areas, moving through the package and then contacting the product (O'Brien, 1998). This process could not be achieved without the use of porous barrier materials. Examples of material used in these processes include medical grade paper, perforated films, and a spunbound polyolefin (Tyvek).

From Dupont, Tyvek is made from very fine, high-density polyethylene fibers, and is used for a wide range of applications (Swain, 2001). It has been used in the medical device industry for over thirty years, and it is compatible with both steam and

EtO sterilization. The porous nature and MVTR of the material are helpful in reducing EtO sterilization times. In the case of steam sterilization, Tyvek will hold its dimensional stability and integrity at a temperature range of 250° to 260° F at fifteen psi for thirty minutes. Therefore these sterilization temperatures must be controlled (Scholla, 1997).

When porous package designs are needed, it is important to select a material that has sufficient breathability to allow for adequate penetration of the sterilization dilutent, while at the same time providing enough protection to prevent bacterial contamination.

The performance testing of a medical device package allows designers to gather quantitative information about different designs and materials. Additionally, these tests give manufacturers and designers information they need to select proper materials and to measure the strength of various design options (Nolan, 1996). Test methods must be reliable and reproducible to be helpful in this design and material selection process. It is the responsibility of the manufacturer to qualify and validate a package design to ensure proper performance of the package, so that the product is sterile when it arrives to the end user. This study will focus on how the selection of a package material--in this case Tyvek--lends additional variability to the testing process and can lead to inaccuracies in the final test results. Additionally, the data gathered will help validate whether or not Burst testing is an acceptable way to test medical device packages as well as a benchmark for performance.

1.2 Testing Porous Medical Packages

Package testing is one of the key steps in the medical device manufacturing process. If a package fails, the sterility of the device is compromised (Beagley, 1998). In 1995 the

American Society of Testing and Materials (ASTM) published a standard guide for "Integrity Testing of Porous Barrier Medical Packages," meant for use in determining the overall package integrity. The standard provides a guide for whole package integrity testing of medical products with porous packages. It assumes that the raw materials have been specified accordingly and found suitable for the application being tested. Determining the integrity of a sterile package is achieved by demonstrating that its seal is intact after being exposed to a standard challenge test (vacuum, leak, visual examination, dye penetration, particulate transmission, or microbial). It should be noted that measuring the strength of a medical package is different from measuring the integrity of a medical package. The strength of a porous barrier medical package can be determined by four different methods: Burst (internal pressure), Creep (internal pressure), Seal Strength or Peel Strength.

Determining the actual strength of a porous package can be subjective, and the results can be substantially influenced by operator technique, equipment variability, raw material selection, and package geometry. Peel strength testing (ASTM D903-49) is the most widely accepted methodology used to measure seal strength and provides valuable information about the sealing process.

The strength of the seal plays a key role in the performance of the package by the end user, and therefore extensive testing must be completed. The seal cannot be too aggressive, or the end user may have to struggle to open the package and compromise the integrity of the device, or tear the package material and introduce airborne contaminants into the sterile environment. On the other hand, the seal cannot be too weak or the device may be compromised during the sterilization process. EVA, a common component of the

seal material, may vary from as low as fourteen percent to as high as forty percent (Yambrach, 1997). The lower the content, the more aggressive the seal will be. This variation in the seal material and the end use of the package must be considered, and peel strength is a key test in evaluating these parameters.

Peel strength test results change as seal parameters change; they are considered a good indicator of variation in the sealing process. Results of tensile strength testing vary based on material stiffness and angle of peel (90° or 180°). The main concern with this test method is that it is ineffective in determining the strength of the entire package. The extensive preparation time is another argument against using tensile testing to evaluate the performance of a peelable package (Hackett, 1998).

By default, Creep and Burst testing are the more desirable test methods for measuring overall package strength. Burst is defined by ASTM (ASTM F1585-95) as "a measurement of the ability of a sealed package to resist rupture when pressure is applied in a controlled and repeatable manner to its interior space." Creep is a non-destructive test method that also uses internal pressure to determine the strength of a package. Creep is an attribute test that yields only a pass/fail result. Since Burst testing gives variable output, it is statistically a more powerful tool. Burst testing incorporates raw material, design, and sealing process elements into a quantifiable output (Wachala, 1991). This approach gives the individual conducting the test a way to assess a package's ability to resist destructive forces during the manufacturing process (gas sterilization) and in the distribution environment. Manufacturers may attempt to test to failure and then use this information to set their own standard (Beagley, 1998). Again, this research will examine

the effects of the variability of material in a porous medical device and the effect on Burst testing.

1.3 The Science of Burst Testing

Using internal air pressure to determine the strength of a package has been common practice within the medical device industry since 1982. In May 1988, the American Society for Test Methods (ASTM) published a standard test method for "Failure Resistance of Unrestrained and Nonrigid Packages for Medical Applications" (F1140-88). This test method brought about standardization of test equipment, conditions, and nomenclature. The Burst test portion (Method A) indicated the area of pressurization was dependent upon the sensitivity of the indicator.

However, Burst testing may not be embraced by the packaging industry due to variability. There is still work to be done in the area of quantifying Burst test process variables as well as determining their significance (Franks and Barcan, 1999).

1.4 Burst Testing Equipment

Early Burst testing equipment consisted of a vacuum chamber used to create a pressure differential between the inside of the package and the environment. Eventually the chamber was partially filled with water; by immersing a sealed package in the water it was possible to determine the exact location of a failure by the appearance of bubbles.

Open-package Burst testing uses a clamping device with internal air supplied by a tube sandwiched between jaws of the clamp. Initially, open-package Burst testing used a needle gauge to record the maximum internal air pressure achieved when the package ruptured. Manually controlled vacuum and air pressure valves were eventually rendered

obsolete with the introduction of pressure transducers that use solid state controllers. These systems use one air line to supply air pressure and a second to measure pressure inside the package when the package bursts

Manually controlled pressurization systems had greater variability in the results and were considered too operator dependent. When pressure transducers and solid state controllers were introduced, it was possible to quantify the rate of pressurization and automate the test sequence (Jones, 1995).

Thesis Objective

2.1 Discussion on Material Variability and the Relation to Burst Testing

The goal of the primary research of this thesis is to examine the effect of Tyvek porosity rates on the burst strength of medical device pouches. The manufacturing process of this material lends itself to variability, and this has yet to be examined as a function of the end use package. The use of other materials such as medical grade papers will not be examined in this research since a high percentage of medical device packages use Tyvek. Burst testing is a widely accepted test method in the medical device industry, and the validity of the results may be impacted due to variability in the porosity present in the lidstock material.

Porous packaging designs have special considerations that need to be accounted for when using a burst test. The input rate of the air from the burst tester must be greater than the rate at which air escapes through the porous material. Due to the inherent variability in the material, in this case Tyvek, an additional degree of variability is added to the test methodology. This fact further hinders any attempt at achieving industry wide burst test standardization. It also reinforces why most medical device manufacturers avoid using burst testing for breathable package designs.

This work will continue the evaluation of burst test variability that was previously examined in Johnson's 1997 thesis " Evaluation of What Factors Effect Burst Test Results using Rigid Porous Packages." This previous work had attempted to quantify test method variability in the area of closed package burst testing. A primary conclusion

drawn from this previous research as that "in both studies the porosity of the lidding material was found to be a significant factor relative to the pressure required to burst this package" (Johnson, 1997). Additional conclusions included the fact that package geometry plays a larger role than peel strength when determining where a package will burst, and that the rate at which a package is filled can affect the burst value. Johnson drew these conclusions by completing the following test plan:

1. Identifying the nominal porosity measurements of the two lidstock lots
2. Performing a sealing process validation with the designated test materials and standard tooling, and determining nominal sealing parameters for sample preparations.
3. Establishing high and low air flow settings for the burst test
4. Conducting burst tests on two sample sets of rigid porous packages

Based on the previously stated conclusion drawn from the test plan above, Johnson recommended that burst test equipment be frequently calibrated to ensure accuracy, and that equipment manufacturers and test labs discuss the standardization of calibration methods and the burst test process validation.

2.2 Hypothesis Statements

This study will focus on how material selection will effect the burst test results of the final package. A detailed section involving burst test factors can be found in the section 3.0. Based on the above discussion, the following hypothesis statements were generated:

Null Hypothesis: Burst Test values of flexible medical device pouches are not related to the variability of the porosity that makes up the sample pouches.

Hypothesis: Burst Test values vary significantly due to material porosity variability

2.3 Burst Test Process Variables

This section provides a detailed outline of the elements that may contribute to burst test variability.

2.3.1 Material Factors

Porosity Rate

The air resistance of a material is measured by using a Gurley densitometer to record the amount of time it takes 100 cm^3 of air under 124 mm of pressure (H_20 gauge) to pass through 6.4 cm^2 (1 in^2) of material. Results from the Gurley-Hill porosity test (TAPPI T460) are recorded in sec/100 cm^3. Gas sterilized medical packaged designs use either Medical Grade paper, paperboard, or Tyvek as the porous membrane

2.3.2 Package Design Factors

Seal Strength

Burst testing is an indication of the strength of a seal. The sealing process parameters of time, temperature, and pressure will have a significant effect on the strength of the seal. The sealing temperature and dwell time are usually determined by the melt temperature of the material used as a sealant in the pouch.

Seal Width

The width of the seal will determine the amount of time required to burst a package; wider seals will require a longer time to burst. The relevance of this factor appears to be reduced given that burst testing is a dynamic test; therefore the amount of time associated with a wider seal is less significant. Wider seals provide greater resistance to seal creep, "the reduction in width of the heat seal due to force exerted by a bulky product, pouch distortion or internal air pressure" (ASTM F1585-95).

Porous Area

For a pouch design, the porous area is determined by the dimensions of the inside seal. In theory, the internal pressure of the package decreases as the air escapes through the porous area of the package. This assumes that the rate at which the air escapes is significant relative to the rate at which the air is supplied. The rate at which air is supplied to the package is far

greater than the escaping air, but there is no study that has been performed to quantify the interaction between porous area and internal air pressure.

2.3.3 Test Equipment and Process Factors

Input pressure flow rate

When vacuum and air pressure burst test devices were first introduced they used a manually controlled pressure regulators. This allowed operators an opportunity to manipulate test results by either quickly or slowly building the pressure inside a package or vacuum inside the chamber. The more modern burst test controllers are equipped with electronically controlled pressure regulators that greatly reduce this variable by controlling the rate of inflow. Despite the degrading affects of rapid pressurization during gas sterilization, the affect of pressurization rate on burst test results has yet to be proven.

Air Supply Attachment Method

Leaks around the attachment area of the seal can create false or misleading readings. As the package inflates and the seal area deflects, these leaks are sealed off and become less evident. In addition, most burst testers use a pre-inflation cycle that helps to reduce this effect.

Test Conditions

ASTM F1140 requires packages to be exposed to standard test conditions (73+/- 4° and 50 +/-5% relative humidity) for at least 24 hours, and that any deviation from these conditions while the test is conducted should be documented.

Standard test conditions have a much lower temperature than the melt temperature of most heat seal materials. Therefore, this is expected to have minimal to no effect on the test results. When attempting to correlate burst values to sterilization effects, consideration should be given to what effect excessive temperature and humidity may have on burst values.

Primary Research

3.1 Test Plan

3.1.1 Material Sample Selection

For this research, 2 lots of Tyvek were selected. These lots were provided by a converter who provides material to the medical device industry and were coated with the same EVA copolymer. In addition, this coating was added by the material manufacturer to these lots using the same process, therefore the blend and thickness would be the same. These 2 different lots were identified by their porosity as a "high Gurley" (Sample Lot A), and the other a "low Gurley" (Sample Lot B) material. The Gurley reference is to that of TAPPI 460. This test measures the air resistance of a material by using a Gurley densitometer to record the amount of time it takes 100 cm^3 of air under 124 mm of pressure (H_20 gauge) to pass through 6.4 cm^2 (1 in^2) of material. Results from the Gurley-Hill porosity test (TAPPI T460) are recorded in sec/100 cm^3. A lot consisted of 50 samples.

3.1.2 Porosity Measurement

Each sheet's porosity was measured in three locations. The measurement locations correspond to those illustrated in Figure 1. All tests were done in accordance with TAPPI 460, and were completed using a closed top Gurley Densitometer Model 4110 at Ethox, Inc. of Buffalo, NY.
This piece of equipment was calibrated on January 9, 1998, and the measurements were taken on January 22-23, 1998.

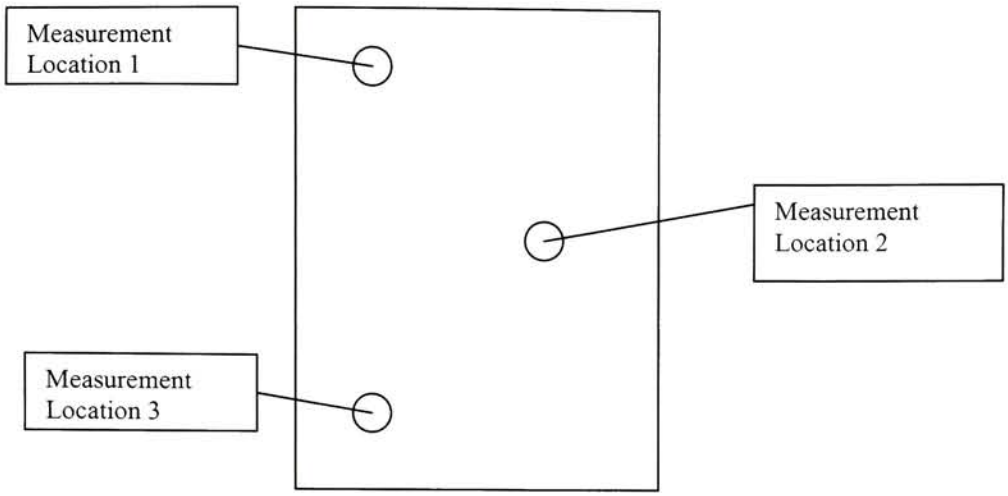


Figure 1- Measurement Locations

3.1.3 Pouch Conversion/Heat Sealing

For the next step in the test plan, the Tyvek material had to be converted into pouches. To accomplish this, 2 mil uncoated polyethylene was heatsealed to the 2 lots of Tyvek. The polyethylene was sealed to 3 sides to form an open-ended pouch (figure 2). The heatsealing was done using a Vertrod heatsealer, serial number 7-42057, model number 24 PCS. The heat setting was set to 6, and the dwell set to 3. The sealing conditions were the same for all pouches since all were determined to be similar in seal requirements as they were manufactured at the same time. In addition, the seal bar provided equal heat at all locations. This was verified by the use of the same heatseal equipment for many student lab activities.

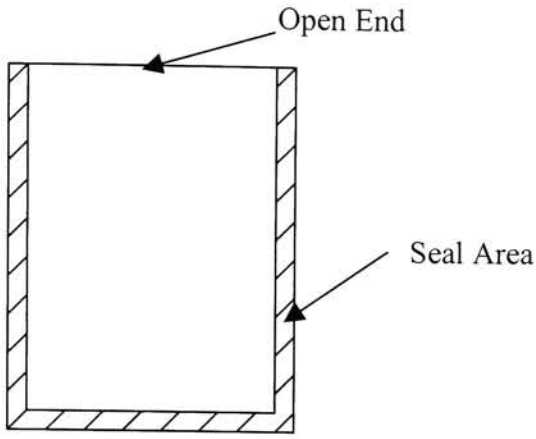


Figure 2: Pouch

3.1.4 Burst Testing

The final step in the test plan was the burst test. The burst testing was completed on the converted pouches using an ARO burst tester, model number F100-2500-1, serial number 181.

3.1.5 Test Plan Assumptions

Based on the test plan above a few assumptions regarding the material and test equipment have been made. First, in relation to the material, it is assumed that the material provided was within the specification of the manufacturer. There was no material specification provided, however the material was from a production run so there is no reason to suspect it was not within specification. The second assumption is that the test equipment was properly calibrated. All of the calibration information has been provided, and again there is no reason to assume that the equipment was not in proper working order.

3.2 Test Results

3.2.1 Porosity Test Results

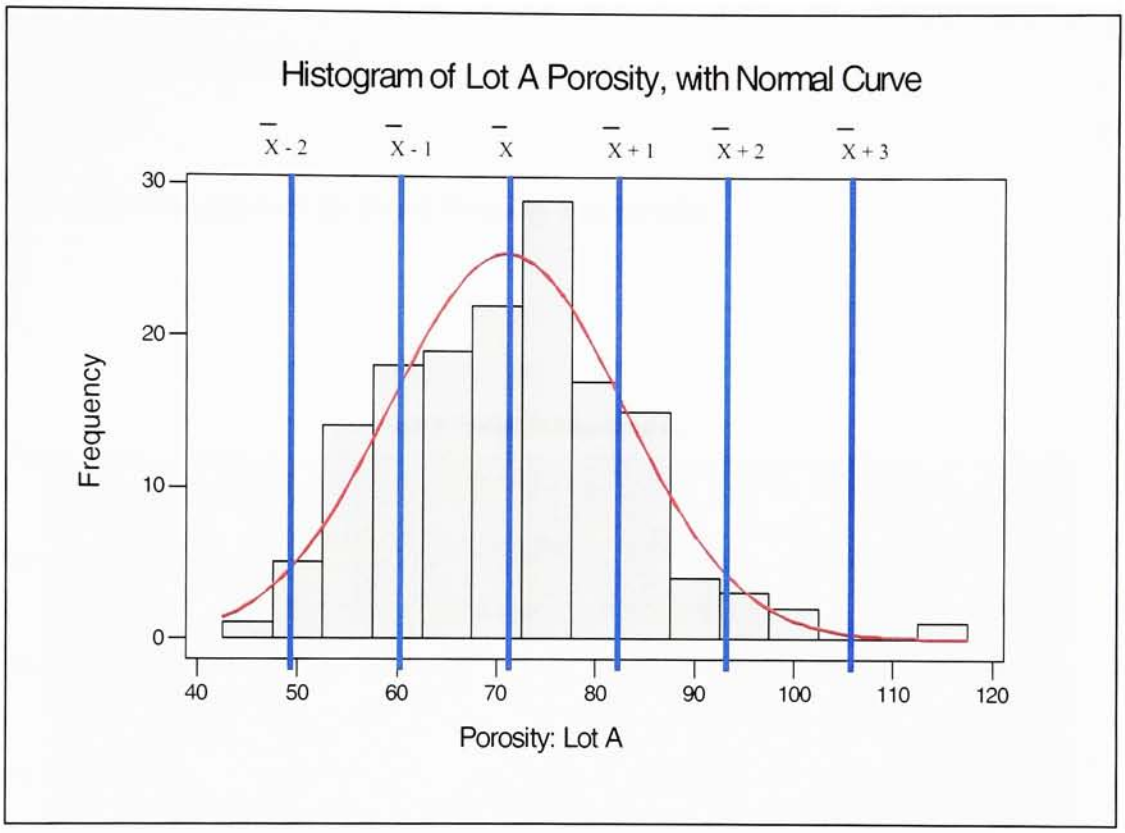
The raw data from the porosity measurements taken for Lot A can be found in the appendix, Section 5.1

3.2.2 Descriptive Statistics – Lot A Porosity

Lot A Porosity	
# of Samples	150
Mean	71.015
Median	70.8
Mode	76.2
Standard Deviation	11.75
Range	69.2
Minimum	47
Maximum	116.2

Table 1 – Descriptive Statistics: Porosity Measurements- Lot A

3.2.3 Histogram with normal curve – Lot A Porosity

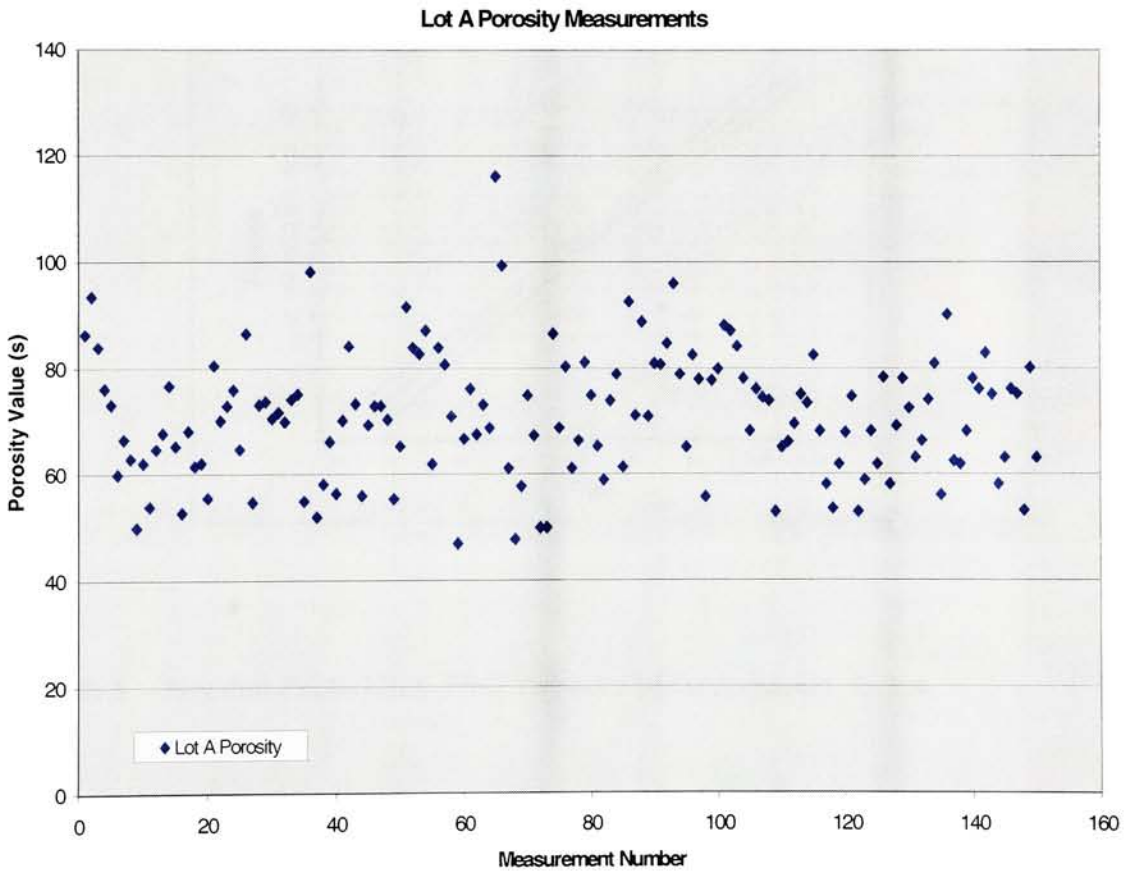


Graph 1 – Histogram: Porosity Measurements- Lot A

The graph above uses the descriptive statistics outlined in section 3.2.1 to graphically illustrate the data for the Lot A porosity and the normal curve plot for this data. The six standard deviations are also plotted, and out of this data one point fell outside of the six-sigma level.

The graph above uses the descriptive statistics outlined in section 3.2.2 to graphically illustrate the data for the Lot B porosity and the normal curve plot for this data. The six standard deviations are also plotted, and out of this data one point fell outside of the six-sigma level.

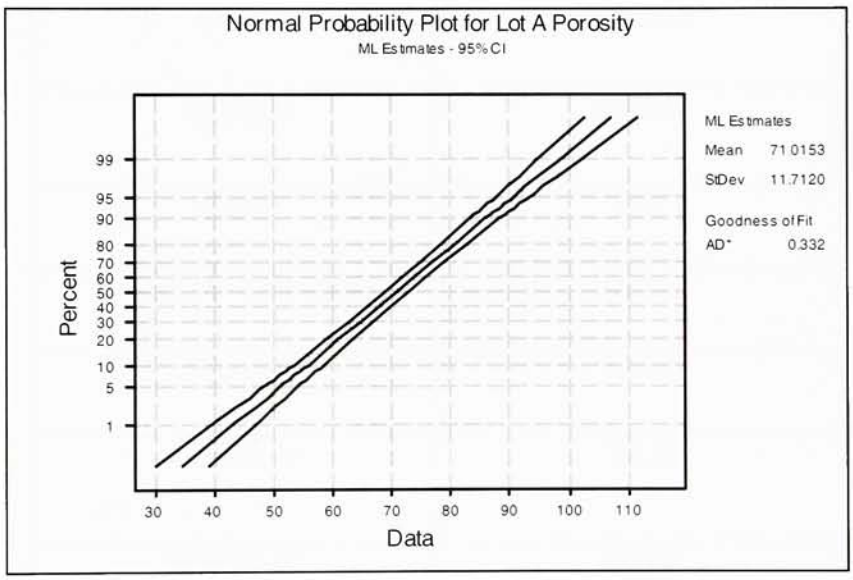
3.2.4 Sample Lot A- Sheet Porosity Scatterplot



Graph 2 – Scatterplot: Lot A Porosity

The scatterplot illustrates the range of the porosity data collected for Lot A. As seen in this chart the low reading for the data set was 47 seconds and the high 116.2 seconds giving a range of 69.2 seconds.

3.2.5 Normal Probability Plot – Lot A Porosity



Graph 3 – Normal Probability Plot: Porosity Measurements- Lot A

3.2.6 Porosity Test Results

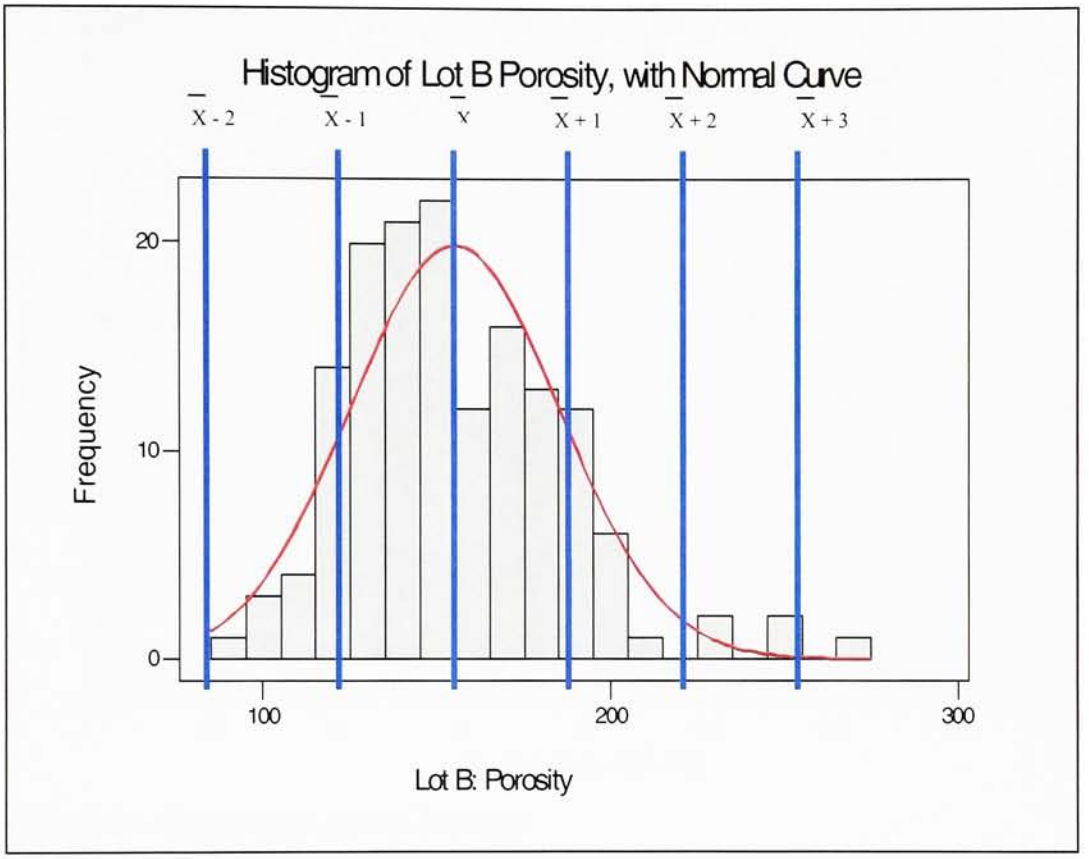
The raw data from the porosity measurements taken for Lot B can be found in the appendix, Section 5.2

3.2.7 Descriptive Statistics – Lot B Porosity

Lot B Porosity	
# of Samples	150
Mean	155.019
Median	151.4
Mode	152
Standard Deviation	30.14
Range	174.4
Minimum	91.2
Maximum	265.6

Table 2 – Descriptive Statistics: Porosity Measurements- Lot B

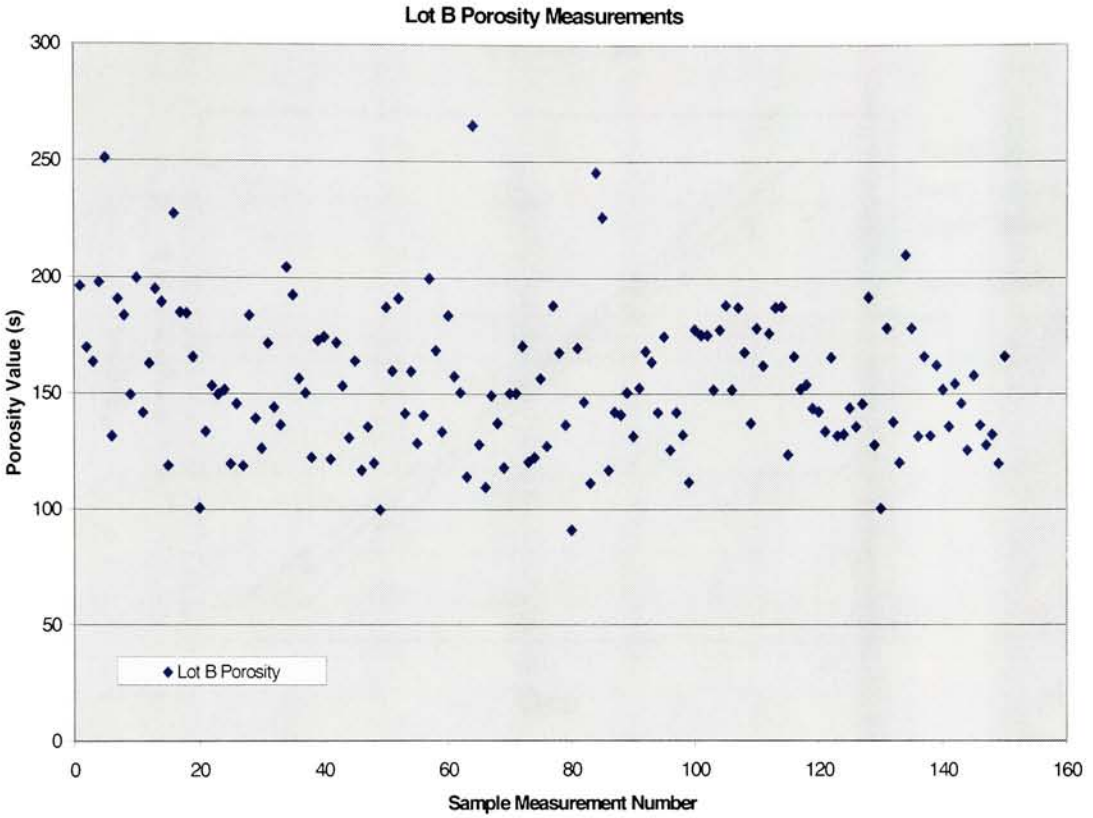
3.2.8 Histogram w/normal curve – Lot B Porosity



Graph 4 – Histogram: Porosity Measurements- Lot B

Again, the graph above uses the descriptive statistics outlined in section 3.2.7 to graphically illustrate the data for the Lot B porosity and the normal curve plot for this data. The six standard deviations are also plotted, and out of this data two points fell outside of the six-sigma level. In addition, the data range for this sample set was much larger (174.4 seconds vs. 69.2 seconds for Lot A).

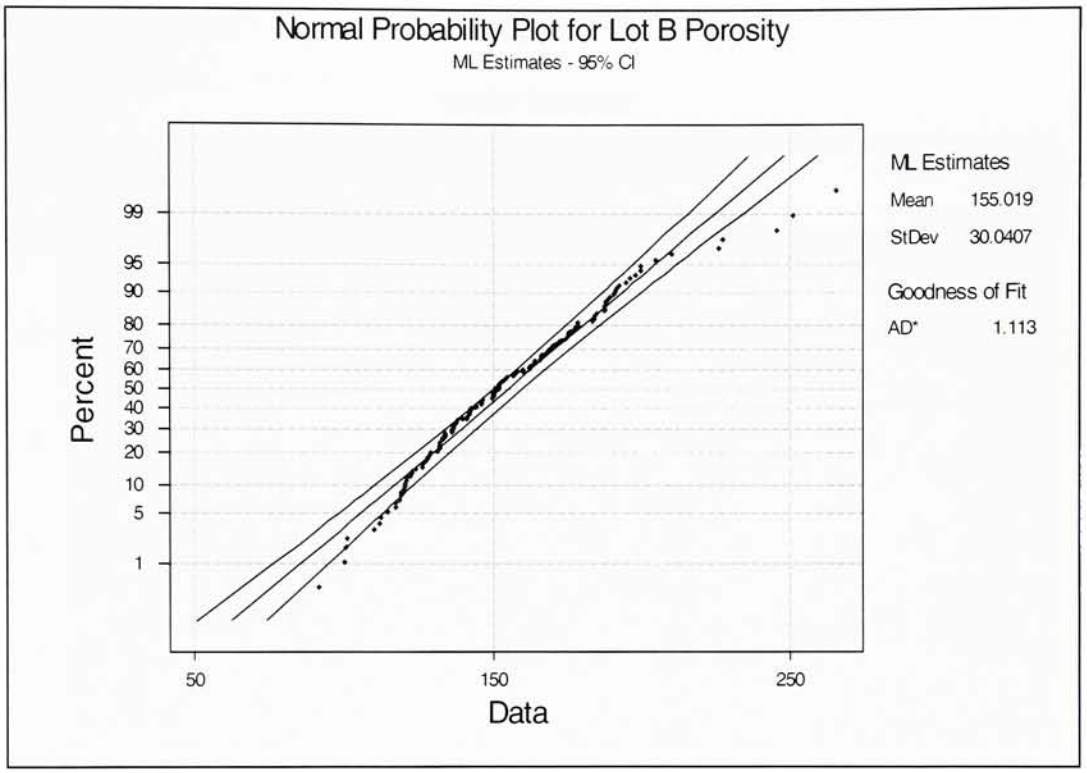
3.2.9 Sample Lot B- Sheet Porosity Scatterplot



Graph 5 – Scatterplot: Lot B Porosity

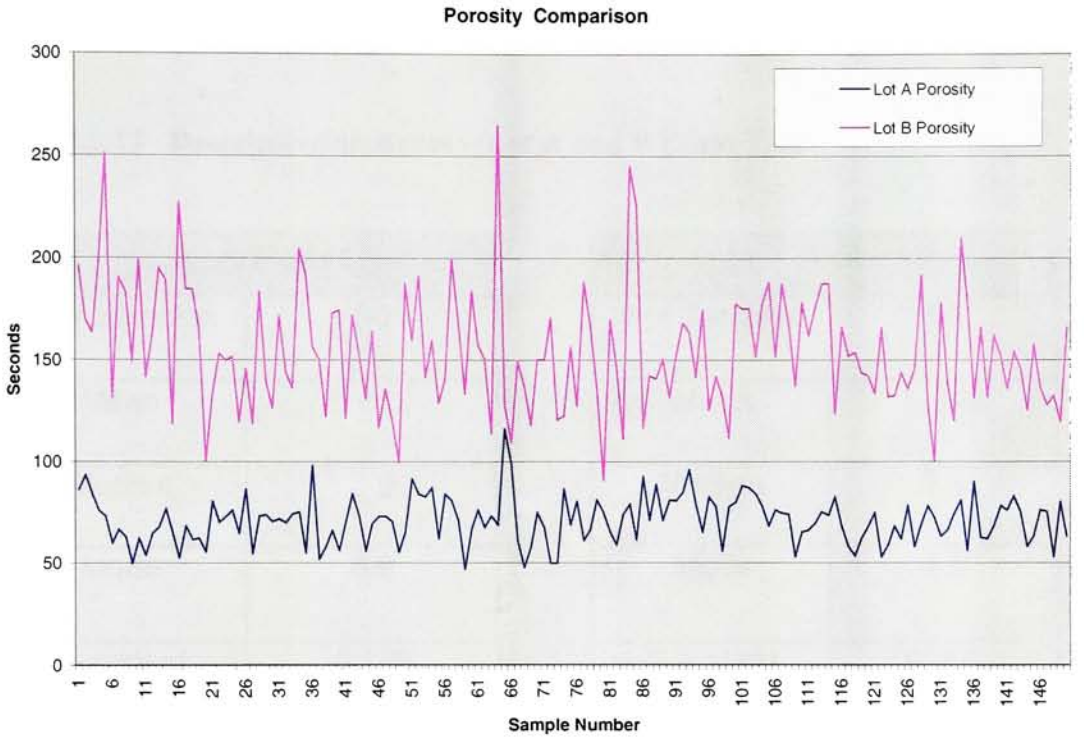
The scatterplot above illustrates the range of the porosity data collected for Lot B. As seen in this chart the low reading for the data set was 91.2 seconds and the high 265.6 seconds giving a range of 174.4 seconds, a much higher range than that of Lot A.

3.2.10 Normal Probability Plot – Lot B Porosity



Graph 6 – Normal Probability Plot: Lot B Porosity

3.2.11 Lot A vs. Lot B Porosity Range



Graph 7 – Lot A vs. Lot B Porosity

In sections 3.2.4 and 3.2.9 the individual scatterplots for Lot A and Lot B porosity were individually plotted. On the line graph above, both data sets are plotted on the same set of axis so that a visual comparison of the data can be seen. As seen on this graph, the Lot B porosity measurements have a much greater level of porosity variability than those of lot A. The range of Lot B is 2.5 times greater than that of Lot A.

3.2.12 Burst Test Results

The raw data from the porosity measurements taken for Lot B can be found in the appendix, Section 5.3

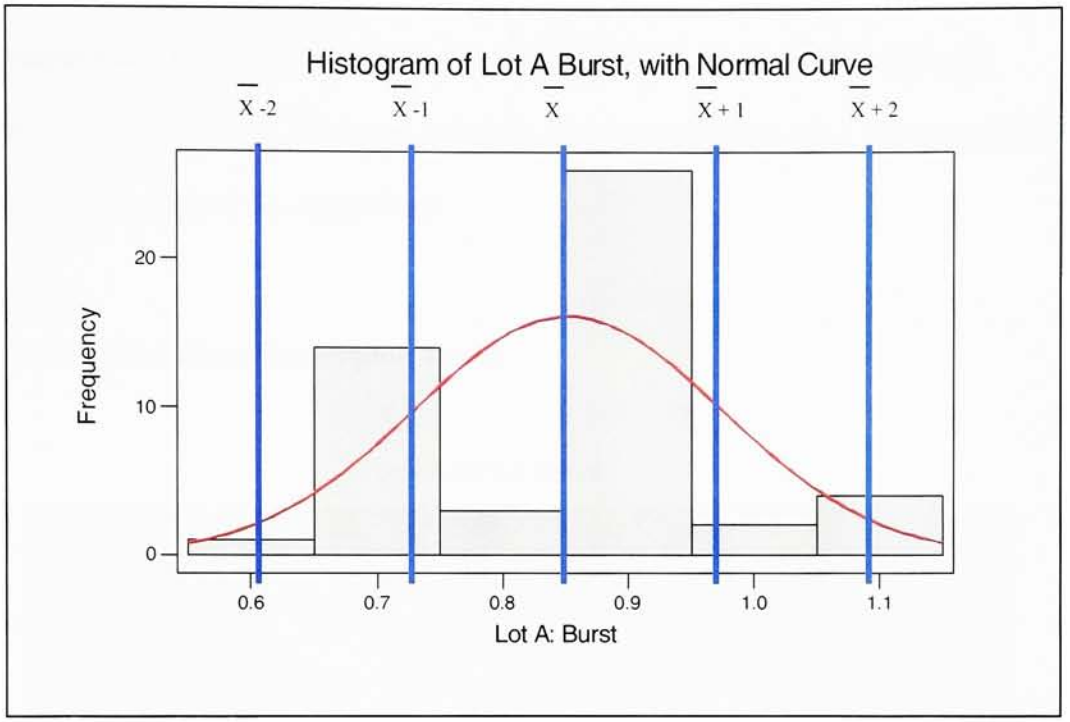
3.2.13 Descriptive Statistics – Lot A and B Burst Test

Lot A Burst	
# of Samples	50
Mean	0.852
Median	0.9
Mode	0.9
Standard Deviation	0.123
Range	0.5
Minimum	0.6
Maximum	1.1

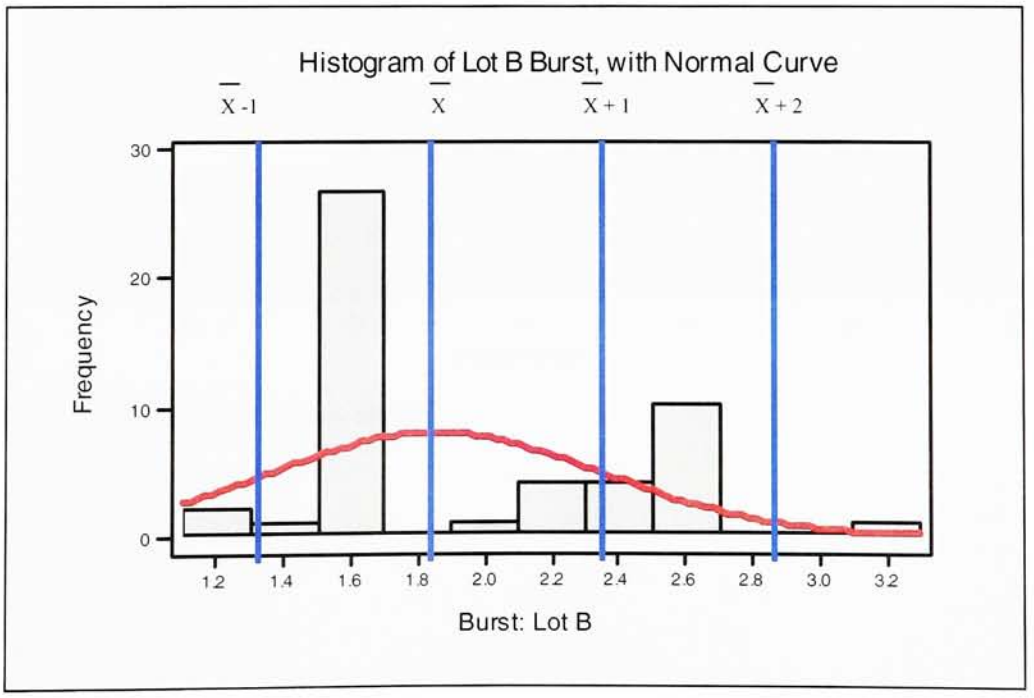
Lot B Burst	
# of Samples	50
Mean	1.848
Median	1.5
Mode	1.5
Standard Deviation	0.499
Range	2.2
Minimum	1.1
Maximum	3.3

Table 3 – Descriptive Statistics: Burst Test Results

3.2.14 Histograms with Normal Curves – Lot A and B Burst Test



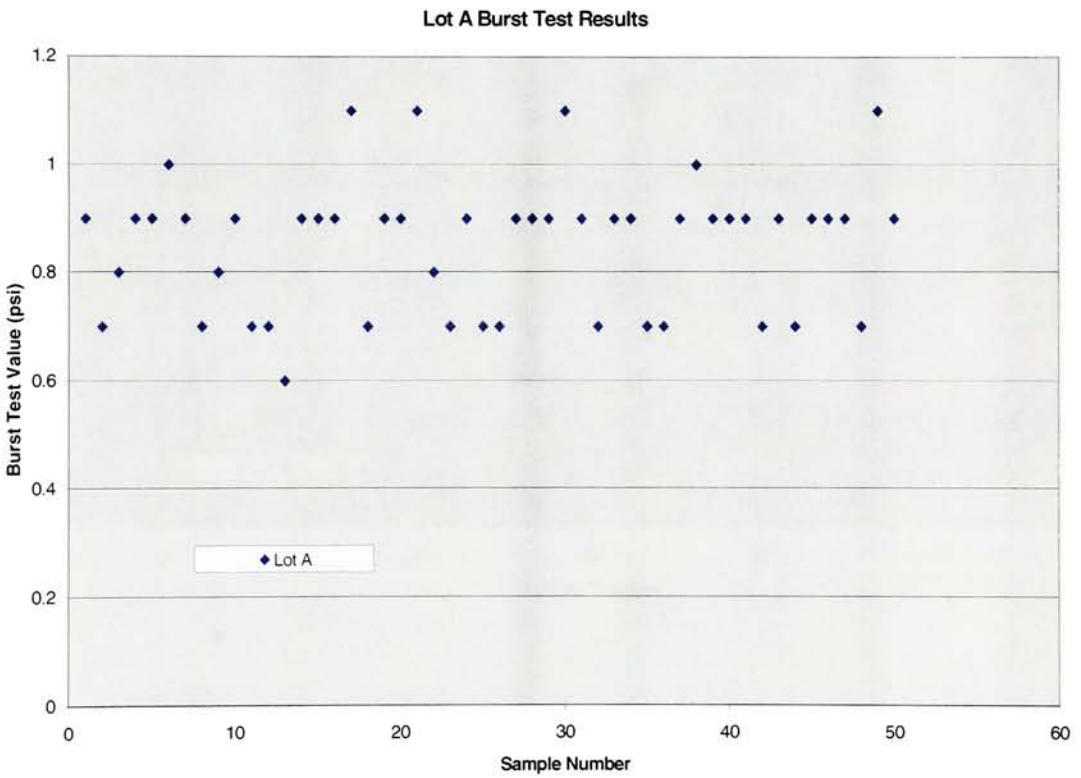
Graph 8 – Histogram with Normal Curve: Lot A Burst



Graph 9 – Histogram with Normal Curve: Lot B Burst

The graphs on the previous page use the descriptive statistics outlined in sections 3.2.13 to graphically illustrate the burst data for Lots A and B in histogram form with their respective standard deviations. In the case of Lot A, all values fall within the accepted six sigma levels. However, in Lot B, the data point with a 3.3 value would fall outside of the accepted six sigma level.

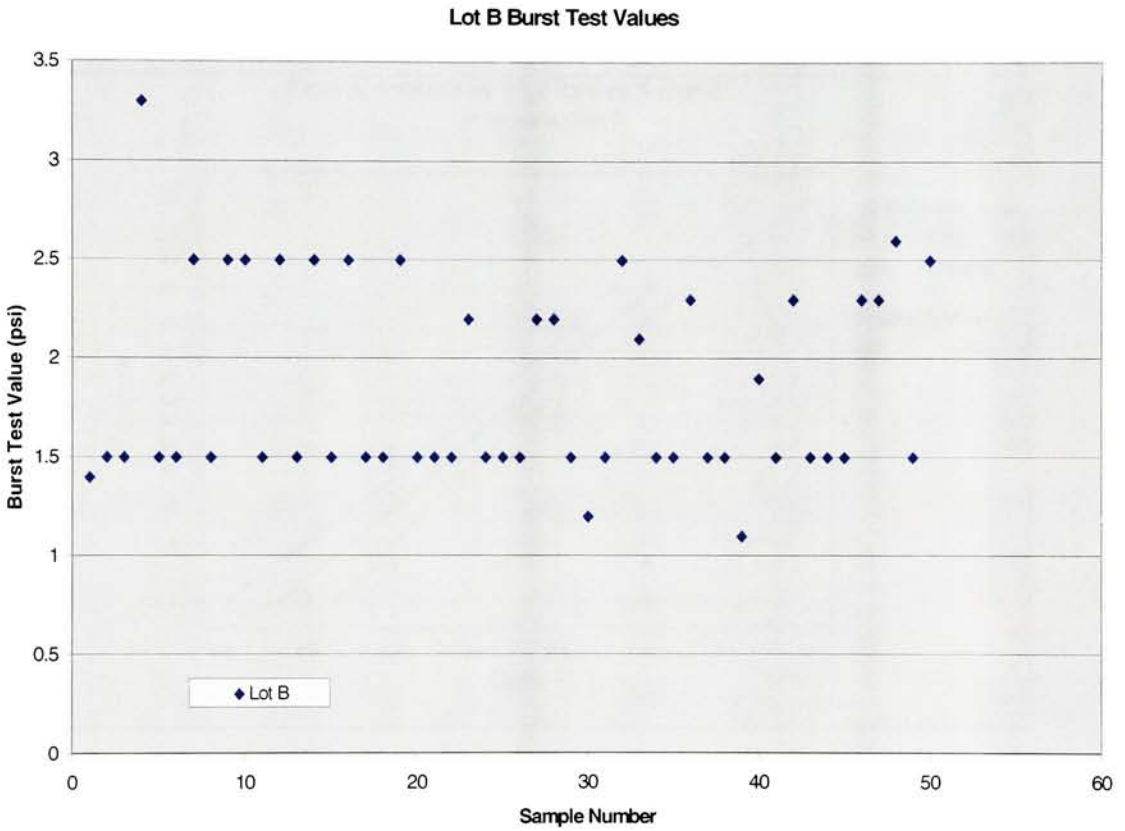
3.2.15 Burst Test Data Scatterplot: Lot A



Graph 10 –Scatterplot: Lot A Burst

The scatterplot on the previous page illustrates the range of the burst data collected for Lot A. The range for this sample lot ranges from 0.6 to 1.1 psi.

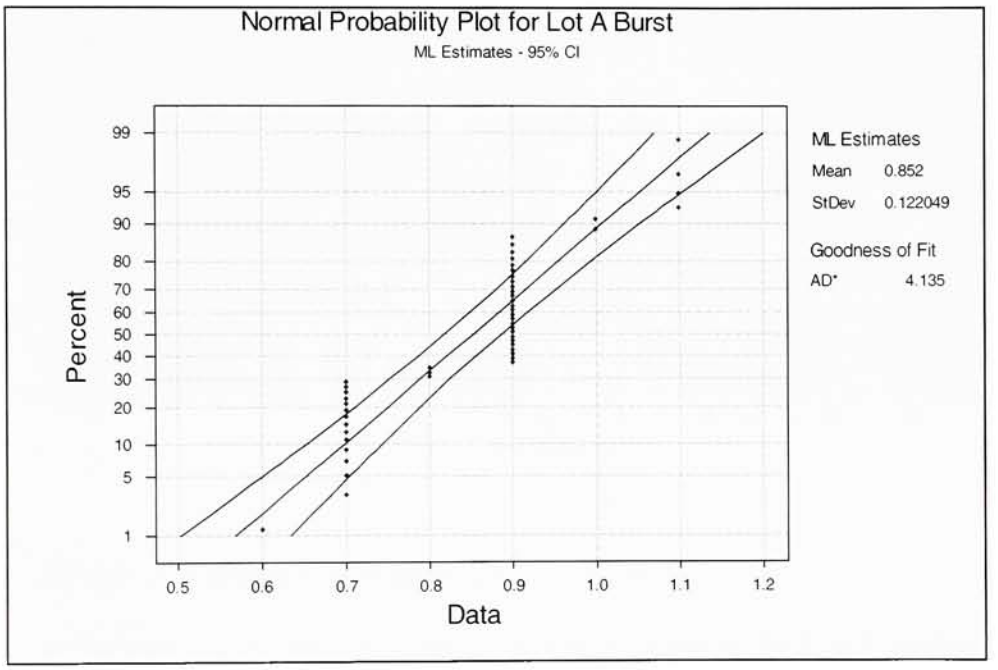
3.2.16 Burst Test Scatterplot: Lot B

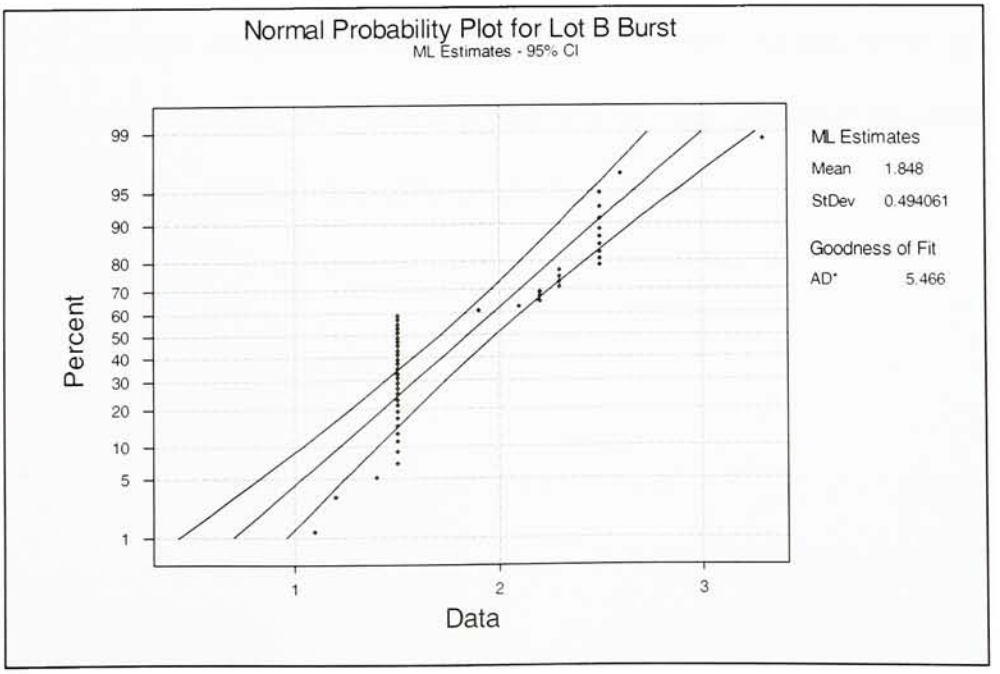


Graph 11 – Scatterplot: Lot B Burst

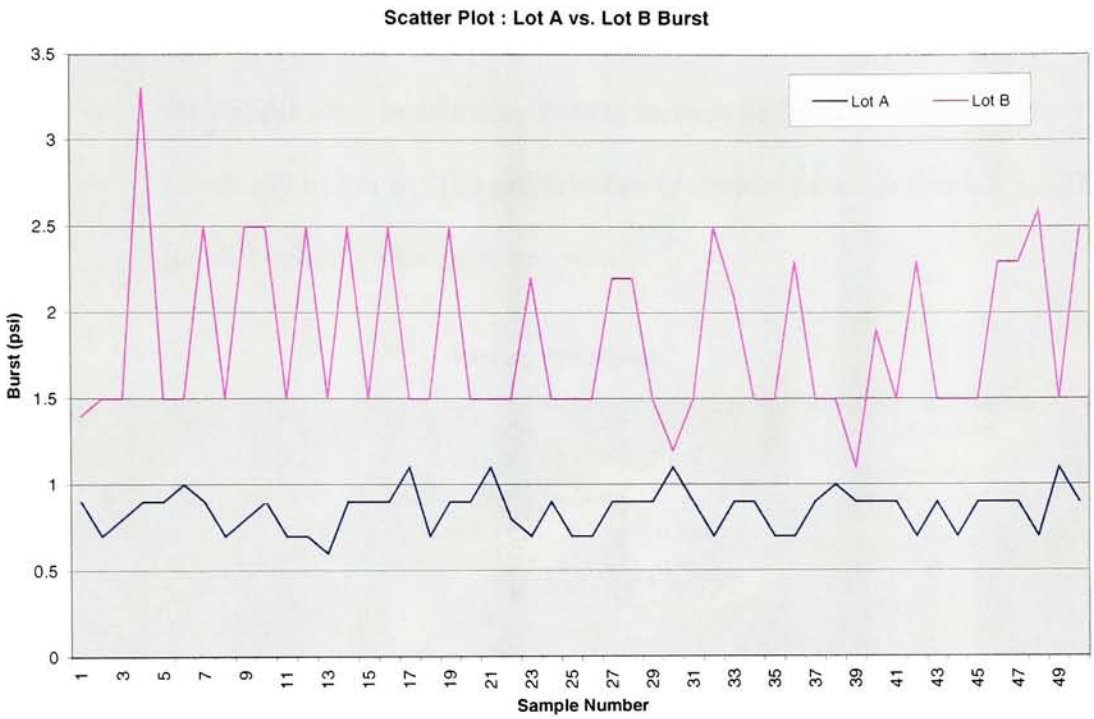
Again, the scatterplot on the previous page illustrates the range of the burst data collected for Lot B. This ranges is much greater than the range seen in Lot A. The range for this data set goes from 1.1 psi to 3.3 psi (2.2 psi delta vs 0.5 for Lot A).

3.2.17 Normal Probability Plots – Lot A and B Burst Test





3.2.16 Burst: Lot A vs. Lot B

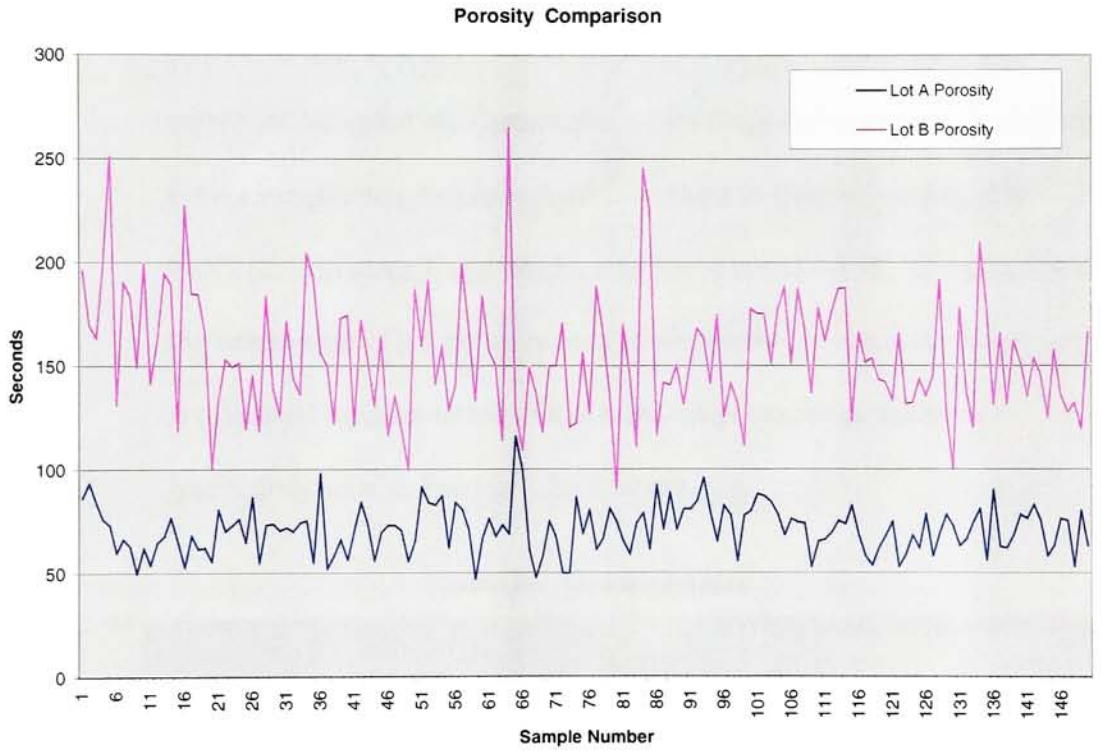


Graph 13 – Burst Test Results: Lot A vs. Lot B

In sections 3.2.16 and 3.2.17 the individual scatterplots for Lot A and Lot B burst were individually plotted. On the line graph above, both data sets are plotted on the same set of axis so that a visual comparison of the data can be seen. As seen on this graph, the Lot B burst measurements have a much greater level of burst variability than those of lot A. The range of Lot B is 4.4 times greater than that of Lot A.

3.3 Conclusions

3.3.1 Variability in porosity measurements exists in Tyvek. Upon reviewing the data it is evident that there is porosity variability in both of the sample lots. In addition, there is an even higher level of porosity variability in Lot B. The graph below (previously seen in Section 3.2.11 graph 7) clearly illustrates this point:

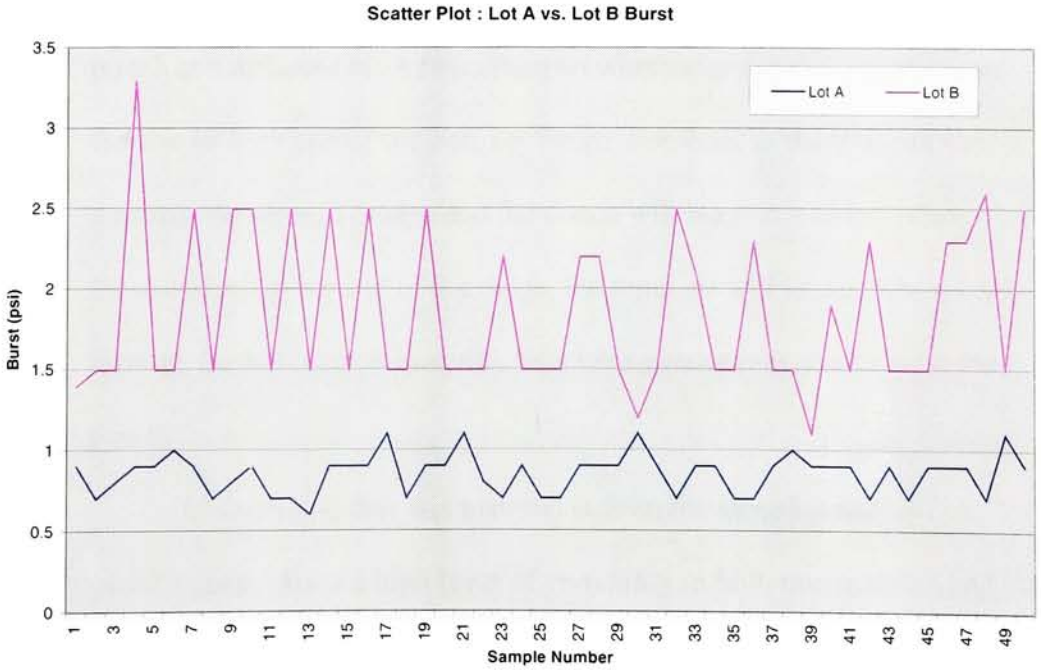


The range of values for Lot A is fairly tight (69.2 seconds) versus that of Lot B (174.4 seconds).

In addition, upon examination of the plot of the statistical mean and standard deviations, it can be seen that both Lot A and Lot B produced samples that fell outside of the 3rd standard deviation thus falling outside of the six sigma quality initiative. This could have an impact on the

sterilization cycle for the medical device package. If the sterilization cycle is set for a given package porosity and the material falls outside of the accepted range, sterility could be impacted.

3.3.2 The variability in porosity contributes to variability in the burst testing of the sample pouches. The range of burst test values (psi) for the sample pouches converted from the Lot A samples ranged from 0.6 to 1.1 (0.5 psi range), and had an average value of 0.852. These values all fall within the accepted six sigma values. The range of burst test values (psi) for the sample pouches converted from the Lot B samples ranged from 1.1 to 3.3 (2.2 psi range), and had an average value of 1.848. The pouch with the burst value of 3.3 psi does not fall within the accepted six-sigma range. A graphical representation of this burst range can be seen below (previously seen in Section 3.2.18 graph 12):



Sample Lot B had a much higher variability in porosity than that of Sample Lot A (174.4 second range vs. 69.27 second range). Understanding the definition of a burst test as that of a test "that measures the ability of a sealed package to resist rupture when pressure is applied in a controlled and repeatable manner to its interior space," (ASTM F1140-88) a conclusion can be drawn that the variability of the materials that form the pouch contribute to the overall variability of the end use package. This is evident in both the data for Lot A and Lot B. However, this conclusion is clearer in the data for Lot B since the overall porosity variability is much greater. With the samples of this lot, the porosity measurements had a large range (174.4 seconds) as well as a large burst test range (2.2 psi).

In the context of the burst test, the air filling the pouch will escape at different rates depending on porosity. With the range of porosity values being spread out over a range of 174.4 seconds, the air will escape the pouch at a different rates depending on whether or not the material is at the low or high end of the porosity range. For those at the low end (more porous), the air will escape and the pouch will burst at a lower value. For those on the higher end of the range, the input air will escape less quickly through the less porous material, thus taking more pressure to burst the pouch.

Considering that this material is from the same lot and specification, this is a high level of variability in both raw material and the

end use pouch. This data also supports the hypothesis statement from section 2.2 that burst test values vary significantly due to material porosity variability.

3.4 Recommendations

If Tyvek is going to be used as a raw material in medical device packaging, it must be accepted that the material has some porosity variability and that this variability will lead to variable burst test results. It will be at the discretion of the packaging engineer responsible for material selection to determine if this variability will have too great of an impact on the final package design. Ultimately the use of Tyvek could have an impact on cost for a few reasons. First, the use of this material may generate scrap in end use packages. If an end use package was constructed of the low gurley material and the porosity values were on the high side of the values measured in this study, there could be a high rate of faulty seals due to burst upon completion of the sterilization cycle. Secondly, sampling costs could potentially higher. If the material is inconsistent, a higher number of sample packages will be needed to ensure the sterilization cycle was successful.

If it is determined that Tyvek is a desired material for the package, and burst testing will be used to verify the integrity of the package system, a range of acceptable values will have to be pre-determined. Since we know that there is variability in the raw material, simply defining one value as a pass/fail criteria

could lead to false test results. Since the porosity rate of the package impacts on the stresses that the seals face, variability in this area is especially vital to the integrity of the medical device package.

In addition, sterilization cycle times will have to be examined. Due to the porosity variation and the fact that it can fall outside of the six-sigma range, the product may not see adequate sterilization and thus not provide a sterile product to the end user.

As the medical device industry attempts to standardize their testing methods, the factors that influence these tests must continue to be evaluated. If burst testing is going to be one of these standardized tests, there must be a continued understanding of the materials used and their properties and processes. The idea of having a standardized industry test procedure is important because it will eliminate discrepancies in lab procedures from manufacturer to manufacturer. Currently, the responsibilities of the package design as well as the commonly used physical and visual tests have been identified for the manufacturer. However, what is lacking is a true industry step by step instruction on how to conduct the tests (Allen, 1999). Further understanding of the materials used in the final package will aid in accomplishing the delivery a well-protected sterile medical device to the end user, while also helping to eliminate variability.

In the area of future research on this topic, it would be recommended that a Design of Experiment (DOE) be outlined for this testing. A DOE is a structured, organized method for determining the relationship between factors affecting a process and the output of that process. At the time this test plan was constructed, the resources were not available for the development and execution of a DOE. The DOE would include the following factors: operator, material porosity, package geometry, coating thickness, seal strength, temperature and humidity. These factors all have an impact on the overall experiment and results. The first factor, operator, is important because different operators would operate the test equipment differently. This difference in technique could introduce variability into the test plan. For the DOE, the operators would be noted as 1 and 2.

The second variable, material porosity, is also of great importance. For this experiment there would be two materials identified, a low porosity and a high porosity. As we have seen in the data presented in the previous sections, the material porosity is variable, and this does have an effect on the burst test values of the end use package.

Package geometry is another factor that could have an impact on the test results. For the DOE the geometry would be noted as either flexible or rigid. This notation refers to the end use package, and an example of a flexible package would a pouch design similar to that of those tested for this research. A rigid package design could consist of a thermoformed tray with lidstock heatsealed to it.

The third factor is thickness of the EVA coating that is applied to the material. In the DOE, this would be identified as either thick or thin. This is an important factor because the thickness of the coating applied to the material would impact the aggressiveness of the seal. The lower the content of EVA, the more aggressive the seal will be. This seal aggressiveness plays a large part in determining the burst test result for the end use package.

The last two factors, temperature and humidity, are included to understand the effects of the environment on the experiment. Both conditions would be identified as either high or low.

A sample DOE could be constructed as follows:

Std	Run	Block	Factor 1 Porosity	Factor 2 Pkg. Geometry	Factor 3 Thickness (EVA)	Factor 4 Seal Str.	Factor 5 Temp.	Factor 6 Humidity
9	1	Operator 1	High	Flexible	Thin	Low	Low	Low
100	2	Operator 1	High	Rigid	Thin	Low	High	High
150	3	Operator 1	High	Flexible	Thick	High	High	Low
125	4	Operator 1	Low	Flexible	Thin	High	High	Low
77	5	Operator 1	High	Rigid	Thick	High	Low	High
53	6	Operator 1	Low	Rigid	Thin	High	Low	High
114	7	Operator 1	Low	Rigid	Thick	Low	High	High
54	8	Operator 1	Low	Rigid	Thin	High	Low	High
146	9	Operator 1	High	Flexible	Thick	High	High	Low
107	10	Operator 1	High	Flexible	Thick	Low	High	High
122	11	Operator 1	Low	Flexible	Thin	High	High	Low
15	12	Operator 1	Low	Rigid	Thin	Low	Low	Low
106	13	Operator 1	High	Flexible	Thick	Low	High	High
110	14	Operator 1	High	Flexible	Thick	Low	High	High
38	15	Operator 1	High	Rigid	Thick	Low	Low	Low
96	16	Operator 1	High	Rigid	Thin	Low	High	High
84	17	Operator 1	Low	Flexible	Thin	Low	High	High
79	18	Operator 1	High	Rigid	Thick	High	Low	High
25	19	Operator 1	Low	Flexible	Thick	Low	Low	Low
8	20	Operator 1	High	Flexible	Thin	Low	Low	Low
48	21	Operator 1	High	Flexible	Thin	High	Low	High

124	22	Operator 1	Low	Flexible	Thin	High	High	Low
55	23	Operator 1	Low	Rigid	Thin	High	Low	High
136	24	Operator 1	High	Rigid	Thin	High	High	Low
46	25	Operator 1	High	Flexible	Thin	High	Low	High
155	26	Operator 1	Low	Rigid	Thick	High	High	Low
76	27	Operator 1	High	Rigid	Thick	High	Low	High
83	28	Operator 1	Low	Flexible	Thin	Low	High	High
49	29	Operator 1	High	Flexible	Thin	High	Low	High
153	30	Operator 1	Low	Rigid	Thick	High	High	Low
10	31	Operator 1	High	Flexible	Thin	Low	Low	Low
97	32	Operator 1	High	Rigid	Thin	Low	High	High
21	33	Operator 1	Low	Flexible	Thick	Low	Low	Low
137	34	Operator 1	High	Rigid	Thin	High	High	Low
23	35	Operator 1	Low	Flexible	Thick	Low	Low	Low
51	36	Operator 1	Low	Rigid	Thin	High	Low	High
22	37	Operator 1	Low	Flexible	Thick	Low	Low	Low
40	38	Operator 1	High	Rigid	Thick	Low	Low	Low
7	39	Operator 1	High	Flexible	Thin	Low	Low	Low
148	40	Operator 1	High	Flexible	Thick	High	High	Low
12	41	Operator 1	Low	Rigid	Thin	Low	Low	Low
39	42	Operator 1	High	Rigid	Thick	Low	Low	Low
151	43	Operator 1	Low	Rigid	Thick	High	High	Low
82	44	Operator 1	Low	Flexible	Thin	Low	High	High
11	45	Operator 1	Low	Rigid	Thin	Low	Low	Low
111	46	Operator 1	Low	Rigid	Thick	Low	High	High
154	47	Operator 1	Low	Rigid	Thick	High	High	Low
121	48	Operator 1	Low	Flexible	Thin	High	High	Low
98	49	Operator 1	High	Rigid	Thin	Low	High	High
37	50	Operator 1	High	Rigid	Thick	Low	Low	Low
14	51	Operator 1	Low	Rigid	Thin	Low	Low	Low
24	52	Operator 1	Low	Flexible	Thick	Low	Low	Low
115	53	Operator 1	Low	Rigid	Thick	Low	High	High
85	54	Operator 1	Low	Flexible	Thin	Low	High	High
36	55	Operator 1	High	Rigid	Thick	Low	Low	Low
109	56	Operator 1	High	Flexible	Thick	Low	High	High
138	57	Operator 1	High	Rigid	Thin	High	High	Low
52	58	Operator 1	Low	Rigid	Thin	High	Low	High
62	59	Operator 1	Low	Flexible	Thick	High	Low	High
147	60	Operator 1	High	Flexible	Thick	High	High	Low
108	61	Operator 1	High	Flexible	Thick	Low	High	High
113	62	Operator 1	Low	Rigid	Thick	Low	High	High
47	63	Operator 1	High	Flexible	Thin	High	Low	High
149	64	Operator 1	High	Flexible	Thick	High	High	Low
123	65	Operator 1	Low	Flexible	Thin	High	High	Low
140	66	Operator 1	High	Rigid	Thin	High	High	Low
50	67	Operator 1	High	Flexible	Thin	High	Low	High
6	68	Operator 1	High	Flexible	Thin	Low	Low	Low
64	69	Operator 1	Low	Flexible	Thick	High	Low	High
61	70	Operator 1	Low	Flexible	Thick	High	Low	High

78	71	Operator 1	High	Rigid	Thick	High	Low	High
63	72	Operator 1	Low	Flexible	Thick	High	Low	High
99	73	Operator 1	High	Rigid	Thin	Low	High	High
152	74	Operator 1	Low	Rigid	Thick	High	High	Low
13	75	Operator 1	Low	Rigid	Thin	Low	Low	Low
81	76	Operator 1	Low	Flexible	Thin	Low	High	High
65	77	Operator 1	Low	Flexible	Thick	High	Low	High
112	78	Operator 1	Low	Rigid	Thick	Low	High	High
80	79	Operator 1	High	Rigid	Thick	High	Low	High
139	80	Operator 1	High	Rigid	Thin	High	High	Low
159	81	Operator 2	High	Rigid	Thick	High	High	High
141	82	Operator 2	Low	Flexible	Thick	High	High	High
34	83	Operator 2	Low	Rigid	Thick	Low	Low	High
42	84	Operator 2	Low	Flexible	Thin	High	Low	Low
116	85	Operator 2	High	Rigid	Thick	Low	High	Low
57	86	Operator 2	High	Rigid	Thin	High	Low	Low
127	87	Operator 2	High	Flexible	Thin	High	High	High
145	88	Operator 2	Low	Flexible	Thick	High	High	High
27	89	Operator 2	High	Flexible	Thick	Low	Low	High
4	90	Operator 2	Low	Flexible	Thin	Low	Low	High
19	91	Operator 2	High	Rigid	Thin	Low	Low	High
120	92	Operator 2	High	Rigid	Thick	Low	High	Low
131	93	Operator 2	Low	Rigid	Thin	High	High	High
66	94	Operator 2	High	Flexible	Thick	High	Low	Low
32	95	Operator 2	Low	Rigid	Thick	Low	Low	High
26	96	Operator 2	High	Flexible	Thick	Low	Low	High
74	97	Operator 2	Low	Rigid	Thick	High	Low	Low
88	98	Operator 2	High	Flexible	Thin	Low	High	Low
117	99	Operator 2	High	Rigid	Thick	Low	High	Low
92	100	Operator 2	Low	Rigid	Thin	Low	High	Low
73	101	Operator 2	Low	Rigid	Thick	High	Low	Low
56	102	Operator 2	High	Rigid	Thin	High	Low	Low
133	103	Operator 2	Low	Rigid	Thin	High	High	High
86	104	Operator 2	High	Flexible	Thin	Low	High	Low
35	105	Operator 2	Low	Rigid	Thick	Low	Low	High
43	106	Operator 2	Low	Flexible	Thin	High	Low	Low
1	107	Operator 2	Low	Flexible	Thin	Low	Low	High
70	108	Operator 2	High	Flexible	Thick	High	Low	Low
156	109	Operator 2	High	Rigid	Thick	High	High	High
129	110	Operator 2	High	Flexible	Thin	High	High	High
2	111	Operator 2	Low	Flexible	Thin	Low	Low	High
102	112	Operator 2	Low	Flexible	Thick	Low	High	Low
87	113	Operator 2	High	Flexible	Thin	Low	High	Low
29	114	Operator 2	High	Flexible	Thick	Low	Low	High
16	115	Operator 2	High	Rigid	Thin	Low	Low	High
119	116	Operator 2	High	Rigid	Thick	Low	High	Low
135	117	Operator 2	Low	Rigid	Thin	High	High	High
45	118	Operator 2	Low	Flexible	Thin	High	Low	Low
72	119	Operator 2	Low	Rigid	Thick	High	Low	Low

134	120	Operator 2	Low	Rigid	Thin	High	High	High
30	121	Operator 2	High	Flexible	Thick	Low	Low	High
104	122	Operator 2	Low	Flexible	Thick	Low	High	Low
44	123	Operator 2	Low	Flexible	Thin	High	Low	Low
5	124	Operator 2	Low	Flexible	Thin	Low	Low	High
101	125	Operator 2	Low	Flexible	Thick	Low	High	Low
126	126	Operator 2	High	Flexible	Thin	High	High	High
67	127	Operator 2	High	Flexible	Thick	High	Low	Low
91	128	Operator 2	Low	Rigid	Thin	Low	High	Low
75	129	Operator 2	Low	Rigid	Thick	High	Low	Low
89	130	Operator 2	High	Flexible	Thin	Low	High	Low
118	131	Operator 2	High	Rigid	Thick	Low	High	Low
20	132	Operator 2	High	Rigid	Thin	Low	Low	High
17	133	Operator 2	High	Rigid	Thin	Low	Low	High
59	134	Operator 2	High	Rigid	Thin	High	Low	Low
69	135	Operator 2	High	Flexible	Thick	High	Low	Low
157	136	Operator 2	High	Rigid	Thick	High	High	High
90	137	Operator 2	High	Flexible	Thin	Low	High	Low
33	138	Operator 2	Low	Rigid	Thick	Low	Low	High
105	139	Operator 2	Low	Flexible	Thick	Low	High	Low
41	140	Operator 2	Low	Flexible	Thin	High	Low	Low
130	141	Operator 2	High	Flexible	Thin	High	High	High
93	142	Operator 2	Low	Rigid	Thin	Low	High	Low
160	143	Operator 2	High	Rigid	Thick	High	High	High
142	144	Operator 2	Low	Flexible	Thick	High	High	High
58	145	Operator 2	High	Rigid	Thin	High	Low	Low
3	146	Operator 2	Low	Flexible	Thin	Low	Low	High
28	147	Operator 2	High	Flexible	Thick	Low	Low	High
143	148	Operator 2	Low	Flexible	Thick	High	High	High
94	149	Operator 2	Low	Rigid	Thin	Low	High	Low
158	150	Operator 2	High	Rigid	Thick	High	High	High
18	151	Operator 2	High	Rigid	Thin	Low	Low	High
31	152	Operator 2	Low	Rigid	Thick	Low	Low	High
60	153	Operator 2	High	Rigid	Thin	High	Low	Low
71	154	Operator 2	Low	Rigid	Thick	High	Low	Low
144	155	Operator 2	Low	Flexible	Thick	High	High	High
95	156	Operator 2	Low	Rigid	Thin	Low	High	Low
68	157	Operator 2	High	Flexible	Thick	High	Low	Low
103	158	Operator 2	Low	Flexible	Thick	Low	High	Low
132	159	Operator 2	Low	Rigid	Thin	High	High	High
128	160	Operator 2	High	Flexible	Thin	High	High	High

4.0 Appendix

4.1 Lot A Porosity Data

Sample Lot A – High Gurley

Measurement #	Value	Measurement #	Value	Measurement #	Value
1	86.4	51	91.6	101	88.2
2	93.5	52	84	102	87.2
3	84	53	82.8	103	84.2
4	76.2	54	87.2	104	78.2
5	73.2	55	62	105	68.3
6	60	56	84	106	76.2
7	66.6	57	80.8	107	74.6
8	63	58	71	108	74
9	50	59	47	109	53
10	62.2	60	66.8	110	65.2
11	54	61	76.2	111	66.2
12	64.8	62	67.6	112	69.6
13	67.8	63	73.2	113	75.2
14	76.8	64	68.8	114	73.6
15	65.4	65	116.2	115	82.6
16	52.8	66	99.4	116	68.2
17	68.2	67	61.2	117	58.2
18	61.6	68	47.8	118	53.6
19	62.2	69	57.8	119	62
20	55.6	70	75	120	68
21	80.6	70	67.4	121	74.8
22	70.2	72	50	122	53
23	73	73	50	123	59
24	76	74	86.6	124	68.2
25	64.8	75	68.8	125	62
26	86.6	76	80.4	126	78.4
27	54.8	77	61.2	127	58.2
28	73.2	78	66.4	128	69.2
29	73.8	79	81.2	129	78.2
30	70.6	80	75	130	72.6
31	71.8	81	65.4	131	63.2
32	70	82	59	132	66.4
33	74.2	83	74	133	74.2
34	75.2	84	79	134	81
35	55	85	61.4	135	56.2
36	98.2	86	92.6	136	90.2
37	52	87	71.2	137	62.6
38	58.2	88	88.8	138	62

39	66.2	89	71	139	68.2
40	56.4	90	81	140	78.2
41	70.2	91	80.8	141	76.2
42	84.2	92	84.8	142	83
43	73.4	93	96	143	75.2
44	56	94	79	144	58.2
45	69.4	95	65.2	145	63.2
46	73	96	82.6	146	76.2
47	73	97	78	147	75.3
48	70.4	98	55.8	148	53.2
49	55.4	99	77.8	149	80.2
50	65.4	100	80	150	63.2

Measurements are in seconds

4.2 Lot B Porosity Data

Sample Lot B – Low Gurley

Measurement #	Value	Measurement #	Value	Measurement #	Value
1	196.4	51	160.1	101	175.6
2	169.9	52	191.4	102	175.6
3	163.8	53	141.8	103	152
4	198	54	160	104	178
5	251.2	55	129	105	188.6
6	131.8	56	141	106	152
7	190.8	57	200	107	187.6
8	183.8	58	169	108	168.2
9	149.8	59	133.8	109	137.6
10	200	60	184	110	178.6
11	142	61	157.8	111	162.4
12	163.2	62	150.8	112	176.4
13	195.2	63	114.4	113	187.6
14	189.6	64	265.6	114	188
15	119.2	65	128.4	115	124
16	227.6	66	109.8	116	166.4
17	185.2	67	149.6	117	152.3
18	184.8	68	137.6	118	154.2
19	166	69	118.4	119	144
20	100.8	70	150.4	120	142.6
21	134	70	150.4	121	134
22	153.6	72	170.8	122	166
23	150	73	120.8	123	132.2
24	152	74	122.8	124	132.8
25	120	75	156.8	125	144.2
26	146	76	127.6	126	136

27	119.2	77	188.4	127	146
28	184	78	168	128	192
29	139.6	79	136.8	129	128.2
30	126.8	80	91.2	130	100.6
31	172	81	170	131	178.6
32	144.4	82	146.8	132	138.2
33	136.8	83	111.6	133	120.6
34	204.8	84	245.6	134	210.2
35	192.8	85	226.4	135	178.6
36	156.8	86	117.2	136	132
37	150.6	87	142.4	137	166.4
38	122.8	88	141.2	138	132.2
39	173.2	89	150.8	139	162.6
40	174.8	90	132	140	152.2
41	122	91	152.8	141	136.2
42	172.4	92	168.6	142	154.6
43	153.6	93	164	143	146.2
44	131.2	94	142.2	144	126
45	164.4	95	175	145	158.2
46	117.2	96	126	146	136.8
47	136	97	142.2	147	128.2
48	120.4	98	132.6	148	132.8
49	100	99	112	149	120.2
50	187.6	100	178	150	166.4

Measurements are in seconds

4.3 Burst Test Data

Burst Test Values for Lot A: High Gurley

Sample Number	Lot A
1	0.9
2	0.7
3	0.8
4	0.9
5	0.9
6	1
7	0.9
8	0.7
9	0.8
10	0.9
11	0.7
12	0.7
13	0.6
14	0.9

Burst Test Values for Lot B: Low Gurley

Sample Number	Lot B
1	1.4
2	1.5
3	1.5
4	3.3
5	1.5
6	1.5
7	2.5
8	1.5
9	2.5
10	2.5
11	1.5
12	2.5
13	1.5
14	2.5

15	0.9
16	0.9
17	1.1
18	0.7
19	0.9
20	0.9
21	1.1
22	0.8
23	0.7
24	0.9
25	0.7
26	0.7
27	0.9
28	0.9
29	0.9
30	1.1
31	0.9
32	0.7
33	0.9
34	0.9
35	0.7
36	0.7
37	0.9
38	1
39	0.9
40	0.9
41	0.9
42	0.7
43	0.9
44	0.7
45	0.9
46	0.9
47	0.9
48	0.7
49	1.1
50	0.9

15	1.5
16	2.5
17	1.5
18	1.5
19	2.5
20	1.5
21	1.5
22	1.5
23	2.2
24	1.5
25	1.5
26	1.5
27	2.2
28	2.2
29	1.5
30	1.2
31	1.5
32	2.5
33	2.1
34	1.5
35	1.5
36	2.3
37	1.5
38	1.5
39	1.1
40	1.9
41	1.5
42	2.3
43	1.5
44	1.5
45	1.5
46	2.3
47	2.3
48	2.6
49	1.5
50	2.5

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