From: Burrill, Dan
Sent: 11/16/2011 01:47:35 PM
To: Cuddy, Christopher
Subject: Marlex HGX-030-01 Equivalency Testing
Attachments: Marlex HGX-030-01 Equivalency Testing Rev AB-CC and DB Comments.doc

Chris,

I believe you only made comments, did not actually change anything. To better see your comments removed the red lines from document. Please review attached as I have attempted to address your comments.

Thanks,

Dan

Document Title:	Marlex® HGX-030-01 Equivalency Testing
Document Number:	90708859
Project Name:	Uro/Gyn Sustaining
Project Number:	U0311
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TABLE OF CONTENTS

1. Executive Summary:

Phillips Sumika has discontinued production of Marlex® HGX-030-01, a Polypropylene Homopolymer grade. Therefore, Boston Scientific (BSC) obtained the same polymer from a second source (material distributor). This document outlines the results of the analytical testing that BSC conducted to ensure the new lot of Marlex® HGX-030-01, received from Emai Plastic Raw Material, is equivalent to the existing lot of Marlex® HGX-030-01 received from Channel Prime Alliance.

The existing lot of Phillips Sumika Marlex® HGX-030-01 Polypropylene Homopolymer (sample 1) was obtained from the material distributor Channel Prime Alliance in Charlotte NC. A Certificate of Analysis (CoA) was supplied for this lot of Marlex® HGX-030-01 (refer to Attachment 1). The second lot of material (sample 2) was obtained from the material distributor Emai Plastic Raw Material (Dongguan) Inc. While the material has been supplied in the correct Phillips Sumika bags all with the same distributor lot number, there was no CoA supplied with this lot, and the distributor is not able to reproduce the CoA. Both distributors obtain Marlex® HGX-030-01 from Phillips Sumika and do not perform and additional processing or value added work to the material.

Comment [CMC1]: should this be "produce"

Comment [DB2]: think it is fine either way, I will change to produce

In addition to the two lots of material mentioned above a third sample (sample 3) of Marlex® HGX-030-01 was obtained from Proxy Biomedical for comparison purposes. This sample was provided with a CoA from Phillips Sumika.

The results for the Differential Scanning Calorimetry, Oxidation Induction Time, Fourier Transform Infrared Spectroscopy, Melt Flow Index, Gel Permeation Chromatography, Gas Chromatography – Mass Spectrometry, Inductively Coupled Plasma Spectroscopy and Optical Microscopy indicate that the new lot of HGX030-01 obtained from distributor Emai Plastic Raw Material (Dongguan) Inc., is equivalent to the existing qualified lot of HGX030-0.1. The minor differences observed in the test results were not unexpected when testing lots made from various points in time.

2. Objective:

The purpose of this document is to outline the analytical testing strategy, acceptance criterion and test results that were used to establish the chemical equivalency of two Phillips Sumika Marlex® HGX-030-01 Polypropylene Homopolymer lots obtained from two different material distributors.

3. Applicable Documents:

Document Description	Document #	Document Version
Procedure to evaluate equivalency of polymers for shelf life	90559224	AA
Global SOP AVL Management	90265075	AJ

4. Materials / Traceability:

Three lots of Phillips Sumika Marlex® HGX-030-01 Polypropylene Homopolymer were tested as part of this work.

Sample	Distributor Lot No.	Phillips Sumika Lot No.	C of C Date	Product Description
1	PP0353133-02	2951877	06/15/2005	Existing Qualified lot of HGX030-01 obtained from Channel Prime Alliance
2	6120105	Unknown	Unknown	New lot of HGX030-01 obtained from distributor Emai Plastic Raw Material (Dongguan) Inc
3	Unknown	2980056	03/05/2008	Lot obtained from Proxy Biomedical for comparison testing, Proxy provided CoA from Phillips Sumika

5. Experimental Method:

Polypropylene can be made from the monomer propylene by Ziegler-Natta polymerization or by metallocene catalysis polymerization. These commercial manufacturing processes are large and typically generate thousands of pounds per hour. Given the size of these processes and the nature of the material bagging operations, it is expected that any given bag represents the entire lot. Therefore samples were selected from a single bag of material. The material samples were evaluated by Cambridge Polymer Group, Inc., an independent external testing laboratory BSC determined to be capable of conducting required test to all applicable ASTM/ISO standards. This laboratory is documented as an approved supplier per Global SOP AVL Management 90265075.

Table 1 lists the testing that was conducted to determine equivalency. In determining equivalency of the polymer samples one and two, not only were the individual test results assessed, based on the analysis techniques listed in Table 1, but all data was assessed in aggregate by internal and independent external subject matter experts (SME).

Sample 3 was evaluated as part of this work as it was a second lot of HGX030-01 with a known origin. This sample was used as a second known data point to help assure that testing was conducted properly and to provide some insight on potential lot to lot differences.

6. Results:

All testing details, results and graphs can be found in Attachment 6 - Cambridge Polymer Group Report # 11440-2 of this report. The following is a summary of these results.

Comment [CMC3]: maybe say all details are discussed in section (XX) of this report and the details can be found in.....

Comment [DB4]: Okay I'm confused, testing details in attached report, this section is summary of those results

Table 1: Summary of Test Results

Test Name	Test Purpose	Expected Results / Analysis Technique	Results
Differential Scanning Calorimetry ASTM D3418	Measure thermal transition characteristics of the polymers.	Melt Temperature (T_m) will be evaluated. Samples are expected to be within 5°C of each other.	Acceptable
Oxidative Induction Time (OIT) ASTM D3895	Highly accelerated stress test used to determine long term stability equivalence of polymers.	Samples are expected to be within 20% of each other (ASTM D3895 indicates within 75%)	Acceptable[1]
Fourier Transform Infrared Spectroscopy (FTIR)	Evaluates the degree of similarity in bulk composition of polymers.	Spectral outputs to be qualitatively assessed by SME.	Acceptable
Melt Flow Index ASTM D1238	Empirical measures of the viscosity of polymers which is an indicator of required processing conditions.	Samples are expected to be within 0.5 grams/10 minutes of each other	Acceptable[2]
Gel Permeation Chromatography (GPC)	Measure of molecular weight and molecular weight distribution.	Samples are expected to be within 15% of each other (excluding PDI). Qualitative assessment of spectral output by SME will also be conducted.	Acceptable
Gas Chromatography/ Mass Spec (GC-MS)	Determines masses of volatile additives, for determining the chemical composition of a sample: as well as contaminant detection.	Qualitative assessment of spectral output by SME.	Acceptable
Inductively Coupled Plasma Spectroscopy (ICP)	Determines primary heavy metal contaminants	Qualitative assessment of spectral output by SME.	Acceptable
Optical Microscopy	Determine presence of bulk contamination	Qualitative visual assessment of pellets by SME.	Acceptable

[1]Results were outside of expected results range; refer to section 6.2 for rationale.

[2]The third lot (Sample 3), which was tested for reference only, was outside of the expected range; however, lots 1 and 2 were within the expected results range.

Comment [CMC5]: I might go on here about how this shoed the potential lot to lot variation, but the lot under test, Sample 2 was a nominal values and well within the expected range.

Comment [DB6]: See Section 6.4

6.1 Differential Scanning Calorimetry (DSC):

The DSC results in Table 2 indicate that all three samples have similar thermal characteristics, and that the melt temperature of each sample is within the expected 5°C range.

Table 2: DSC Summary Results

Heat Cycle 1			
Sample	Onset Melt Temperature (°C)	Peak Melt Temperature (°C)	Enthalpy (J/g)
1	150.48	164.49	104.9
2	152.26	161.87	112.1
3	151.69	164.54	111.3
Heat Cycle 2			
Sample	Onset Melt Temperature (°C)	Peak Melt Temperature (°C)	Enthalpy (J/g)
1	154.14	163.44	106.9
2	154.60	161.79	109.5
3	157.52	163.67	113.2

6.2 Oxidative Induction Time (OIT):

The OIT results are listed in table 3. Sample 1 and Sample 2 are within ~ 32%, and all samples are within the ASTM D3895 range of 75% to be considered equivalent. While the difference between sample 1 and sample 2 is slightly larger than the anticipated 20% listed in Table 1 the results are within minutes of one another and shall be deemed equivalent based upon the ASTM recommendation of 75%. The increased oxidation induction time for sample 2 is an indicator of greater oxidative stability. Given the potential age difference between these lots it is not unexpected to see the below differences in the OIT. As the material ages and antioxidant constituents are consumed the OIT will decrease. Additionally there is inherent to lot to lot variability in OIT performance.

Comment [CMC7]: I'm surprised we don't talk about this a little more…that these results are favorable for sample 2 and are likely due to sample 2 being newer.

Comment [DB8]: What additionally could be said here? We are evaluating equivalency not goodness

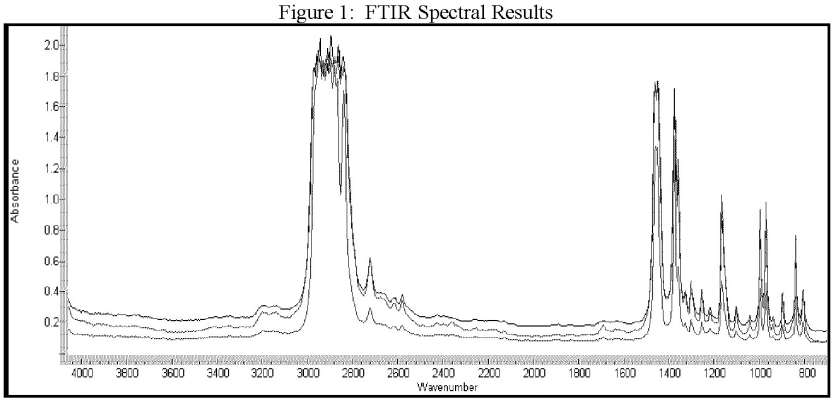
Table 3: OIT Summary Results

Sample	**Oxidation Induction Time (min)**
1	5.61
2	8.23
3	4.49

6.3 Fourier Transform Infrared Spectroscopy (FTIR):

Figure 1 summarizes the FTIR results. There are minimal (insignificant) differences between the three samples spectra; there were no additional peaks identified that would indicate a material difference.

Figure 1: FTIR Spectral Results



Sample 1 - **Green Line** Sample 2 – **Blue Line** Sample 3 – **Pink Line**

6.4 Melt Flow Index (MFI):

Table 4 summarizes the MFI results. Each sample was tested twice and averaged. Samples 1 and 2 are within the expected range of 0.5 g/10 min. Sample 3, which was run for comparison purposes only, has a slightly higher MFI rate than samples 1 & 2. This is an indicator of the potential lot to lot variation in MFI for Marlex® HGX-030-01.

Table 4: MFI Results

Sample	Time (s)	Mass Extruded (g)		Average Melt Flow Rate (g/10 min)
		Run 1	Run 2	
1	60	0.391	0.389	**3.90**
2	60	0.375	0.370	**3.72**
3	60	0.473	0.468	**4.70**

6.5 Gel Permeation Chromatography (GPC):

Table 5 summarizes the molecular weight moments for all three samples. The results for Mn, Mw and Mz are all within the expected 15% range. The polydispersity index (PDI) M_w/M_n does not have the same expected results as the individual moments (Mn, Mw and Mz). Typically polymers with PDI values from 3-5 are considered to have narrow molecular weight distributions. The PDI values observed in this work are consistent for a polypropylene with a narrow molecular weight distribution.

Table 5: Molecular Weight Moments (g/mole)

Sample	M_n	M_w	M_z	PDI
1	6.80E+04	2.65E+05	7.77E+05	3.90
2	5.80E+04	2.82E+05	8.74E+05	4.86
3	6.08E+04	2.60E+05	8.16E+05	4.27

6.6 Extraction for Elutables:

Table 6 summarizes the extraction for elutables test results for each sample. The samples were refluxed in Hexane for 72 hours; refer to section 3.6.1 of Attachment 6 for further details. While samples 1 and 3 are very similar, sample 2 has almost twice the amount of extract. There is no acceptance criteria for the amount of extract as this is the initial step of sample prep for the Gas Chromatography – Mass Spectrometry testing, this is simply an observation.

Table 6: Extract Results

Sample	Mass of Sample (g)	Extract (mg)	Percent of Total Mass Extracted (%)
1	5.85	37.6	0.64
2	6.01	86.1	1.43
3	6.21	37.9	0.61

6.7 Gas Chromatography – Mass Spectrometry (GC-MS):

The mass spectrometric identification of compounds is summarized in Table 7 (refer to section 3.6.2 Gas Chromatography – Mass Spectroscopy in Attachment 6). The three samples had similar fragments detected in the extract. All the extracted compounds are long chain aliphatic hydrocarbons, which is to be expected from polypropylene. Aromatic fragments identified as Bis Dimethylethyl Phenol and Hydroxy Benzoic Acid was found in sample 2. These are common by-products of polymer stabilizers. Given the increased OIT performance of sample 2 and the higher level of extract obtained it is not unexpected to see additional levels of stabilizer present in Sample 2.

Table 7: GC-MS Results Summary

Component	Sample 1	Sample 2	Sample 3
Bis dimethylethyl phenol	ND	✓	ND
Docosane	ND	✓	ND
Heptadecane	✓	✓	ND
Hydroxy benzoic acid	ND	✓	ND
Nonadecane	✓	✓	ND
Pentacosane	✓	✓	ND
Pentadecane	ND	✓	✓
Tetracosane	✓	✓	✓
Unidentified compound	✓	ND	✓

Note: ND means fragment was not detected

6.8 Inductively Coupled Plasma (ICP) Spectroscopy:

Table 8 summarizes the ICP results for elemental survey scan. Sample 1 shows a larger array of trace metals than sample 2 &3, potentially due to post polymerization handling differences. Sample 2 shows the presence of Titanium (Ti), used in the polymerization process as part of catalysis package. All three samples show the presence of Selenium (Se) a polymer stabilizer used with polypropylene.

Table 8: ICP Results for Survey Scan

	Concentration by weight (ppm)			
Element	**Sample 1**	**Sample 2**	**Sample 3**	**Detection Limit**
Be	43.0	ND	ND	0.01
Na	ND	ND	ND	0.05
Mg	ND	ND	ND	0.05
Al	106	ND	25.9	0.01
K	ND	ND	ND	0.10
Ca	ND	ND	ND	0.01
Ti	ND	280	ND	0.01
V	20.9	ND	ND	0.01
Cr	33.1	ND	ND	0.01
Mn	6.8	ND	ND	0.01
Fe	36.1	ND	ND	0.01
Co	16.4	ND	ND	0.01
Ni	27.4	ND	ND	0.01
Cu	14.7	ND	ND	0.01
Zn	ND	ND	ND	0.01
As	ND	ND	ND	0.01
Se	1500	1700	2160	0.01
Sr	29.2	ND	14.8	0.01
Mo	ND	ND	ND	0.01
Cd	ND	ND	ND	0.01
Sn	ND	ND	ND	0.01
Sb	ND	ND	ND	0.01
Ba	10.4	15.7	34.3	0.01
Tl	ND	ND	ND	0.01
Pb	ND	ND	ND	0.01

Note: ND means element was not detected within detection limits

6.9 Optical Microscopy:

There was no visible evidence of contamination in the form of specks or debris on any of the samples. Small differences in pellet shape, size and opacity were observed. These differences are not unexpected and are typical lot to lot variation most likely caused by differences in cooling conditions during pelletization.

7. Conclusion:

The comparison of test results from sample 1 and 3, both lots of HGX030-0.1 with CoA, indicates that there were no testing issues encountered during this work.

The results for the DCS, OIT, FTIR, MFI, GPC and Optical Microscopy tests clearly indicate that samples 1 and 2 are equivalent. The results for the GC-MS tests of hexane extractible materials indicate that sample 1 and 2 have similar fragment types in the extract although sample 2 has a higher level of these compounds. While the majority of the extracted compounds are long chain aliphatic hydrocarbons, there are a few aromatic fragments, indicative of common anti-oxidants, detected in sample 2 that were not detected in samples 1 or 3. Additionally the ICP testing found a low level of Ti in sample 2 and did not detect any in samples 1 or 3. These small differences found between samples 1 and 2 in extractables and trace metals are not significant enough to present a short term or long term mechanical performance difference.

Based upon this testing the new lot of HGX030-01 obtained from distributor Emai Plastic Raw Material (Dongguan) Inc. is equivalent to the existing qualified lot of HGX030-01. The minor differences observed in the test results were not unexpected when testing lots made from various points in time and exposed to different storage conditions.

Comment [CMC9]: I think it would be good if we could describe where in the project plan we are. While this is a conclusion that sample 2 is Marlex, it is not a conclusion that it is fit for use…yet. We still have work to do. I'd like to find a way to describe that of we could. Discuss how we have biocompatibility testing and mechanical performance testing to follow this, maybe?

Comment [DB10]: Conclusions address the purpose of this work. This is not a project plan or a DVMP. I think those things belong in the MRB, SCAR or whatever the appropriate quality document is.

8. Attachments:

Attachment	Description
Attachment 1	Sample 1 CoA: Existing lot obtained from Channel Prime Alliance
Attachment 2	Marlex® HGX-030-01 Technical Data Sheet
Attachment 3	Marlex® HGX-030-01 MSDS
Attachment 4	Photos of bags containing new resin lot (sample 2)
Attachment 5	Sample 3 CoA; supplied with Proxy Biomedical sample
Attachment 6	Cambridge Polymers Test Report #11440-2