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DATE: April 30, 2020

TO: Karen Hays, Air Branch Chief, Georgia EPD

FROM: Kimbrell R Darnell, Sr Manager QA Labs

SUBJECT: Engineering Studies Report

The purpose of this report is to provide information pursuant to Condition 2(h) and (i) to the First Amendment to the Consent Order, as well as other pertinent material as follows:

1) Summary of engineering study to more completely identify, define, and quantify fugitive emissions of ethylene oxide (EO) released from packaging materials and other materials subjected to sterilization.
2) Summary of an engineering study designed to evaluate the potential reduction in fugitive emissions of EO achieved by switching from using a wood pallet to a pallet composed of an alternate material.
3) Conclusions, recommendations, and next steps.

1) Summary of engineering study to evaluate emissions of ethylene oxide released from packaging materials and other materials subjected to sterilization

A study was carried out by BD to evaluate the level of residual EO in product sterilized in two qualified EO processes. This evaluation assessed product over an extended time period to understand the desorption characteristics of residual EO under ambient storage conditions. For this activity representative product loads were sterilized in EO Cycle 7 and Cycle 15 whereby sample of packaging and product were tested for residual EO prior to heated aeration and then at intervals of 0, 1, 10, 20, and 30 days after 16 hours of heated aeration with the product load residing in the work-in process warehouse area under ambient storage conditions. The study analyzes EO levels in these materials over time to the point near full desorption with comparisons made between the two cycles. It should be noted that the data in this report is

representative data, and that some variation is to be expected, depending on the specific load configuration, specific product and package configuration, and the setpoints met during each phase of the cycle within the validated process parameters (e.g. time, temperature, EO gas concentration). Additionally, some variability is expected between production lines running the same cycles. EO residuals for Cycle 15 were slightly higher at the end of heated aeration than for Cycle 7 in this study, however, it should be noted that Cycle 7 ran at the top end of the validated temperature range during the sterilization cycle which is expected to contribute to more efficient EO removal, as compared to previous studies.

The data from the study is presented in Tables 1.1 (Cycle 7) and 1.2 (Cycle 15). The data for both cycles demonstrates that, as expected, the residual EO steadily decreases over time with the sharpest decrease at the beginning of the ambient storage period and flattening somewhat as the EO desorption progresses. The largest decrease is seen on the first day. By day 20 and 30 almost every component of the product has fully desorbed. The exceptions to this are a few packaging components as well as the [redacted] with trace amounts of EO. The values obtained for both 20 and 30 day time points are very close to each other and are very close to the limit of detection for the assay.

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Table 1.1. Evaluation of Residual EO Over Time for Cycle 7*

Product Info	Cycle 7	Pre-aeration		Day-0		Day-1		Day-10		Day-20		Day-30	
	Component	Internal case Pre-aeration mgEO/device	External case Pre-aeration mgEO/device	Internal case Post-aeration mgEO/device	External case Post-aeration mgEO/device	Internal case Post-aeration mgEO/device	External case Post-aeration mgEO/device	Internal case Post-aeration mgEO/device	External case Post-aeration mgEO/device	Internal case Post-aeration mgEO/device	External case Post-aeration mgEO/device	Internal case Post-aeration mgEO/device	External case Post-aeration mgEO/device
Cat #897218 Lot NGDZ3107	[redacted]												
		0.09	0.17	0.10	0.15	0.09	0.09	0.09	0.00	0.10	0.00	0.10	0.10
		2.21	3.03	1.56	2.57	1.93	0.00	1.56	0.00	0.00	0.00	0.00	0.00
	Subtotal	**2.30**	**3.20**	**1.66**	**2.72**	**2.02**	**0.09**	**1.65**	**0.00**	**0.10**	**0.00**	**0.10**	**0.10**
	Unit Packaging												
	[redacted]	1.02	0.71	0.38	0.32	0.22	0.20	0.16	0.14	0.13	0.13	0.14	0.12
		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
		15.65	14.49	3.16	2.14	2.54	1.32	0.45	0.30	0.00	0.00	0.00	0.00
		1.39	1.19	0.62	0.45	0.22	0.35	0.22	0.21	0.00	0.00	0.00	0.00
		0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
		0.21	0.23	0.11	0.10	0.06	0.07	0.04	0.04	0.03	0.03	0.03	0.03
	Subtotal	**18.27**	**16.64**	**4.27**	**3.01**	**3.04**	**1.94**	**0.87**	**0.69**	**0.16**	**0.16**	**0.17**	**0.15**
	Subtotal/cs (x10)	**182.70**	**166.40**	**42.70**	**30.10**	**30.40**	**19.40**	**8.70**	**6.90**	**1.60**	**1.60**	**1.70**	**1.50**
	Product												
	[redacted]	0.60	0.43	0.12	0.07	0.07	0.05	0.00	0.00	0.00	0.00	0.00	0.00
		0.26	0.26	0.13	0.07	0.06	0.07	0.02	0.02	0.02	0.02	0.02	0.00
		0.30	0.31	0.13	0.08	0.08	0.04	0.02	0.00	0.01	0.02	0.01	0.01
		1.55	1.44	0.24	0.18	0.15	0.10	0.00	0.00	0.00	0.00	0.00	0.00
		0.26	0.22	0.04	0.03	0.04	0.02	0.00	0.00	0.00	0.00	0.00	0.00
		0.30	0.30	0.19	0.11	0.10	0.06	0.00	0.00	0.00	0.00	0.00	0.00
		0.26	0.26	0.11	0.10	0.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00
		2.69	2.37	0.85	0.65	0.44	0.34	0.12	0.09	0.04	0.04	0.00	0.00
		21.49	21.56	5.81	4.62	4.90	2.96	1.14	0.00	0.00	0.00	0.00	0.00
		0.20	0.26	0.17	0.15	0.18	0.17	0.20	0.13	0.08	0.07	0.05	0.05
		0.05	0.07	0.03	0.03	0.03	0.03	0.02	0.02	0.03	0.02	0.02	0.02
	Subtotal	**27.96**	**27.48**	**7.82**	**6.09**	**6.16**	**3.84**	**1.52**	**0.26**	**0.18**	**0.17**	**0.10**	**0.08**
	Subtotal/cs (x10)	**279.60**	**274.80**	**78.20**	**60.90**	**61.60**	**38.40**	**15.20**	**2.60**	**1.80**	**1.70**	**1.00**	**0.80**
	Total per case (10 units + shipper) (mg)	**464.60**	**444.40**	**122.56**	**93.72**	**94.02**	**57.89**	**25.55**	**9.50**	**3.50**	**3.30**	**2.80**	**2.40**
	Total EO/pallet of cases (13 internal 53 external) (mg)	**29593**		**6560.44**		**4290.43**		**835.65**		**220.4**		**163.6**	
	Wood Pallet	**4415.02**		**670.04**		**552.05**		**108.49**		**0.00**		**0.00**	
	Plastic Wrap	**0.00**		**0.00**		**N/A**		**N/A**		**N/A**		**N/A**	
	Residual EO per Pallet	**34,008.02mg / 0.0749lbs**		**7,230.48mg / 0.0159lbs**		**4,842.48mg / 0.0107lbs**		**944.14mg / 0.0021lbs**		**220.4mg / 0.00049lbs**		**163.60mg / 0.00036lbs**	

*Cycle in which samples were processed demonstrated temperatures at upper end of specified range during final air and nitrogen washes which may have contributed to residual EO removal.

Table 1.2. Evaluation of Residual EO Over Time for Cycle 15

Product Information	Cycle 15	Pre-aeration		Day-0		Day-1		Day-10		Day-20		Day-30	
	Component	Internal case Pre-aeration mgEO/device	External case Pre-aeration mgEO/device	Internal case Post-aeration mgEO/device	External case Post-aeration mgEO/device	Internal case Post-aeration mgEO/device	External case Post-aeration mgEO/device	Internal case Post-aeration mgEO/device	External case Post-aeration mgEO/device	Internal case Post-aeration mgEO/device	External case Post-aeration	Internal case Post-aeration mgEO/device	External case Post-aeration mgEO/device
Cat # 897218 Lot NGDZ3107	**Shipping Pkg**												
	[redacted]	N/A	N/A	0.31	0.30	0.11	0.10	0.12	0.00	0.00	0.00	0.09	0.10
		52.83	57.89	13.23	6.89	2.02	2.02	0.00	1.47	0.00	0.00	0.00	0.00
	Subtotal	**52.83**	**57.89**	**13.54**	**7.19**	**2.13**	**2.12**	**0.12**	**1.47**	**0.00**	**0.00**	**0.09**	**0.10**
	Unit Packaging												
	[redacted]	1.32	1.41	0.43	0.24	0.24	0.23	0.11	0.12	0.10	0.10	0.08	0.10
		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
		18.55	15.85	3.13	2.79	1.72	1.82	0.19	0.18	0.00	0.00	0.00	0.00
		2.16	2.05	0.55	0.41	0.39	0.42	0.19	0.19	0.00	0.00	0.00	0.00
		0.02	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
		0.34	0.36	0.06	0.06	0.06	0.06	0.03	0.03	0.02	0.02	0.02	0.02
	Subtotal	**22.39**	**19.68**	**4.18**	**3.50**	**2.41**	**2.53**	**0.52**	**0.52**	**0.12**	**0.12**	**0.10**	**0.12**
	Subtotal/cs (x10)	**223.90**	**196.80**	**41.80**	**35.00**	**24.10**	**25.30**	**5.20**	**5.20**	**1.20**	**1.20**	**1.00**	**1.20**
	Product												
	[redacted]	0.65	0.78	0.12	0.12	0.11	0.15	0.00	0.00	0.00	0.00	0.00	0.00
		0.40	0.32	0.11	0.07	0.05	0.08	0.00	0.02	0.00	0.00	0.00	0.00
		0.47	0.54	0.10	0.07	0.07	0.07	0.01	0.01	0.01	0.01	0.00	0.01
		2.77	3.02	0.44	0.30	0.14	0.16	0.00	0.00	0.00	0.00	0.00	0.00
		0.34	0.35	0.04	0.04	0.03	0.03	0.00	0.00	0.00	0.00	0.00	0.00
		0.44	0.61	0.12	0.05	0.08	0.08	0.00	0.00	0.00	0.00	0.00	0.00
		0.28	0.27	0.11	0.11	0.10	0.00	0.00	0.00	0.00	0.00	0.00	0.00
		3.14	3.18	1.12	0.99	0.52	0.52	0.06	0.06	0.00	0.00	0.00	0.00
		26.34	24.71	6.75	6.51	2.93	2.82	0.00	0.00	0.00	0.00	0.00	0.00
		0.13	0.11	0.20	0.19	0.16	0.12	0.15	0.09	0.08	0.07	0.05	0.04
		0.05	0.03	0.03	0.03	0.03	0.03	0.02	0.03	0.02	0.02	0.01	0.01
	Subtotal	**35.01**	**33.92**	**9.14**	**8.48**	**4.22**	**4.06**	**0.24**	**0.21**	**0.11**	**0.10**	**0.06**	**0.06**
	Subtotal/cs (x10)	**350.1**	**339.2**	**91.4**	**84.8**	**42.2**	**40.6**	**2.4**	**2.1**	**1.1**	**1**	**0.6**	**0.6**
	Total per case (10 units + shipper) (mg)	**626.83**	**593.89**	**146.74**	**126.99**	**68.43**	**68.02**	**7.72**	**8.77**	**2.30**	**2.20**	**1.69**	**1.90**
	Total EO/pallet of cases (13 internal 53 external) (mg)	**39,624.96**		**8638.09**		**4494.65**		**565.17**		**146.5**		**122.67**	
	Wood Pallet	**8035.11**		**1024.72**		**641.48**		**30.48**		**32.53**		**25.8**	
	Plastic Wrap	0		0		N/A		N/A		N/A		N/A	
	Residual EO per Pallet	**47,660.07mg / 0.1050lbs**		**9,662.81mg / 0.0213lbs**		**5,136.13mg / 0.0113lbs**		**595.65mg / 0.0013lbs**		**179.03mg / 0.00039lbs**		**148.47mg / 0.00031lbs**	

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2) Summary of an engineering study evaluate residual EO in pallet materials

A study was carried out by BD to evaluate the levels of residual EO in pallets used to convey product through the sterilization process and the data is presented in Table 2.1. The study encompassed pallets composed of two different materials including the conventional wooden pallet and a pallet composed of polypropylene. Polypropylene was chosen as the alternative material as it is known to be a stable material that is somewhat resistant to EO absorption, and suitable for use at target process temperature. The study compares the difference in residual EO in each pallet material and estimates the potential annualized difference in fugitive EO between the two materials.

The data from the study shows that the level of EO in the wooden pallet material is significantly higher than the polypropylene material at the beginning of heated aeration with the polypropylene material completely free of measurable EO at the end of heated aeration compared to the wooden pallet which retains over 1100 mg/pallet of EO. The estimated amount of EO potentially released from the wooden pallets based on a run rate of about 125,000 pallets of product per year is approximately 300-500 lbs per year.

Table 2.1 Comparison of Residual EO in Wood vs Polypropylene Pallet Materials

Cycle 7	Run 1	Run2		Run 1	Run2	
	Pre-aeration EO mg	Pre-aeration EO mg	**Average**	Post-aeration EO mg	Post-aeration EO mg	**Average**
Wood Pallet	6066.07	6535.38	**6300.73**	1186.00	1761.64	**1473.82**
Polypropylene Pallet	202.14	137.65	**169.90**	0.00	0.00	**0.00**

3) Conclusion, Recommendations, and Next Steps

Based on this information, with regards to packaging, we conclude that the type and configuration of packaging has a measurable impact on fugitive emissions from a product. These emissions decrease over time, with the largest reductions occurring in the first day after heated aeration. However, neither the Covington and Madison facilities or the GDC, have the ability to change the product or package design. Thus, BD will consider ways that it can utilize improved packaging design to further minimize fugitive emissions in future product design.

With regard to pallets, we conclude that polypropylene pallets do not retain measurable levels of EO residuals following heated aeration, however, there are significant issues with functionality and durability and we have yet to find a pallet that will withstand repeated use and the wear the tear caused by the automated pallet transfer system. Thus, we do not currently plan to substitute the wooden pallets for another material as we have yet to find one that can withstand the thermal cycling associated with sterilization, nor a pallet design suitable for use with the custom automated transfer system.

Notably, the studies also further confirm that Cycle 15 achieves lower EO residuals at the product level and overall lower EO residues over time, as well as lower EO consumption per cycle (by approximately 21%), as compared to Cycle 7, when properly accounting for variables such as load configuration, product, and the setpoints met during each phase of the cycle within the validated process parameters (e.g. time, temperature, EO gas concentration). BD will continue implementation of Cycle 15 for qualified lines in Covington and Madison as regulatory approvals are received and change control activities are completed.

Based on the results of this and previous studies, BD will update the mass balance formula, air quality modeling, and resubmit the air permit application for Covington.

Please recognize that this is an initial assessment and we are unaware of other similar studies. Our assessment of these data is based on our knowledge of our products and local conditions at the time of the study. It is not necessarily applicable to other products or different conditions.

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