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PRESCRIPTION DIVISION

INFLUENCE OF A NOVEL POLYAMIDE RING DESIGN ON LEACHABLES LEVELS GENERATED IN A HFA pMDI

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SUMMARY / INTRODUCTION

The aim of this study is to demonstrate the influence of a novel polyamide ring component, used in a metered dose valve, on the leachable (1) fatty acids levels from EPDM gaskets in a HFA pMDI.

The advantages of using a polyamide ring in pMDIs have already been evaluated: reducing dead volume inside the canister at the end of product life and acting as a moisture sink to prevent excessive levels of moisture coming into contact with the drug product (2, 3). In addition, there are other benefits to using such a specific designed ring with respect to product performance. A metering valve is subject to relatively high stresses during component assembly, crimping the valve onto the canister, pressure filling, and high pressures due to elevated temperatures during testing etc. This stress can potentially lead to irreversible deformations of the plastic components, and especially the valve body, resulting in negative impact on valve functionality and product performance. A solution to the above issues would be to use a specific designed polyamide ring (referred to as PRE4) which is able to absorb most of this mechanical stress *(Figure 1)*

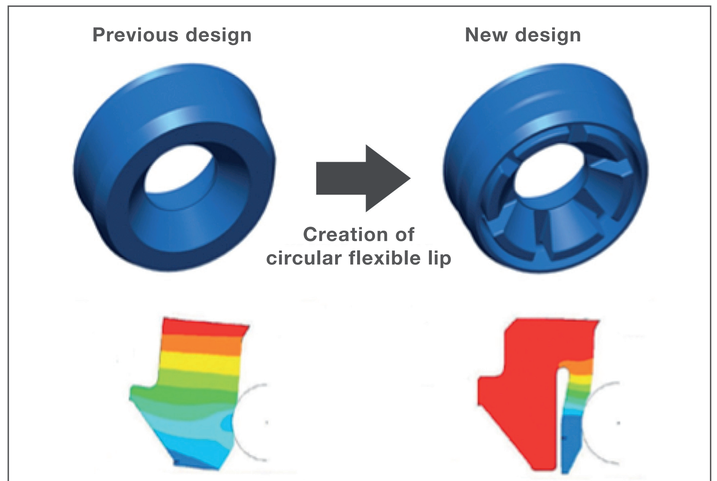

Figure 1. Absorption of mechanical stress by the new PRE4 ring design.

MATERIALS AND METHODS

A metered dose valve (DF316/48µl, Aptar Pharma) and pMDI canister (Presspart C128) were used for the study. Two ring components (standard PRE1A and PRE4) were evaluated in terms of leachables. The novel PRE4 ring component differs from the standard ring design, PRE1A, in that it incorporates a circular flexible outer lip designed to absorb physical stresses and reduces potential contact between the can contents and the sealing gasket.
The ring components and the corresponding metered dose valves were crimped onto aluminum cans with a diameter setting of 17.70 ± 0.05mm and a height setting of 5.70 ± 0.05mm.
The cans were then filled with 8.5g of HFA134a + 1.5g of ethanol (15% w/w). The samples were then stored inverted in stability ovens at 40°C/ 75% RH.
The cans were sampled after 1, 6 and 12 months storage (5 samples per configuration).
The sampled cans were placed for 1 hour in a freezer at -80°C, opened, and the content of each can transferred into 250ml flask. To ensure full recovery of leachables the can was rinsed 3 times with 2 ml of ethyl acetate.
The HFA 134a was evaporated at ambient temperature, and the resulting solution was transferred to a 20ml flask and the volume adjusted with ethyl acetate.
Leachable analysis was carried out by GCFID (gas chromatography flame ionization) using a validated analytical method developed in-house at Aptar Pharma.

RESULTS

The amounts of fatty acid leachables measured are presented in Table1.

		1 month (n=5)		6 month (n=5)		12 month (n=5)	
		Palmitic acid	Stearic acid	Palmitic acid	Stearic acid	Palmitic acid	Stearic acid
PRE4 ring	Average	59	112	68	112	141	216
	sd	1	3	3	2	8	4
	RSD%	2	3	4	2	6	2
PRE1A ring	Average	75	135	167	239	212	293
	sd	0	8	3	15	11	10
	RSD%	0	6	2	6	5	3
Without ring	Average	135	216	193	254	248	320
	sd	4	9	14	21	14	6
	RSD%	3	4	7	8	6	2

Table 1. Fatty acids results (µg/pMDI)

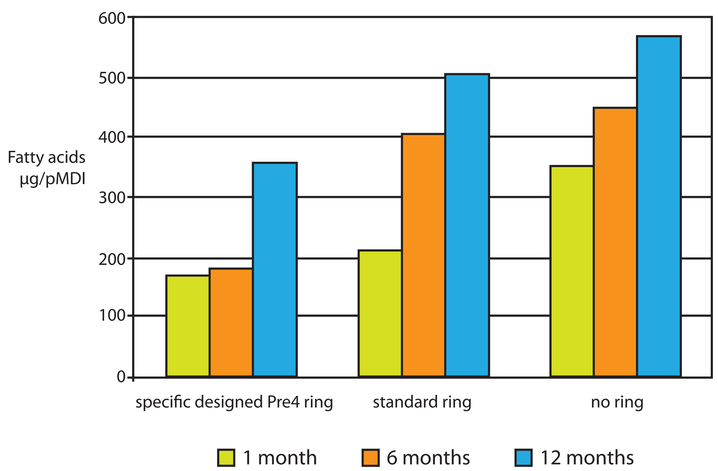

Table 2. Influence of ring on fatty acid leachable levels

The results clearly show lower levels of fatty acids in a pMDI fitted with the specific PRE4 ring design, when compared with the levels obtained for the pMDI fitted with a standard ring and pMDI without ring. This conclusion is confirmed by the good repeatability of measurements, whatever the storage time and configuration. The flexible outer lip design of the PRE4 ring component results in a better inner seal between the can and the valve, which in turn leads to less contact between the can contents or formulation and the sealing gasket. As a result of this improved seal, there is less opportunity for leachables to be taken up into the formulation during storage and hence lower levels of extractables over time, which is confirmed in this study.

CONCLUSION

The use of a novel polyamide ring component in a pMDI valve clearly reduces the fatty acids leachable levels in comparison with a standard polyamide ring and a reference pMDI without ring. In addition, the specifically designed ring has a protective role for the pMDI components and reduces intercomponent stress forces. During the assembling operation of the metering valve on the can, the ring component also allows for less stringent crimping specifications. One further benefit of using a ring component in polyamide is that it can reduce the moisture uptake inside a pMDI.

References

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