IMPROVEMENT OF PMDI PERFORMANCE THROUGH OPTIMISATION OF THE METERING VALVE MATERIAL AND DESIGN

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OBJECTIVE

The goal was to develop a metering valve with alloy gasket technology that shows good drug compatibility and mechanical stress resistance. The specifications were to:

- Eliminate continuous leakage
- Eliminate side-streaming
- Reduce loss of prime
- Eliminate sticking
- Improve chemical compatibility

METHODS

Metering valve prototypes were prepared and assembled using semi-automatic pilot tools. A matrix of combinations was designed to evaluate different first gasket diameters (in order to optimize leakage and loss of prime) and different materials for neck gaskets (in order to optimize drug compatibility and mechanical performance). Dosages tested were 3 at the beginning, 4 at the middle and 3 at the end of the can life. The active drugs tested were recovered using appropriate solvents and quantitatively determined using HPLC analysis.

RESULTS

Among the different configurations evaluated, only configurations #1, #5, #6 and #7 were evaluated for mechanical stress resistance. The specifications were to:

- Eliminate continuous leakage
- Eliminate side-streaming
- Reduce loss of prime

Two different HFA based formulations were prepared to be evaluated. The first formulation is based on a combination of Fluticasone Furoate and Salmeterol Xinafoate and contains no Ethanol. The second is a Budesonide suspension prepared using a low Ethanol content. These formulations were prepared on a pilot scale, and the valves were filled by pressure filling. All cans were primed and let for equilibration for 14 days, then were placed at 40°C / 75% RH for accelerated ageing for 3 and 6 months for delivered dose uniformity testing, and 1 and 3 months for mechanical testing.

Delivered dose uniformity (DDU) analysis was performed using a DUSA apparatus at 28.3 L/min (n=5 cans). Cone tests were 3 at the beginning, 4 at the middle and 3 at the end of the can life. The active drugs tested were recovered using appropriate solvents and quantitatively determined using HPLC analysis.

CONCLUSION

Among the different configurations tested, one of them (configuration #8) showed good results in term of mechanical testing, as well as drug compatibility (delivered dose uniformity and compatibility testing), at initial testing and after several months of accelerated ageing. This study confirms the importance of the gasket material selection and that gasket alloys are a promising opportunity for future valve optimizations.

BIBLIOGRAPHY


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