

## **A new high performance dual-layer coating for inhalation hardware**

**P A Jinks**

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### **Summary**

The physical and chemical surface properties of Metered Dose Inhaler (MDI) and Dry Powder Inhaler (DPI) hardware play a critical role in system performance and stability. For many years lacquer-based coatings have been employed on MDI cans to prevent chemical interactions with the formulations and in more recent years to reduce loss of the active substance to the can walls by deposition. Such coatings however are not suitable for the coating of more intricate geometries, such as the components of a valve for a MDI, or the powder contacting components of a DPI.

This paper explores the performance benefits of a new dual-layer coating, which comprises a sub-micron, plasma deposited inorganic layer which is surface functionalised with a networked fluorine containing layer. Data highlighting performance benefits of the coating for MDIs, with regard to reducing deposition and aiding valve function are presented.

### **Background**

Driven by the need for compliance to the Montreal Protocol<sup>(1)</sup>, most MDI formulations today consist of suspensions of one or more micronised active pharmaceutical ingredient (API) dispersed in a propellant mixture based on hydrofluoroalkanes (HFAs). Due to the strongly electronegative mantle of the HFA molecule causing intense interparticulate and particle to surface interactions<sup>(2)</sup>, such formulations are prone to deposition of the API/s onto internal surfaces of the can and the metering valve. These interactions can lead to low or erratic product dosing due to deposition (caking) of the dispersed API particles onto surfaces and partial re-entrainment of the deposits into the dispersion as non-respirable agglomerates. In addition to causing erratic dosing, agglomerates have the potential to cause blockage of the spray orifice of the mouthpiece actuator and hence are clearly undesirable.

In a move to address the above product behaviour, the use of fluoropolymer-based lacquers for MDI cans has become widespread, with Ventolin™ Evohaler™ being an example of a marketed product employing such technology.

The use of fluoropolymer lacquered cans however, only addresses part of the deposition problem. Of potentially greater significance is deposition of API particles downstream from the can, in particular on the surfaces of the valve and actuator.

The transition to HFAs has also presented challenges in the functionality of the metering valve due the low solvency of HFAs for the previously employed surfactants. Whilst stronger springs can be employed to overcome higher friction, this may lead to wear of the elastomeric seals which in turn may give rise to particulates and changes in product dosing performance through life.

Clearly deposition and friction are both surface phenomena and might be tackled by the employment of a suitable coating. Any such coating however would need to be more versatile than the fluoropolymer lacquers, which due to their curing temperatures of around 400degC and high fluid viscosity and resultant thickness, limit their use to metal components with fairly simple geometry.

### **Experimental**

The dual layer coating referred to in all of the following discussion comprises a plasma deposited inorganic sub-layer with a thickness of around 100nm, which is further surface functionalised with a networked fluorine containing layer. The coating processes are low temperature and hence are suitable for plastic as well as metal substrates.

#### **Example 1 Qualitative assessment of dual layer coating on plastic and glass surfaces**

The dual layer coating was applied to one of the two flat glass side viewing ports of a laboratory pressure vessel and also to a sample of clear PET (polyethylene terephthalate) plastic vials.

A suspension MDI formulation comprising a micronised inhalation corticosteroid compound suspended in an HFA based propellant system comprising ethanol, oleic acid and HFA 227, was added through a non-metering valve affixed to both the pressure vessel and to the PET vial. Both systems were then left to stand for one week.

The formulation was then drained from the pressure vessel and the glass walls removed and examined. The PET vial was tilted to observe the region where the fill line had been during the week's storage.

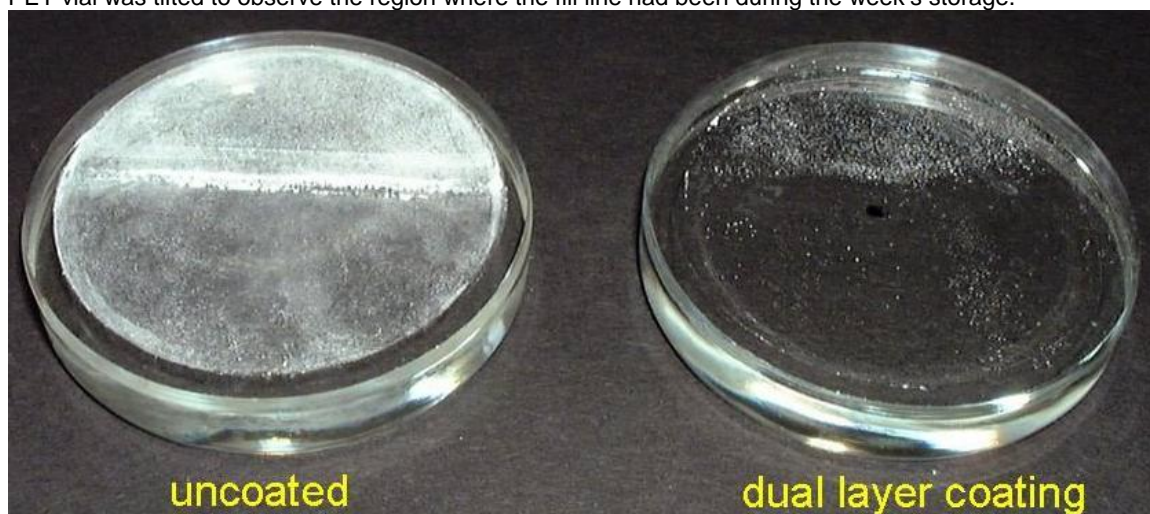


Fig 1 Glass pressure vessel walls – uncoated versus dual-layer coated after exposure to formulation for 1 week



Fig 2 Appearance of the fill line zone on PET vials with no coating (left) and dual-layer coating (right) after exposure to formulation for 1 week

In Figs 1 and 2 the effect of the coating on the fill line deposition for both the glass and the plastic substrates is pronounced, showing the potential benefit of the coating to formulation systems prone to deposition.

### Example 2 Quantitative deposition assessment of model suspension formulation onto dual-layer coated plastic valve components

The dual-layer coating was applied to acetal stems and polybutylene terephthalate (PBT) metering chambers of a test 50ml metering valve. The coated components were then assembled into valves and valves with non-coated stems and metering chambers served as controls. Valves (3 coated and 3 non-coated control valves) were crimped onto cans containing the following model formulation to provide six test units.

	mg/ml	%w/w
Micronized Brilliant Blue food dye	1.2	0.0991
Oleic acid	0.0606	0.0050
Dehydrated ethanol	24.2285	2.0000
HFA 134a	1185.9373	97.8959

Each test unit was primed using 5 actuations and then actuated 89 times. Valve forces were then determined using a JJ Lloyd tensile tester and finally the units were chilled down to -60°C and the valves detached from the cans. The valves were then carefully disassembled, and deposition on each valve stem and metering chamber was photographed and then quantified by photometric assay.

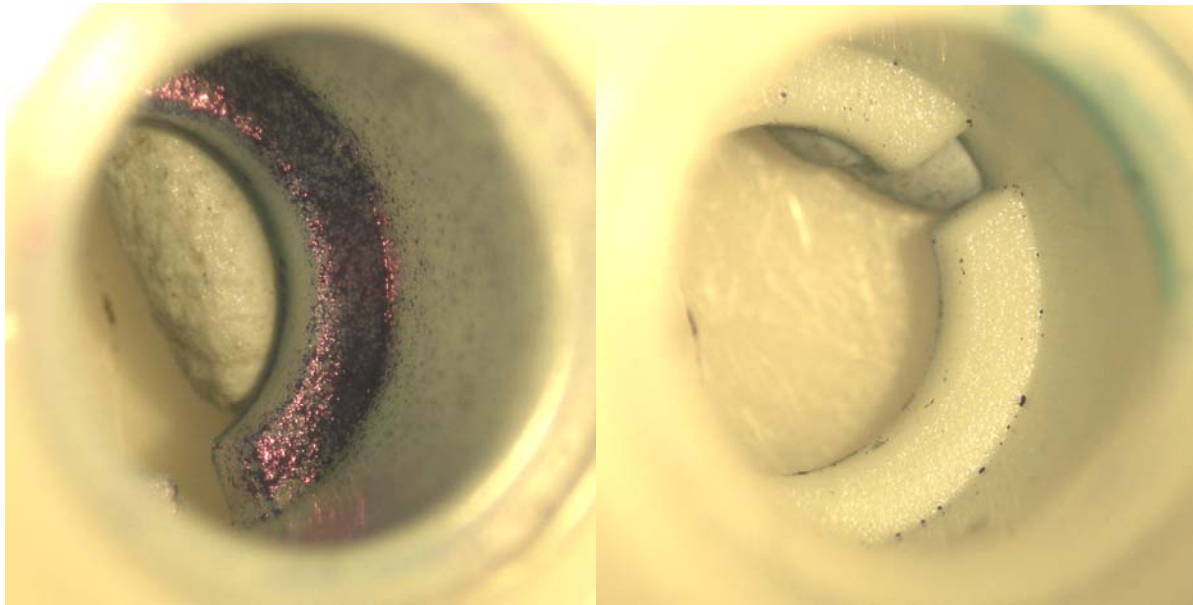


Fig 3 Example photography of internal surfaces of uncoated (left) and coated (right) PBT metering chambers prior to assay showing extent and location of brilliant blue deposition

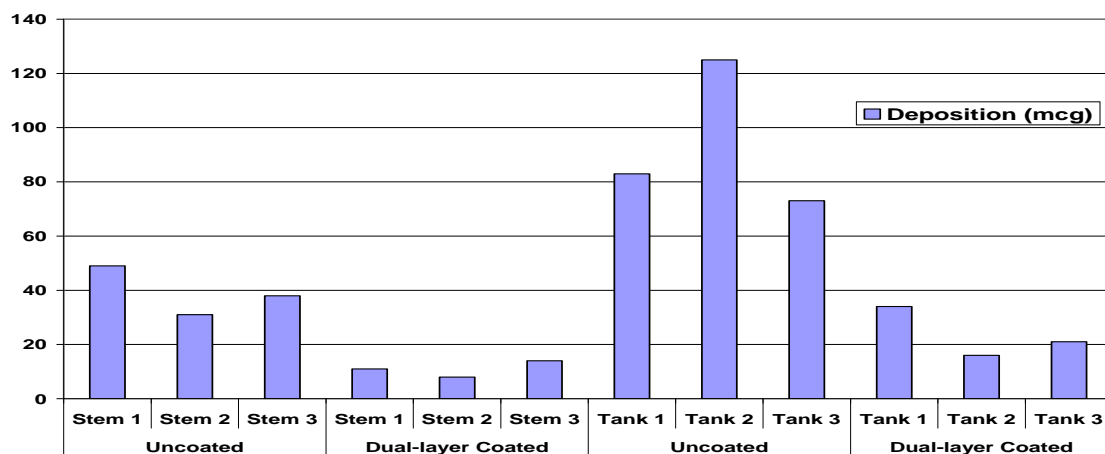


Fig 4 Quantification of brilliant blue deposition on coated and uncoated acetal valve stems and PBT metering chambers (tanks)

#### Valve friction results

Uncoated: Average 10.2 Newtons, SD 0.35 Newtons  
 Dual-layer coated: Average 7.9 Newtons, SD 0.96 Newtons

The dual-layer coating clearly has a marked effect on reducing levels of deposition on the stem and metering chamber and in addition, the friction data confirm that the coating acts as a bound lubricant.

#### Example 3 Quantitative deposition assessment of salbutamol active suspension formulation onto dual-layer coated metal valve components

Spraymiser™ valves were assembled using metal components™ coated with the dual-layer coating. Control valves were built with the same base components but without the coating. The following formulation was employed.

	mg/ml	%w/w
Salbutamol Sulphate (micronised)	2.0000	0.163
HFA 134a	1224.4127	99.837

Formulations were filled into aluminium vials using a laboratory scale cold filling technique. After equilibration for 1 week, both product systems were actuated through life (200 actuations) and valve force measurements were then performed. Finally the units were disassembled and the mass of salbutamol deposited on each stem, spring and metering tank valve component was quantified.

**Return force  
(Newtons)**

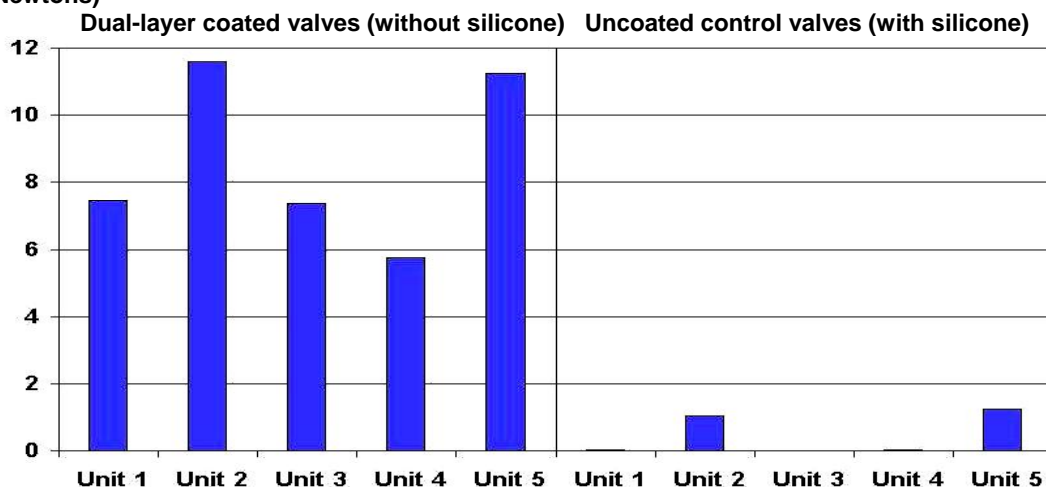


Fig 5 End of life return force on dual-layer coated and uncoated valve product systems

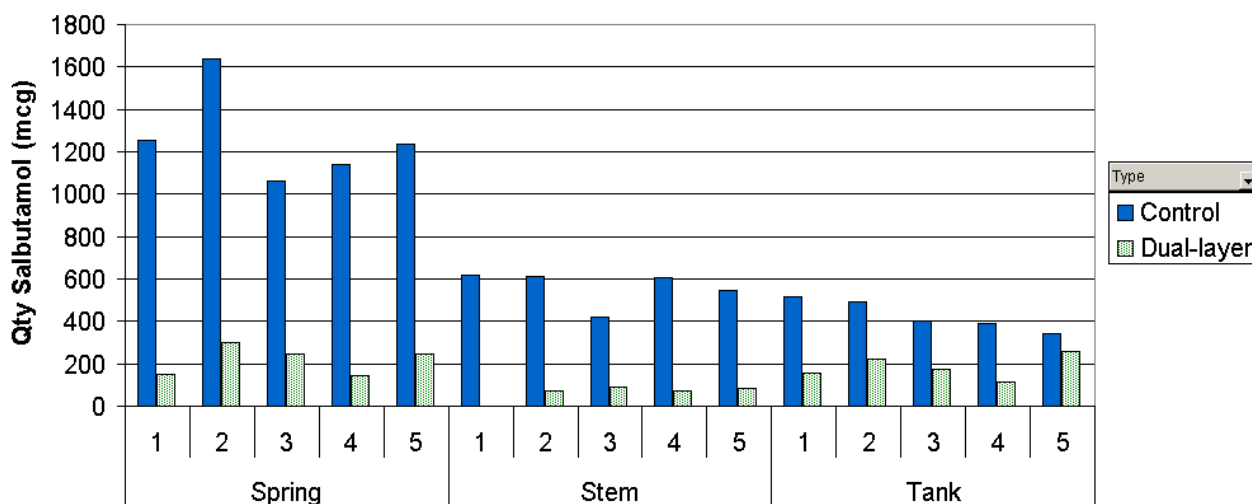


Fig 6 End of life salbutamol deposition on dual-layer coated and uncoated valve components

For the salbutamol MDI test system, both valve function and deposition levels were very significantly improved with the dual-layer coating compared with the uncoated control valves.

**Conclusions**

The use of a new dual-layer coating for inhalation hardware has been described, with data highlighting deposition and frictional benefits across a number of product systems when applied to MDI valves. The multifunctionality of the coating is particularly attractive since in MDI systems, deposition and frictional issues commonly occur together. Work is ongoing to develop a more complete understanding of the properties and potential utility of the coating and to optimise coating process parameters to achieve maximum product system performance.

**References**

- (1) The Montreal Protocol on Substances that Deplete the Ozone Layer, 2000, United Nations Environment Programme.
- (2) Vervaet, C., Byron, P.R., 1999. Drug-surfactant-propellant interactions in HFA formulations. International Journal of Pharmaceutics 186 13-30.