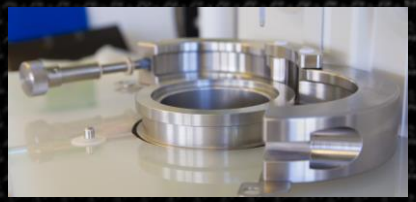
Case Study #1

Leachables from Dry Powder Inhalers (DPI)

Leachables from Dry Powder Inhalers (DPI)

According to the table of leachables risk in USP <1664> “ASSESSMENT OF DRUG PRODUCT LEACHABLES ASSOCIATED WITH PHARMACEUTICAL PACKAGING/DELIVERY SYSTEMS” there is a low possibility of interaction between a powder and packaging components of a DPI.

A major pharmaceutical client had a problem with an unidentified leachable in their newly designed DPI.

This leachable was a non-volatile that did not contain a chromophore.

It was not detected in the extractables testing, since LV/UV was used to screen the extracts.

A combination of LC/MS and fraction collecting followed by NMR determined that the leachable was a commonly used anti-static additive.

Anti-static additives are compounds formulated into polymer systems that are designed to migrate to the surface of finished molded articles to reduce the static charge.

This allows for the free flow of the powdered drug formulation through the drug contacting components of the DPI.

Since the anti-static additive was on the surface of the DPI polymer components, it was readily available to become a leachable in this solid dosage form.

Lessons learned:

- Surface additives, such as anti-static, anti-microbial, and slip additives, are a high risk for becoming leachables-even in solid dosage forms
- Multiple detection systems, such as UV and MS, should be utilized with HPLC analysis of extractables and leachables, so that compounds without a chromophore and/or chemicals that cannot be ionized in the MS will be detected.
- Low risk does not mean any risk.