External Washing Protocol

Recent research has illustrated that many vials of cytotoxics are not free from detectable levels of external contamination. Such contaminated vials represent a risk for staff involved in handling cytotoxic drugs, having specific health effects such as:

- **Cancer**[1]
- **Birth defects**[1]
- **Leukemia**[2]
- **Spontaneous abortions**[2]
- **Congenital malformations**[2]
- **Skin rashes**[3]
- **Infertility**[3]

Accord is committed to putting user safety at the heart of our offering. Accord is a dynamic young company unencumbered by past practice and with an appetite for refreshing the way in which safe and efficacious pharmaceuticals are delivered to users.
Unlike many companies operating within the area of generic oncology, Accord owns and controls all aspects of its pharmaceutical manufacturing, through 2 GMP-approved* state-of-the-art facilities. This gives Accord greater ability to control and optimize all aspects of products that could impact on user safety. Accord recognizes that we need to employ both **Preventative** and **Protective** measures in a systematic way to prevent occupational exposure.

HOW WE PREVENT EXTERNAL VIAL CONTAMINATION

Accord recognises that to provide the best standards in minimising external residue requires a systematic and consistent risk minimising approach.

Filling:

To ensure that all required cytotoxic material enters the vial cavity, Accord employ's an **in-line volume/weight control** as a core in process check on 100% of filling operations. Deviation from this check leads to vial rejection. Many competitor sites continue to use ad hoc sampling with a reduction in confidence.

Lyophilisation:

Accord's research and operational specialists design into our advanced freeze dried processes a **smooth sublimation step**. This minimises the chance of bubbling and risk of migration of cytotoxic to the external surface for freeze dried products, as well as producing an elegant product cake.

*MHRA, FDA.

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Incidental vial breakage:

In process vial breakage is a potential source of external residues on other vials. One key way in which Accord minimises this risk is by **optimising the vertical load during vial crimping**. A secondary benefit of this optimisation is ensuring optimum container-closure integrity. This helps reduce in transit leakage risk.

Visual Inspection

Accord's risk minimisation approach reduces the chance of external contamination. However, Accord doesn't stop here; instead we ensure that before leaving our factories 100% of our cytotoxic products undergo an extensive **validated washing cycle** and **visual inspection:**

Washing protocols

Accord's **validated washing protocols** utilise industrial equipment that subjects each vial to a double rinse with purified water and then dried with compressed air. The validation of the washing process included extensive analysis of washing efficiency at a range of machine operating speeds, different vial sizes and for the most insoluble product in the range. Analysis of the vials after washing found that at operating speeds, all vials sizes sampled were below the test limit.

Final visual inspection

100% of cytotoxic vials are subjected to **final visual inspection** across a preset range of parameters including; lack of external residue, crimp integrity, no vial defects.

References:

1. DHHS (NIOSH) Publication No. 2009-106 (2008). Personal Protective Equipment for Health Care Workers Who Work with Hazardous Drugs http://www.cdc.gov/niosh/docs/wp-solutions/2009-106/pdfs/2009-106.pdf
2. NIOSH: Hazardous drug exposures in health care.
3. Huynh T., Jalundhmala Y., Subramaniam V. Hazardous Drugs. Maintaining Standards of Safe Pharmacy Practice. *Pharmacy Practice News*. 2010; 37 http://www.cdc.gov/niosh/topics/hazdrug/

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OUR PREVENTATIVE PROCESS