The Seemingly Innocuous Glue in Staked Needle Syringes

By: Alan Xu, Product Manager for Analytical Services at Stevanato Group's Technical Excellence Centers, USA and Italy

Guidelines for container closures cover a variety of elements including particle counts and plunger glide force. But the adhesive used in staked needle syringes is an under-characterized realm. While glue or adhesive suppliers may provide preliminary extractable data, the final gluing and curing process parameters may include – and generate – new compounds that affect the final extractables profile. The true effects, such as loss of drug potency, may not be seen until the drug is in direct contact with the final container. If your drug is losing potency – or you wish to evaluate glue compatibility earlier to prevent late-stage formulation changes – where do you start?

Stevanato Group's Technology Excellence Centers (TEC) can provide a helping hand with the Design of Experiments (DoE) and the associated method development to detect specific glue-derivative compounds that interact with your drug product. SG TEC can also help support method validation and transfer methods to your lot release provider to ensure future lots meet this new quality specification. With locations in Boston and Piombino Dese, Italy, SG TEC has extensive experience in a variety of techniques ranging from chemical investigations, such as adhesive compatibility and tungsten compatibility, to mechanical tests such as container closure integrity testing and break-loose and glide-force testing.

If you're finding an incompatibility between your drug and an existing container, our investigation starts with a fish bone chart (or Ishikawa diagram) to evaluate all aspects of the process – from materials, machines, and the environment to human aspects, methods, and measurement. Next comes risk assessment to evaluate likely and unlikely items from the fish bone chart.

A series of experiments then needs to be designed to confirm the potential root causes. Experiments may include intentionally recreating the issue and testing high-impact process parameters at relatively high and low values. Fringe cases may also need to be evaluated – for example, perhaps the product is affected when the production line is on hold due to sudden maintenance.

For the most robust study, these DoE samples can also be included in a stability study to evaluate the long-term performance and interaction between these optimized parameters and the actual drug product. Based on the test results, an inspection criteria and/or process optimization that minimizes drug interaction can be finalized.

With acrylic-based glues, SG TEC has investigated and developed multiple techniques, including High-Performance Liquid Chromatography (HPLC) and Ion Chromatography (IC) test methods capable of quantifying the presence of acrylic acid and other glue compounds in the final cured adhesive. With our HPLC method, even individual syringes can be evaluated without having to pool multiple samples. Inspecting individual syringes allows a closer look at a process because there may be significant differences – even between pieces of the same batch.

Other crucial elements include specificity/selectivity; accuracy and precision, i.e. the closeness of the results to a true value and to results obtained by the same or different preparations; repeatability to show capability across multiple set-ups; linearity – whether the method correctly detects concentrations ranging from small to large; and robustness, with consistent performance under different variables. Once the method is validated, a method transfer needs to be performed to implement the method at the customer's quality control laboratory, if they would like to implement it as part of the lot release process. Another fish bone and risk assessment is performed to plan the smoothest transition from one laboratory to another. And a failure modes and effects analysis (FMEA) evaluates the entire analytical process – from the infrastructure of the laboratory to the availability of the reagents/materials used in the method and the data analysis/reporting technique.

The attributes from the method validation are re-evaluated and compared between the two laboratories to see if equivalent results are obtained when testing the same material. In-person training is provided, where possible, and videos or live webcam training is provided if travel is not possible. Support for the generation of standard operating procedures at the receiving laboratory is also provided. Future planning may include a well-defined design verification testing plan to avoid problems further down the line.

With the right DoE, method development, and method transfer, container compatibility issues don't need to derail your successful commercial launch of a world-class drug delivery device.

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