INDUSTRIAL PILOT PROJECT

Detection of leakages in prefilled syringes by Neutron Radiography

THE INDUSTRIAL CHALLENGE

Prefilled syringe is a successful format to allow patient self-injection of pharmaceutical treatments. Swedish Orphan Biovitrum AB (Sobi) is a global producer of biological medicines for rare diseases and these are often provided in prefilled syringes. However, there are technical challenges for the pharmaceutical sector to secure the integrity during storage. Leakage can cause liquid to enter the syringe needle and evaporate, leaving dry product to block the needle or even migrate into the rubber needle shield. This is a rare case but nevertheless results in costly investigations. There is therefore a need to establish technologies that can predict and identify leakage mechanism without compromising the syringe integrity.

WHY USING A LARGE SCALE FACILITY

To investigate the leakage within a rubber needle shield, an aqueous liquid must be able to be detected and viewed inside the steel needle without removing the shield around it. Using a neutron source for radiography is currently the only option to address this challenge. X-ray or Neutron Tomography methods would not provide an actual detection of the aqueous liquid in the needle.

HOW THE WORK WAS DONE

The IMAGINE beamline of Laboratorie Leon Brillouin (LLB) neutron facility in France was selected for the experiments. The study design and the practical experimentation were performed in close collaboration between the industrial partner Swedish Orphan Biovitrum AB and neutron experts at RISE and LLB.

Syringes with pre-attached needles were filled with three different aqueous solutions; pure water, protein solution and gadolinium solution. Gadolinium was selected as having excellent contrast with neutrons. Neutron radiography was then used to visualize the liquids through the steel needle, see Figure. Pre-studies were performed to optimize the detection conditions. In order to test relevant stress conditions (vacuum and temperature) during measurement, the team also constructed an equipment. The final tests addressed how different types of syringe behaved.

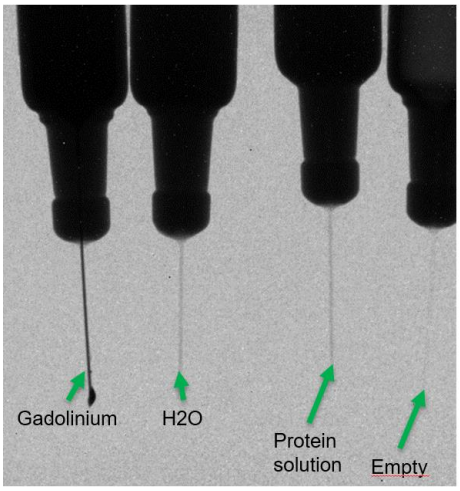

Figure. Liquids in prefilled syringe needles detected by Neutron radiography. Pure water and protein solution showed similar intensity.

THE RESULTS AND EXPECTED IMPACT

Most importantly the experiments have confirmed neutron radiography as an important tool for detection of liquids in needles. The work has also generated a method to actually be able to detect leakage in prefilled syringes without compromising the integrity of either the syringe or the needle shield. This important tool may be used to assess manufacturing issues and syringe design. Further work in this field are planned involving other key stake holders. One can even consider implementing technologies to measure this in manufacturing settings.

"It has been an exciting project to apply large-scale facilities to solve industrial challenges for biological products"
/Jonas Fransson,Swedish Orphan Biovitrum

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Vinnova's project No: 2018-03261 **Duration:** November 2018 -- December 2019

Funded by Sweden's Innovation Agency, Vinnova, in order to build competence and capacity regarding industrial utilisation of large-scale research infrastructures such as MAX IV and ESS.