Development and validation of puncture performance test for MAP products

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Background: Effective development of Microneedle Array Patch (MAP) products will require appropriate test methods to exemplify features of the device that are critical to their safety and efficacy, i.e. their critical quality attributes (CQAs). Validated and widely recognized standardised test methods for CQAs are employed in both the pre-clinical development and quality assurance of pharmaceutical products. Established dosage forms have internationally recognised validated tests methods, e.g. in international Pharmacopoeia, and whilst some of these have been adopted to evaluate MAP products, the unique features of this new dosage form may require adaptations to these methods and/or the development of bespoke tests. A prioritization exercise by the MAP Regulatory Working Group (MAP-RWG)[1], and corroborated by stakeholder consultation, identified a MAP puncture performance test as being a priority area of development that would have wide applicability in the field. This work aims to identify, develop and validate (using *in vivo* human data) a synthetic skin surrogate that has comparable compression properties to human skin, for use in a simple in vitro puncture performance test for MAP products.

Methods: Compression tests on *in vivo* human skin (interior forearm) were carried out using Zwick Roell Z500 testing machine using both (i) flat and (ii) conical indenters up to a maximum of 2N (conical indenter) or 8N (flat indenter). The test was conducted at a quasi-static speed of 100mm/min, using a 500N load cell and testExpert II v3.5 software to record force/displacement curves. Human data (N=25) was obtained under ethical approval* and informed consent.
Commercially available synthetic representations of human skin were identified from published materials and were prepared in accordance with manufacturer's instructions. Practical considerations (e.g. ease of preparation) and the compression behaviour of the material, in comparison to the *in vivo* data set, were used to identify and then optimise candidates most suited to use as a skin surrogate in a MAP puncture test. Different material thicknesses and composites were examined and the temporal stability (20 days) and reproducibility (batch-to-batch and person to person) of the materials was assessed.

Results: Twenty-one candidate materials were identified for screening and two were selected as primary candidates i.e. (i) hydrophobic SmoothOn Silicones (EcoflexGel, Ecoflex30 and SomaFoama15) and hydrophilic Syndaver materials[2] (made of fiber, water and salt) including fat/ subcutaneous fat, muscle and skin parts. Over 250 different thicknesses and composite variations have been tested. Those with compression profiles most similar to human data have been selected for further work.

Conclusions: Commercially available materials have been identified to provide a skin surrogate for development of a MAP puncture test. Future work will identify and integrate a puncture indicating layer into the model to create a first iteration of a MAP puncture test, which will then be optimised and validated to provide stakeholders with a test to exemplify performance of MAP products.

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References
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