Key challenges in development of a long-acting, discreet, embeddable microneedle product for hormonal contraception

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Background: One of the sustainable development goals for 2030 is to "*ensure universal access to sexual and reproductive health-care services, including for family planning, information and education, and the integration of reproductive health into national strategies and programmes*"[1]. The family planning needs of many women remain unmet, notably in low- and middle-income countries (LMICs), where access to a choice of modern contraceptive methods can empower women, improve maternal and infant health, and enhance educational prospects. Novel microneedle (MN)-based contraceptives are being developed to provide women with more choice. This article discusses the key challenges encountered in the development of a hormonal, biodegradable contraceptive MN product.

Methods: Human factor studies[2] identified end-user preference for a contraceptive product that is small, potentially self-administrable, discreet, environmentally safe, long-acting and allows for a relatively rapid return to fertility after discontinuation. However, encapsulating sufficient hormonal contraceptive for 6 months contraceptive effect into micron-sized biodegradable MNs while maintaining an acceptable patch size is practically difficult. This study iteratively developed and tested (in vitro and in vivo) drug loaded biodegradable polymer blends and carefully engineered MN designs.

Results: Fifty percent drug loading has been achieved in a polymer blend, with *in vitro* drug release at therapeutically significant levels over 6 months. Preclinical studies confirmed excellent safety and tolerability of the drug-loaded polymer, but also highlighted a slower release profile than *in vitro*, triggering iterative rounds of polymer optimisation, as well as the development of more representative *in vitro* models. In the proposed product, MNs are designed to separate from the supportive base and remain embedded under the skin, slowly releasing the incorporated drug over 6 months. The challenge of engineering MNs with appropriate mechanical properties to fully penetrate the skin during insertion yet fracture at the base after insertion was overcome with the assistance of predictive *in silico* modelling and the development of an integrated applicator system. The applicator was iteratively developed based on input received from end users regarding its appearance, mechanism of action, usability, and ability to provide patient feedback.

Conclusions: The manufacturing method for MN products aimed at LMICs needs to be precise, reproducible, suitable for commercial mass production, and affordable. Micro injection moulding is potentially the most cost-effective way of manufacturing MN components due to the speed and volume of processing. However, in practice, mould tools, MN design and drug-polymer formulation had to be repeatedly modified to achieve a satisfactory moulding process. In conclusion, whilst it is extremely challenging to develop a long-acting, discreet, embeddable MN product for hormonal contraception in LMICs, our multi-disciplinary consortium has been able to iteratively develop a user-informed, low-cost concept that is now progressing through preclinical testing and manufacturing development.

1) UN. Sustainable development goals. [cited 2023 January 16]. Available from: https://www.un.org/sustainabledevelopment/health/.
2) Gualeni B, Hughes L, Stauber I, Ackers L, Gorman A, Gashuga D, Dzabala N, Chimimba F, Chikowe I, Coulman SA, Birchall JC. Human-centred design of a new microneedle-based hormonal contraceptive delivery system. Gates Open Res. 2021 Jul 30;5:96.