InFact Final publishable summary report

Surgical site infection is one of the most prevalent healthcare-associated infections and heavy microbial colonization is a key reason for non-healing of chronic wounds. In Germany alone, there are approximately 14 million cases of post-operative wounds and 3 million of chronic wounds. In Europe, this results in estimated treatment cost of > € 5 billion per year while the resulting pain, impairment and social isolation lead to reduced quality of life and, in the worst case, hospitalization, and eventually sepsis and death. Currently, wound infection is not diagnosed until becoming pathologically evident. The InFact project has developed novel diagnostic tools for early detection of infection which can be integrated into wound care devices. Considering the global wound care market of USD 21.6 billion in 2018 together with the social need for early infection detection the economic potential of the InFact devices is clearly evident.

The InFact devices were developed based on the fact that the human innate immune system secretes several enzymes, such as myeloperoxidase, neutrophil elastase, and lysozyme in early and established infection. To allow simple indication of infection status, the InFact partners developed specific substrates for these enzymes which rapidly change colour when contacted with infected wound fluid. An alternative visualization strategy invovled trapping systems for dyes released by the enzyme reaction or which migrate in the wound fluid path as a internal control. Moreover, a pH-sensitive substrate was developed providing additional on infection status. The developed substrates are in-sensitive to wound matrix effects (e.g. influence of heme) and develop strong colours (e.g. dark blue) which are clearly visible in red wound fluid. Apart from the enzyme substrates, internal standards were developed to avoid false negative results. In a next step, immobilization procedures (ultrasound and printing) for these enzyme substrates were developed and optimized. Formulations were designed to allow integration into wound dressings by simple printing procedures. In a second application, these substrates were immobilized onto a cellulose matrix to be used as a standalone test device. A risk assessment was carried out for all chemicals present in the final devices. Substrate production was up-scaled for mass production under required quality standards (clean room etc) with concomittant LCA and LCC analysis. The developed individual substrates and the resulting InFact devices (sensors for integration into dressings, standalone test devices) fulfill essential requirements like storage stability, biocompatibily (e.g. no leaching of chemicals), no cytotoxicity and in-sensitivity sterilization where required. Most importantly, however, several clinical studies conducted throughout

the project have demonstrated the functionality of the InFact devices for simple and early detection of wound infection. Interestingly, some of the included enzymes as infection markers show high specificities and lower sensitivities and and others vice versa while the combined result (including pH) clearly has a higher diagnostic value than clinical judgment providing an ealry signal for wound infection. Based on these sucessful results a business plan has been developed considering EU regulatory and commercialization aspects, and additional future challenges such as gaining access to the US market.
The collaboration within the InFact project timeframe resulted in three joint patents, five publications in peer reviewed journals and a number of conference presentations.