# LCA of Nanodrugs: Adding Constraints

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**Context**

It is estimated that inflammatory diseases have now affected more than 80 million people worldwide, and counting. Studies have shown that disorder like rheumatoid arthritis (RA) shortens life span about 10 years. The treatment RA remains a challenge for the medical and scientific community. Vectorisation of active pharmaceutical ingredient(s) (API) is a promising option.

**Project aim**

NANOFOL proposes to develop a new diagnostic/therapy approach using folate based nanobiodevices (FBN) able to provide a new type of cost efficient treatment for chronic inflammatory diseases such as RA. The FBN is expected to generate low(er) side effects, possibly constituting a solution more advantageous than current therapies.

**The concept**

NANOFOL undertakes design, development and production of nanobiodevices (FBN) targeting directly effector cells.

**Drug assessment issues**

Establishing a proof of concept for one or several FBN, and testing it (pre-clinical) is a central aim of the project. However, other aspects of this new therapy shall be assessed – basically consisting in: occupational safety assessment; LCA; socio-economic analysis (SEA). Undertaking these combine difficulties typical of both pharmaceuticals and objects with nanometric caracteristics.

**Work presented**

This communication presents the key questions raised prior to developing the methodology for LCA and SEA , and how these have been answered. Available knowledge in LCA of nanos could be applied to some extent, as well as guidelines of REACH Regulation (EC). Working out the right hypotheses – a challenge in anticipation of clinical phase trials – did involve experts from the chemical, medical, engineering, social and economic sciences. Therapeutical strategies are introduced as scenarios for running LCA and SEA.

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# Generating pore fluid isotope and solute profiles in exceptionally low permeability rocks

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Establishing geochemical and isotopic profiles for aquitard pore fluids is a critical, yet challenging, component of investigations of deep geological settings considered for nuclear waste isolation. A variety of advanced techniques have been developed internationally to extract and analyze pore waters and gases from sediments. However, the exceptionally low-permeability shales and limestones at the Bruce nuclear site, on the eastern margin of the Michigan Basin, demand innovative techniques for the extraction and analysis of pore fluids. Here we describe new methodologies, based on vacuum distillation and diffusive leaching developed to extract water, solutes and gases from rocks with hydraulic conductivities as low as $10^{-15}$ m $s^{-1}$ and effective diffusion coefficients as low as $10^{-12}$ m $s^{-2}$.

Field investigations included the drilling of six cored boreholes to various depths through the ~860 m thick Paleozoic sedimentary sequence at the site. Samples of this high-quality, 76 mm diameter, core were broken to acquire inner material uncontaminated by drilling fluid, and were then crushed to 2-4 mm size to fill four 75 ml Pyrex flasks. Porewater and $CO_2$ were extracted for content and isotope analysis by heating under vacuum and condensing into 12 ml septum-fitted glass vials. Replicate testing of different rock types found optimum conditions to be 150°C for 6 hours. Solutes were analyzed after leaching with deionized water and normalized to the gravimetrically-measured recovered water content to produce molal concentrations.

The method is well suited to the illite-dominated shales (water contents of 6 to 8%) and for the exceptionally-low water content of the limestones (to less than 1%), as it uses a closed system for water extraction, and reduces error by normalization of solute mass to sample specific water contents. New developments to the method use a closed system ball-mill to crush and then heat smaller chip-samples. This offers greater control for investigating temperatures of release of mineral hydration waters and heterogeneities near permeable features.