

## 1008

Making smart nanocarriers applicable to the pharmaceutical industry through the development of an innovative mechano-chemical process



# PROJECT

### Inspiration

A large panel of industrial sectors, such as biotechnology, cosmetics, and pharmaceutical ones, make use of nanomaterials to ensure their attractiveness and competitiveness. In the rise of nanotechnology, the pharmaceutical industry can benefit from the last development of nanoparticles based drug delivery systems in order to constantly improve its drug synthesis, as well as targeted delivery using smart nanocarriers. Despite the considerable interest and research in the development of nanoparticles based drug delivery systems, only few have been commercialized, mainly protein based NPs (e.g. abraxane), liposomes (e.g. doxil), and drug nanocrystals. In fact, promising nanoparticles, such as mesoporous silica nanoparticles (MSNs) and nanostructured lipid carriers (NLC), are facing strong challenges when it comes to be used in pharmaceutical products at an industrial scale, due to high constraints in the current standard manufacturing processes (e.g. aggregation phenomena, uneven particles growth, excess in stabilisers). A new synthetic approach is therefore required.

### Innovation

The 1008 project aims to develop an innovative mechano-chemical process scaling up the production of stable nanocarrier dispersions for an efficient transfer to the pharmaceutical industry. Wet stirred media milling is a standard process in the pharmaceutical industry, mainly used as a comminution method to get drug nanocrystals. With proven experience in nanomaterials, LIST researchers will first couple a highly performing wet bead mill qualified for pharmaceutical applications, developed by its partner Frewitt, with a chemical reactor designed to produce smart nanocarriers such as MSNs and NLC, following already developed LIST recipes.

With the NanoWitt-Lab, materials can be wet milled down to the desired particle size, i.e. 50 or 200 nanometers (nm) while keeping constant product temperature and narrow particle size distribution (PSD). The milling chamber's modular construction (4 chamber sizes) is designed for milling quantities ranging from milligrams up to kilograms of solid. The innovative patented NanoWitt construction allows short milling time at low specific energy with a reduced beads quantity, this resulting in gentle product processing, no hot spot generation, lowest product contamination and tight particle size distribution. In addition, its unique dynamic separator with no filter prevents clogging and hectic operation, which are steady problems with other technologies. In order to provide stable processing conditions, the dynamic separator enables direct in-line sampling and integration of an in-line particle size measurement. Finally, the NanoWitt cGMP design provides furthermore user-friendly operation, easy cleaning, and convenient bead handling, this combined with high product recovery.

The novel mechano-chemical process implemented with the NanoWitt will be then evaluated at a scale up to 1 L dispersion, and shared with a panel of pharmaceutical stakeholders active in the nanocarrier developments. With a long-term view through their project, LIST researchers will also assess the business implementation potential of this innovative process for others industrial sectors.

### Impact

The 1008 project will enable the development of a novel mechano-chemical process allowing the production of stable nanocarrier dispersions. In addition, this new mechano-chemical fabrication process is expected to lead to a significant reduction of the manufacturing costs. As a result, smart nanocarriers such as MSNs and NLC, which show a high interest in the drug delivery systems, should be able to be produced at an industrial scale while meeting the specifications of the pharmaceutical industry.

The effectiveness of the solutions developed in the 1008 project will be shared with a panel of pharmaceutical stakeholders active in the nanocarrier developments. In parallel, the assessment of the business implementation potential will be carried out throughout the 1008 project in order to develop future opportunities both for LIST and Frewitt, as well as potential future industrial partners in the pharmaceutical, cosmetics, and biotechnology markets just to name a few.

By establishing this long-term strategy, LIST, and as a consequence its partner Frewitt, will benefit from a clear vision of the nanomaterials manufacture, use, and integration value chain, and thus, will be able to establish a roadmap of the nanomaterials technology line valorisation.

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### Contact

5, avenue des Hauts-Fourneaux  
L-4362 Esch-sur-Alzette  
tél : +352 275 888 - 1 | [LIST.lu](http://LIST.lu)

Dr David DUDAY ([david.duday@list.lu](mailto:david.duday@list.lu))  
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