



Unique in Uniformity.

www.nanomi.com

monosphere technology for the life sciences™



Nanomi is an independent, privately owned Dutch high-tech company, which specializes in the development of **precisely defined functional emulsions** and **micro** and **nanospheres**. The company was founded in 2004 as an independent spin-off from the University of Twente, and is located in the East of the Netherlands. It has been profitable from the start, and despite being a relatively new business, is already involved in developing products for several **Forbes 2000 companies** worldwide.

Mission

Nanomi partners with companies in the life sciences to provide them with novel, high added value micro and nanospheres enabled by its microsieve™ based process technology.

Proprietary technology

Nanomi's core technology is its proprietary **microsieve™ emulsification process**. The microsieves™ are made by precise semi-conductor technology, which enables the production of **highly monodisperse droplets** and **particles** in a **robust, reproducible** and **cost effective** way.

Key application areas

- Drug delivery and controlled release
- Molecular imaging
- Diagnostics
- Research and Analysis

How we do business

Nanomi develops its proprietary technology platform for the precise production of droplets and particles, and enters into partnerships with companies that have a high value product/application that strongly benefits from our technology. Return on investments comes from royalty payments and technology transfer, which is based on product added value. Nanomi is solely involved in business-to-business partnerships and does not attempt to distribute and market products on its own.

Core values

- innovation
- customer focused
- excellence
- teamwork
- flexibility
- result and product focused

We create value through

Quality research and technology | Providing valuable products through outstanding technology

Innovation and product uniqueness | Creating innovative solutions that meet our partners' needs and providing unique, tailor-made monodisperse products

Expertise and motivation | Focusing our efforts and capabilities on providing expertise to our customers and improving their product performance

Strategic partnering | Close collaboration with market and technology leaders in B2B partnerships

- patent protected technology
- monosphere technology and expertise
- profitable since start-up
- flexible organization
- customers leading the global life sciences market

Nanomi develops microsieve™ emulsification technology for the production of **precisely defined functional emulsions**, and **micro** and **nanospheres**. These have various applications in the life sciences market, such as **drug delivery** and **controlled release**, **diagnostics**, **molecular imaging** and **research and analysis**.

Microsieve™ emulsification

In the microsieve™ emulsification process, mono-disperse droplets are generated by dispersing one fluid into a second, immiscible fluid through a precise microsieve™, which has millions of tiny pores that are of the same size and shape. Since every pore is the same, every droplet generated by the membrane is the same, resulting in either highly uniform, reproducible and size-controlled droplets or, after an appropriate solidification step, particles.

A unique feature of the microsieve™ emulsification technology is the independence of the droplet size to the precise formulation, the size being solely determined by the membrane design. Compared to other conventional or membrane-based droplet and particle production methods, our technology offers several advantages such as:

Total control of droplet/particle size | Products with the required size and uniformity without process or formulation optimization.

No loss of valuable ingredients | No post process fractionation required due to total size control.

Robust, reproducible and stable in operation | The process is insensitive to fluidic and pressure conditions near the membrane surface.

Straightforward scalability | Scalable to any volume by increasing the number of pores of the microsieve™, or by adding more microsieves™ to the process.

Highly efficient encapsulation | Each droplet is formed individually, at negligible imposed shear and pressure. The small pore to droplet diameter ratio allows for the encapsulation of relatively large nanoparticles.

- optimal droplet/particle size
- droplets 5 - 90 µm, particles 2 - 50 µm
- monodisperse: C.V. ≈ 5 %
- reproducible, robust and scalable
- encapsulation/double emulsions
- large freedom in formulation
- low shear and pressure
- high chemical and thermal resistance
- compatible with aseptic processing

Microsieve™ membranes

The heart of the microsieve™ emulsification technology is a silicon membrane that is fabricated by precise semiconductor technology in a cleanroom environment. By means of photolithographic techniques excellent uniformity of pore size and shape is obtained in a highly reproducible way. Currently, microsieves™ for droplet and particle generation in the micron range are available. Microsieves™ for nanoparticles are under development. The microsieves™ have a very high chemical and thermal resistance. They can be cleaned with a wide variety of cleaning agents, and can be sterilized.

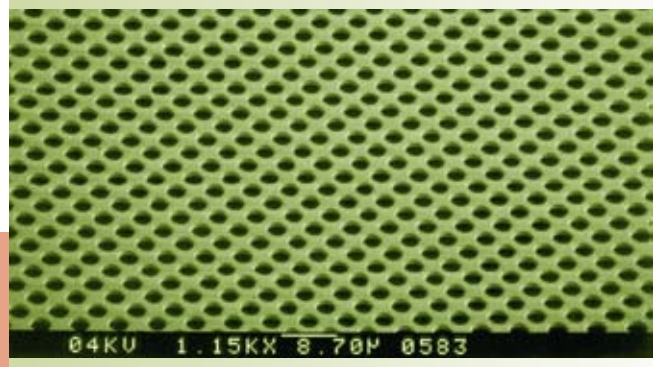
Process compatibility

- Solvent evaporation
- Melt emulsification
- Monomer emulsification
- O/W, W/O, W/O/W, S/W/O and S/O/W systems
- Large range of materials and solvents
- Aggressive cleaning agents and methods, including autoclaving

Strong IP position

Nanomi's microsieve™ emulsification technology is protected by several patent applications and licences, and the company is continuously seeking to expand its patent portfolio.

| SEM image of a microsieve™ (the pore diameter is 3 µm)



Nanomi offers technology for the fabrication of microspheres for **parental, sustained released**, drug delivery applications. Nanomi's proprietary microsieve™ emulsification process enables the **cost efficient processing** of a large variety of polymer/active combinations into microspheres, with **unsurpassed predictability in size and performance**. In many cases your **existing product formulation** can be **used directly** in our process.

Product morphology and encapsulation of active compounds

Microsieve™ emulsification results in monospheres in the micrometer range (C.V. \approx 5 %) with high encapsulation efficiency and controlled release profiles. A large variety of polymers can be processed with dichloromethane as solvent (class III solvents are also available if desired). Proteins, peptides and poorly soluble drugs can be encapsulated reproducibly, and in a cost-effective manner.

Our activity portfolio includes microsphere fabrication with PLGA, PLLA, PLGA-PEG, PLGA-PCL, PMMA and PEG-PBT, and the encapsulation of antibodies, progesterone, doxycycline, cyclosporine A, and model compounds such as lysozyme, BSA and vitamin B12.

Size control

The predictability and accuracy of the particle size obtained by our process is excellent. The particle size depends only on the membrane used and is independent of the formulation. Size control benefits both the product (better injectability and therapeutic proper-

ties) and the patient (smaller needle gauges can be used, thereby resulting in less-painful injections). At the same time, precise control of the particle size in non-vascular injectables is vital for suppressing immunoactivation.

Nanomi's process also enables the production of microspheres with a precisely defined size, for use in intravascular delivery and embolic therapies.

Small processing volumes and mild process conditions

In comparison to traditional double emulsion techniques, microsieve™ emulsification enables the use of much smaller volumes to produce the desired product. Furthermore, low shear and low pressure at room temperature helps to preserve the functionality of the encapsulated compound and the carrier.

Enabling new products and therapies

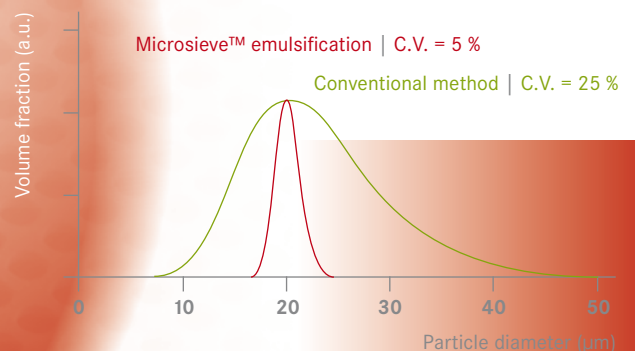
Nanomi's flexible and customizable process makes new products and therapies possible, and transforms difficult to process formulations into novel drug delivery vehicles.

Upscaling and GMP compatibility

The microsieve™ emulsification process can be conveniently scaled to any size by increasing the number of pores on our membranes. The currently available production scale is 10 gram/hour but work is in progress to both scale up to 1 kg/day, and to adapt the equipment for GMP compatibility.

- optimal particle size
- monodispersity, typically C.V. \approx 5 %
- single and double emulsion routes
- formulation independent particle size
- large freedom in formulation
- high loading and encapsulation efficiency
- biodegradable and biocompatible polymers
- low burst and controlled release
- smaller needle gauges/embolic therapies
- GMP compatible

Particle size distribution



Other Applications

Besides applications in drug delivery, Nanomi provides expertise in the production of tailor-made, monodisperse and high-value emulsions and micro and nanospheres, for utilization in other applications such as diagnostics, molecular imaging and research and analysis. Within these applications, Nanomi can encapsulate gases, nanoparticles, colloids and other molecules that are relevant in the life sciences.

Products developed for our customers

For leading companies in the life sciences market, Nanomi has recently developed various droplet and particle-based systems, such as lipid microspheres, fluorescent polyethylene and polystyrene monospheres, ultrasound contrast agents, colored magnetic microspheres, and biodegradable microspheres with encapsulated drugs.

Product examples

Fluorescent polymeric markers | 1

Biodegradable polymeric microspheres for embolic drug delivery | 2

From intramuscular to intravascular (embolic) drug delivery: Nanomi's process can improve the monodispersity and reduce the particle size without changing the formulation.

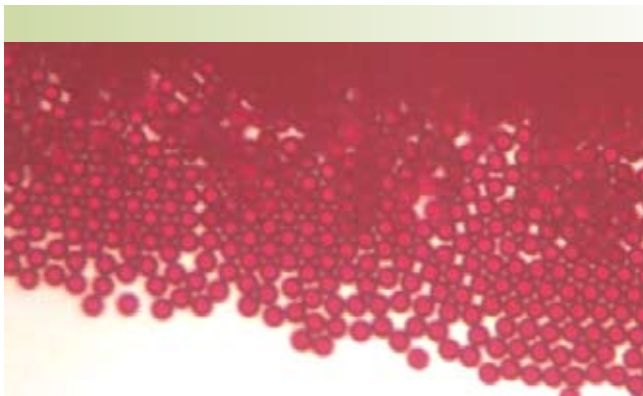
2 | a



2 | b



2 | Biodegradable polymeric microspheres of the same formulation fabricated by (a) conventional technology (50 - 100 μm) and (b) by microsieve™ emulsification (10 μm)



1 | Fluorescent red polymeric markers with a particle diameter of approx. 10 μm produced by microsieve™ emulsification

Please contact us to discuss the possibilities of Nanomi's microsieve™ emulsification technology.

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