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### 1. Description

<b>Components</b>	850 µL FeraSpin™ XL, MRI agent (superparamagnetic iron oxide nanoparticles) or 5 x 850 µL FeraSpin™ XL, MRI agent (superparamagnetic iron oxide nanoparticles).
<b>Capacity</b>	5 x 100 µL injections or 25 x 100 µL injections.
<b>Product format</b>	FeraSpin XL is supplied as a sterile isotonic solution with an iron concentration of 10 mM.
<b>Appearance</b>	Clear, amber liquid.
<b>Storage</b>	Store at 2–8 °C. Do not freeze. The expiration date is indicated on the vial label.

For laboratory and animal research use only. Warning: Not for human or animal therapeutic or diagnostic use. Make sure to comply with all laws and regulations governing research on animals.

#### 1.1 Background information

FeraSpin XL is a nanoparticulate superparamagnetic iron oxide imaging agent specifically formulated for pre-clinical magnetic resonance imaging (MRI).

FeraSpin XL belongs to the FeraSpin Series, which encompasses size-selected, narrowly distributed nanoparticulate agents with well-defined particle sizes derived from FeraSpin R (for details refer to the product portfolio at [www.viscover.berlin](http://www.viscover.berlin)). The FeraSpin Series includes FeraSpin XS, FeraSpin S, FeraSpin M, FeraSpin L, FeraSpin XL, and FeraSpin XXL. Their identical composition allows for exclusive size-dependent studies and

selection of the most suitable imaging agent for the intended application.

FeraSpin XS, S, M, L, XL, and XXL are agents of high relaxivity. They enhance the contrast in T<sub>2</sub>- and T<sub>2</sub>\*-weighted MRI due to a shortening of the spin-spin relaxation time (T<sub>2</sub>) and increase the signal intensity in T<sub>1</sub>-weighted MRI due to a shortening of the spin-lattice relaxation time (T<sub>1</sub>). The T<sub>2</sub>-effect increases with increasing particle size whereas the T<sub>1</sub>-effect increases with decreasing particle size. On accumulation in cells, the T<sub>1</sub>-effect diminishes and the T<sub>2</sub>-effect increases.

Upon intravenous injection, all agents of this series circulate in the bloodstream and are taken up by macrophages. They accumulate in the liver and spleen and are degraded within a few days with their iron being transferred into the physiological iron stores. The macrophage uptake varies in dependence of particle size. Increased uptake by the Kupffer cells (macrophages of the liver) with increasing particle size leads to a rapid accumulation in the liver and spleen and a short blood circulation time. With decreasing particle size, the uptake by the Kupffer cells is reduced leading to a prolonged circulation time and increased uptake by other macrophages.

The following schematic diagram shows the characteristics of the FeraSpin imaging agents in dependence of their particle size.

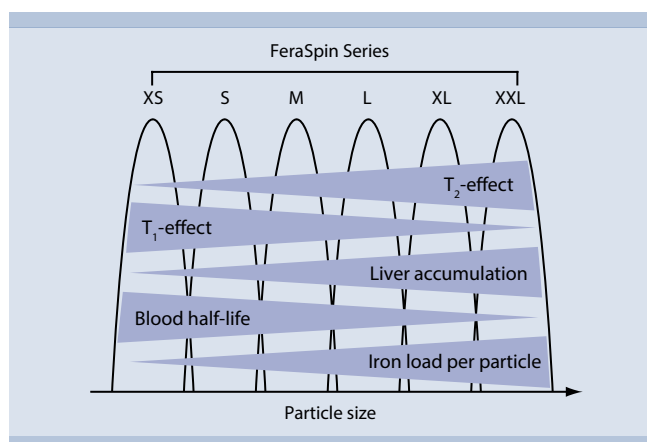


Figure 1: Characteristics of the FeraSpin Series in dependence of particle size.

#### 1.2 Applications

The FeraSpin Series is an innovative research toolbox that offers solutions for a wide range of imaging applications.

It provides the possibility for selection of the MR contrast properties, the pharmacokinetic properties as well as the iron oxide load and, thus, allows a tailoring of the imaging agent to customer needs.

FeraSpin XS, S, M, L, XL, and XXL are indicated for use in MRI of small animals, for example, mice. They can be used in various applications, such as *ex vivo* cell labeling or *in vivo* macrophage labeling for inflammation imaging.

Principally, all agents of this series can be used to facilitate the visualization of the liver and spleen as well as visualization of the vasculature.

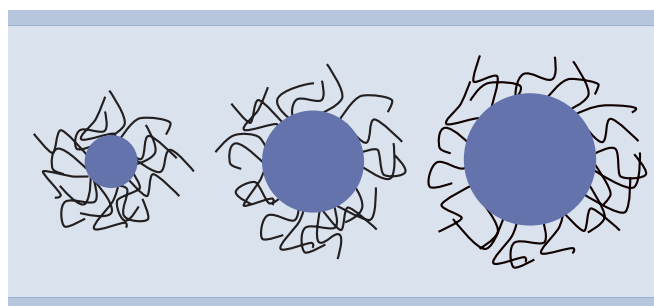
**Note:** For liver and spleen imaging the use of FeraSpin R is recommended. In applications where a long blood circulation time and a strong  $T_1$ -effect are favorable, for example in MR angiography, the use of FeraSpin XS is most suited. For more details refer to the product portfolio at [www.viscover.berlin](http://www.viscover.berlin).

**Note:** The imaging agents of this series are provided with equal composition for reasons of comparability. For custom-tailored concentrations please contact the customer support.

### 1.3 Physico-chemical properties

FeraSpin	Mean particle size <sup>#</sup>	Relaxivity [ $r_2/r_1$ ] <sup>##</sup>
XS	10–20 nm	3-5
S	20–30 nm	5-9
M	30–40 nm	9-22
L	40–50 nm	22-32
XL	50–60 nm	32-39
XXL	60–70 nm	39-46

<sup>#</sup>hydrodynamic diameter, <sup>##</sup>in water, 37 °C, 1.41 T



**Figure 2:** Schematic diagram of small, medium, and large-sized nanoparticles of the FeraSpin Series.

### 1.4 Requirements

#### ☞ Sterile syringes and needles (27–30 G)

**Note:** To allow sufficient volume for  $5 \times 100 \mu\text{L}$  injections per vial, the syringe/needle dead volume should be kept below  $70 \mu\text{L}$ .

**Tip:** Use insulin or tuberculin syringes.

#### ☞ 70 % ethanol

## 2. Protocol

### 2.1 Preparation

#### ☞ Read the entire protocol before starting.

**Tip:** For optimum device settings perform initial studies in a suitable imaging phantom.

#### ☞ The imaging agent is ready for injection as provided.

#### ☞ The dosing varies in dependence of the intended application as well as the selected FeraSpin imaging agent and, thus, has to be adapted accordingly.

#### ☞ For a mouse weighing 20–30 g an injection volume of $100 \mu\text{L}$ corresponds to a dose of $40 \mu\text{mol Fe/kg}$ body weight (for a 25 g mouse).

**Note:** Standard animal-handling procedures and local regulations must be followed.

### 2.2 Injection

#### ☞ Vortex the vial to ensure thorough mixing.

#### ☞ Disinfect the septum with 70% ethanol. Let septum dry.

#### ☞ Warm the mouse tail to dilate the veins and enhance their visibility.

#### ☞ Inject FeraSpin XL via the lateral tail vein of the mouse.

**Note:** FeraSpin XL contains no preservatives. Avoid microbial contamination and discard any unused material after 24 hours.

### 2.3 Imaging

#### ☞ Imaging can be performed on a multitude of devices at all commonly used field strengths including high-field MRI.

#### ☞ FeraSpin XL can be detected by $T_1$ - as well as $T_2$ - and $T_2^*$ -weighted sequences.

#### ☞ Taking a pre-contrast image is recommended.

#### ☞ The time interval between injection and imaging depends on the application. For applications involving imaging of the vasculature begin imaging immediately after injection. For other applications imaging over an extended time period after injection, for example 24 hours, is recommended.

Find examples of FeraSpin Series-enhanced MR images at [www.viscover.berlin](http://www.viscover.berlin).

## 3. References

- Ludwig, F. *et al.* (2012) Optimization of Magnetic Nanoparticles for Magnetic Particle Imaging. *IEEE Transactions on Magnetics*. 48(11): 3780–3783.
- Lohrke, J. *et al.* (2008) Characterization of superparamagnetic iron oxide nanoparticles by asymmetrical flow-field-flow-fractionation. *Nanomedicine* 3: 437–452.
- Metz, S. *et al.* (2004) Capacity of human monocytes to phagocytose approved iron oxide MR contrast agents *in vitro*. *Eur. Radiol.* 14: 1851–1858.
- Allkemper, T. *et al.* (2002) Contrast-enhanced blood-pool MR angiography with optimized iron oxides: effect of size and dose on vascular contrast enhancement in rabbits. *Radiology* 223: 432–438.
- Bremer, C. *et al.* (1999) RES-specific imaging of the liver and spleen with iron oxide particles designed for blood pool MR-angiography. *J. Magn. Reson. Imaging* 10: 461–467.
- Briley-Saebo, K. C. *et al.* (2006) Clearance of iron oxide particles in rat liver. effect of hydrated particle size and coating material on liver metabolism. *Invest. Radiol.* 41: 560–570.
- Tsuda, N. *et al.* (2005) Potential of superparamagnetic iron oxide in the differential diagnosis of metastasis and inflammation in bone marrow: experimental study. *Invest. Radiol.* 40: 676–681.
- Persigehl, P. *et al.* (2007) Antiangiogenic tumor treatment: early noninvasive monitoring with USPIO-enhanced MR imaging in mice. *Radiology* 244: 449–456.
- Frericks, B. B. *et al.* (2009) Magnetic resonance imaging of experimental inflammatory bowel disease: quantitative and qualitative analyses with histopathologic correlation in a rat model using the ultrasmall iron oxide SHU 555 C. *Invest. Radiol.* 44: 23–30.
- Simon, G. H. *et al.* (2006) Ultrasmall superparamagnetic iron oxide-enhanced magnetic resonance imaging of antigen-induced arthritis: a comparative study between SHU555 C, Ferumoxtran-10, and Ferumoxytol. *Invest Radiol* 41: 45–51.

#### 4. Related products

FeraSpin™ R	# 130-095-138, # 130-095-139
FeraSpin™ XS	# 130-095-140, # 130-095-141
FeraSpin™ S	# 130-095-166, # 130-095-167
FeraSpin™ M	# 130-095-168, # 130-095-169
FeraSpin™ L	# 130-095-170, # 130-095-171
FeraSpin™ XXL	# 130-095-174, # 130-095-175
GadoSpin™ M	# 130-095-134, # 130-095-135
GadoSpin™ P	# 130-095-136, # 130-095-137
GadoSpin™ F	# 130-095-162, # 130-095-163
GadoSpin™ D	# 130-095-164, # 130-095-165

A comprehensive product portfolio for the imaging modalities MRI, CT, US, OI, SPECT, and PET is available at [www.viscover.berlin](http://www.viscover.berlin).

#### Warranty

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