



Streptavidin coated magnetic beads (MagSi-STA) specifically suited for IVD assays and assay development

Background: Many IVD assays are based on the tight binding of surface exposed streptavidin towards a biotinylated antibody capturing directly or indirectly an biomarker to be diagnosed in an immunoassay. However, any immunodiagnostic assay can suffer from negative test effects, which fall under the rubric of interference. These effects lead to imprecision or can result in false-positive or false-negative outcomes. One typical effect is the so called *matrix effect* which is used to denote the sum of all interference effects of all components that appear in a specimen and influence the measurement of a target analyte. Using a streptavidin based immunodiagnostic assay one typical matrix effect is the biotin interference caused by natural, free biotin competing with the biotin labelled antibody. One strategy to reduce negative biotin interference is a precise control of the streptavidin concentration exposed to the surface, e.g. coated to magnetic beads. Here we describe the MagnaMedics expertise in optimizing the physical and biological properties of magnetic beads specifically suited for IVD assays.

Step one: Optimizing the size, size distribution and magnetic force of silica based magnetic beads.

In the first step the physical properties of a magnetic bead have to be defined (Fig. 1) to balance the needs of:

- magnetic separation time within the immunoassay
- time in suspension
- possible light scattering
- bead homogeneity within the buffer solution used
- etc.

Fig. 1:

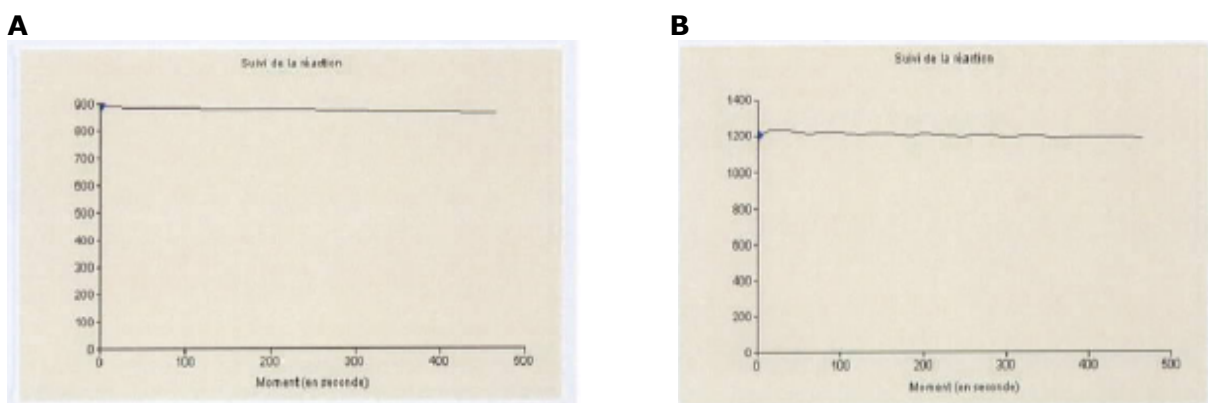


Fig.1: A) Linearity of the MagSi-STA 600 (600 nm sized magnetic beads) in used UV/Vis spectrophotometric assay. B) 300 nm sized competitor magnetic bead tested in linearity measurements.



Step two: Optimizing the streptavidin concentration

Typically the streptavidin concentration is measured and controlled by detection of fluorescein labelled biotin in a spectrophotometric assay. Therefore most suppliers of streptavidin coated magnetic particles use the biotin uptake values to specify their streptavidin coated magnetic beads. Table 1. provides an overview of commercially available streptavidin coated beads:

Table 1: Commercially available streptavidin coated magnetic beads

Company/Product	Biotin uptake (pmoles/mg bead)	mean size	Volume	Conc. mg/ml	Comments
MagnaMedics MagSi-STA 1.0	3000 - 6000	1 μm	2 ml	10	magnetic silica beads
MagnaMedics MagSi-STA 600	3000 - 6000	0,6 μm	2 ml	10	magnetic silica beads
Invitrogen My One Streptavidin T1	>1300	1 μm	2 ml	10	polymeric hydrophobic surface
Invitrogen M270	650 - 1300	2,7 μm	2 ml	10	polymeric hydrophilic surface
Thermo, Sera-Mag Speed beads streptavidin	"high"	1 μm	2 ml	10	polymer based magnetic beads

To reduce matrix effects like biotin interference many immunodiagnostic assays need tightly controlled biotin uptake values to control the competitive binding of free and antibody labelled biotin. Fig. 2 shows the biotin interference [BI] of four different MagSi-STA 600 lots coated with different concentrations of streptavidin. The biotin uptake values range from 5000 pmoles/mg bead (Lot 2: "low") over 6000/6100 (Lot 3 and 4: "mid") to 6500 pmoles/mg bead.

Fig. 2:

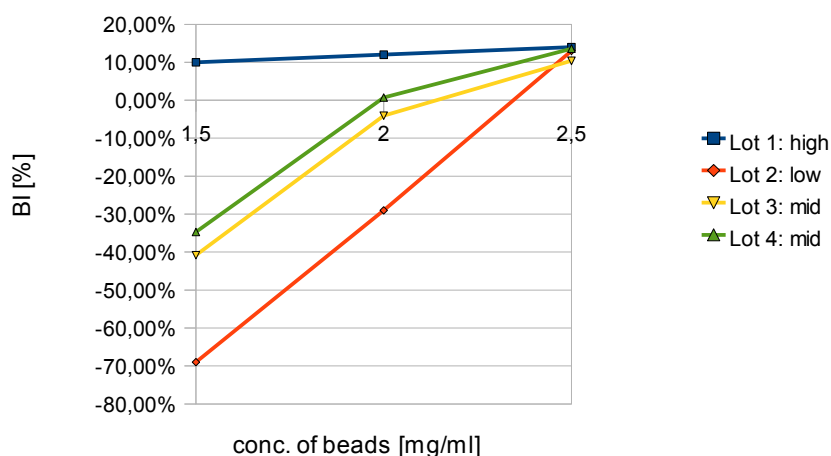


Fig. 2: Biotin interference at different bead concentrations in a specific immunodiagnostic assay. Four different MagSi-STA 600 lots with different streptavidin concentrations (low, mid and high) have been tested.

The optimal and acceptable biotin values out of Fig. 2 have been determined to be **6050 pmoles/mg bead +/- 150 pmoles.**



Step three: controlled synthesis of streptavidin coated magnetic beads during production.

To secure best test to test and batch to batch reproducibility the MagSi-STA beads are synthesized under strict SOP management incl. SOPs for raw material QC, raw material warehousing, state-of-the-art magnetic bead synthesis and streptavidin coating, QC of each production step, final quality control of the end product, stability control of the end product etc. As result MagnaMedics offers customized MagSi beads directly tailored to the clients immunodiagnostic assay (Fig. 1 and Fig. 3).

Fig. 3:

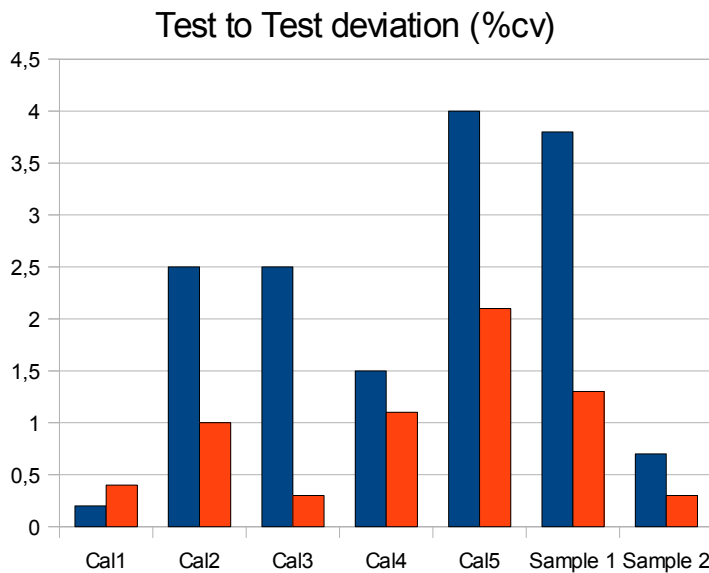


Fig. 3: Test to Test deviation (number of tests n=3) of the MagSi-STA 600 magnetic beads (red) and a competitor magnetic silica bead (blue). Cal1 – Cal5: Calibrators at different conc.; Sample 1 and 2: human blood samples.

As ready to use standard product MagnaMedics is offering the following MagSi beads typically used in immunodiagnostic assays:

MagSi-STA

MagSi magnetic silica particles with a monolayer of high quality streptavidin covalently attached to the bead surface.

Art. Nr.	Product	Conc.	Size	Volume
MD16001	MagSi-STA 600	10mg/ml	600nm	2ml
MD18001	MagSi-STA 600	10mg/ml	600nm	10ml
MD01001	MagSi-STA 1.0	10mg/ml	1µm	2ml
MD03001	MagSi-STA 1.0	10mg/ml	1µm	10ml



MagSi-protein A

MagSi magnetic silica particles with high quality, recombinant Protein A covalently bound to the particle surface.

Art. Nr.	Product	Conc.	Size	Volume
MD10011	MagSi-protein A 600	10mg/ml	600nm	1ml
MD11011	MagSi-protein A 600	10mg/ml	600nm	5ml
MD01011	MagSi-protein A 1.0	10mg/ml	1µm	1ml
MD02011	MagSi-protein A 1.0	10mg/ml	1µm	5ml

MagSi-protein G

MagSi magnetic silica particles with high quality, recombinant Protein G covalently bound to the particle surface.

Art. Nr.	Product	Conc.	Size	Volume
MD10012	MagSi-protein G 600	10mg/ml	600nm	1ml
MD11012	MagSi-protein G 600	10mg/ml	600nm	5ml
MD01012	MagSi-protein G 1.0	10mg/ml	1µm	1ml
MD02012	MagSi-protein G 1.0	10mg/ml	1µm	5ml

MagSi-COOH

MagSi magnetic silica particles coated with a carboxyl group containing polymer, covalently attached to bead surface.

Art. Nr.	Product	Conc.	Size	Volume
MD16004	MagSi-S-COOH 600	10mg/ml	600nm	2ml
MD18004	MagSi-S-COOH 600	10mg/ml	600nm	10ml
MD01004	MagSi-S-COOH 1.0	10mg/ml	1µm	2ml
MD03004	MagSi-S-COOH 1.0	10mg/ml	1µm	10ml

Please note larger batch sizes and bulk quantities are available on request. Please contact MagnaMedics to get an individual quote.

MagnaMedics is also offering customized magnetic (and non-magnetic) particles in nm and µm sizes incl. customized surface and chemistry design. Customized magnetic beads are available from small ml to several ltr. quantities!

MagnaMedics Diagnostics B.V.

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