Magnetic Beads, The Needs and The Opportunity

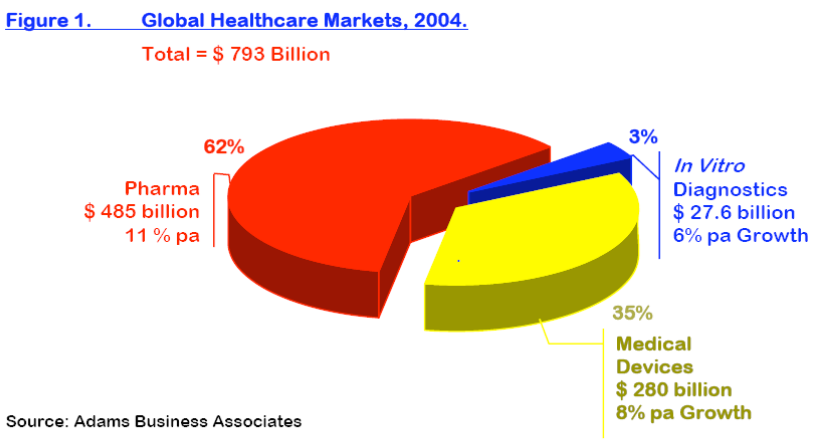
The quest for an improved medical care at lower costs is reshaping the whole healthcare business. Coupled with an aging population, the need for solutions to improve care at reduced costs is urging In Vitro Diagnostic (IVD) companies to find solutions.

A recent analysis by Frost & Sullivan (http://www.healthcare.frost.com) concludes that the IVD industry is rapidly evolving and is presently more dynamic than in over a decade. Diagnostics currently possesses tremendous potential for growth, but harnessing this opportunity requires that market participants concentrate on efforts to raise awareness regarding the importance and benefits of optimizing patient diagnosis.

Frost & Sullivan's Research Analyst Silvia Cerqueira states "Understanding individual markets and clinical needs is becoming increasingly important to overcoming obstacles and promoting the adoption of new technologies. New IVD systems must address unmet needs and provide substantial added value in order to be successful".

Considering that the need for improved care at lower costs entails an improved diagnosis, the quest for an improved test sensitivity have stimulated research by numerous organizations for new technologies to meet the this need. Even 1% decrease in health care costs through better diagnostics will have a major impact on healthcare spending. Improved testing sensitivity means better diagnosis and better clinical management and hence reduced cost of clinical care.

Figure 1. Global Healthcare Markets, 2004.



Considering the investment in developing diagnostic test products and components, and the risks involved with the adoption of these new technologies, far better risk-benefit is obtained by developing diagnostic components. The attached table illustrates the costs and reward of developing products to various healthcare segments.

Figure 2. Costs to Market and Benchmark Success levels, 2004.

Feature	Pharma	Medical Device	Diagnostic
Average Cost to Market	£ 900 Million	£ 250 Million	£ 2-10 Million
Major Product Revenue Mark	£ 1 Billion	£ 50 Million	£ 20 Million
Years to Market	6 – 15 years	3 – 5 years	1 – 3 years
Net Profit Level	10 –15 %	5 -10%	10 – 25%

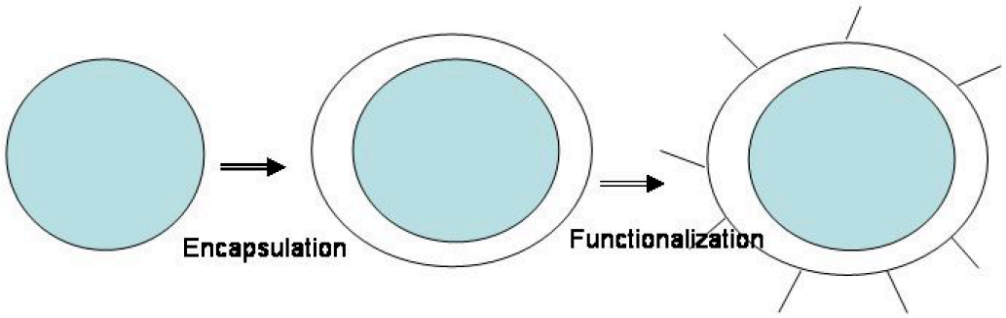
Source: Adams Business Associates

Magnetic Beads

In the last 2 decades, substantial progress has been made in developing technologies in the field of magnetic microspheres and magnetic nanospheres. Currently, magnetic beads are an integral component of immunoassay diagnostic kits for analyzers in the clinical laboratory. Commercial magnetic microspheres (particles or beads) are made of magnetic pigment encapsulated in a polymer shell. The magnetic material is mainly oxide of iron with minor amounts of other elements and is therefore dark, ranging in color from black to dark brown, depending on the percentage of the magnetic pigment.

Enhancing the amount of collected light in any binding assays represents an opportunity to improve test sensitivity and test throughput and therefore improved diagnostic care. Developing new magnetic beads with improved light scattering and light collection efficiency represents less challenging solution to improved test sensitivity. The improved beads, as a reagent, could replace traditional beads in the same platform clinical analyzer.

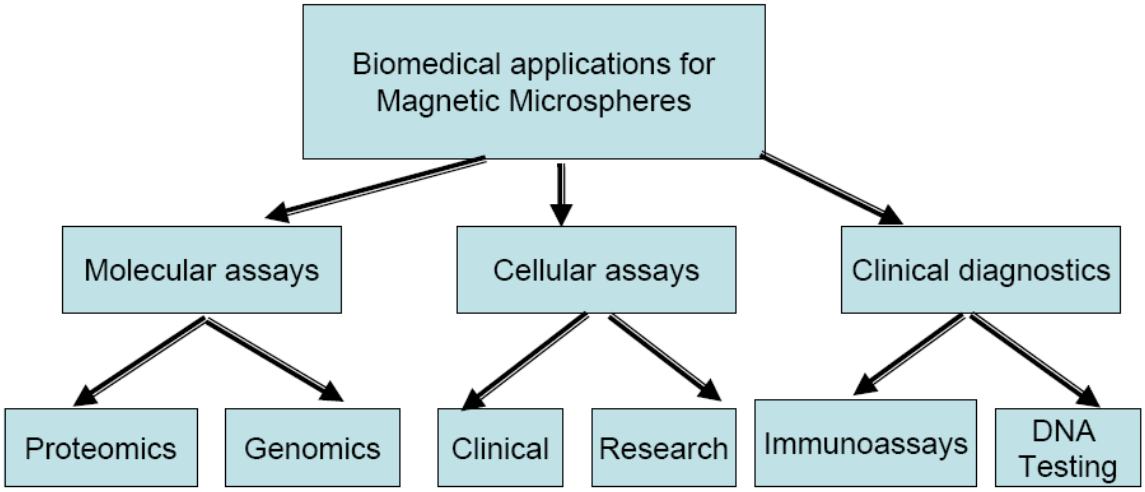
Commercial magnetic beads employed in the biomedical field range in size from less than 1 micron up to 100 microns, most commonly in the size range of 2-10 micron. Iron content of the commercial magnetic beads range from 15% up to 60%, the amount of which determines the response to applied magnetic field and colloidal status, and therefore the ease of manipulation.



Magnetic beads employed in biomedical applications are made out of a core of magnetic material encapsulated in a polymer shell. Functional groups on the polymer surface permit chemical derivatization of magnetic particles. This chemical derivatization process allows the conversion of magnetic particle to binding agent with specificity (by linking agents with specificity to the beads).

Biomedical applications

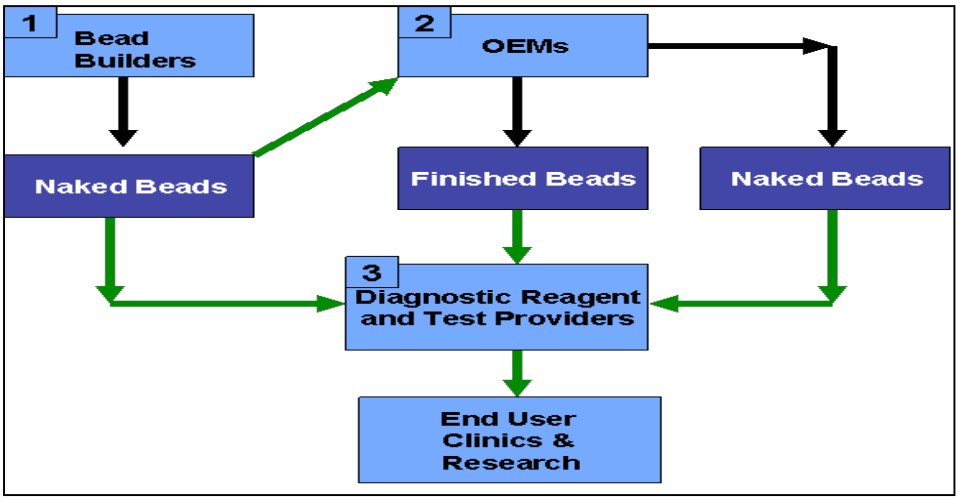
Techniques based on using magnetic particles have found numerous applications in the biomedical field, specifically clinical diagnostics, drug targeting, cell isolation and purification, and nucleic acid purification and detection, the most common of which is immunoassays on clinical laboratory analyzers.



Market size

Currently, magnetic beads are the most widely used solid phase for automated methods for isolation and detection of biomolecules and are the most common solid phase in immunoassay diagnostic kits used in automated clinical laboratory analyzers. Nine of the top 10 *In-vitro Diagnostic* companies employ magnetic particles in their fully automated analyzers. According to latest data available, binding tests (immunoassays and molecular tests) represent one third of the clinical testing market, a global market estimated at $42

billion in 2008. Biological material is attached to magnetic particles makes them specific capture reagent for the analyte under testing on these analyzers.

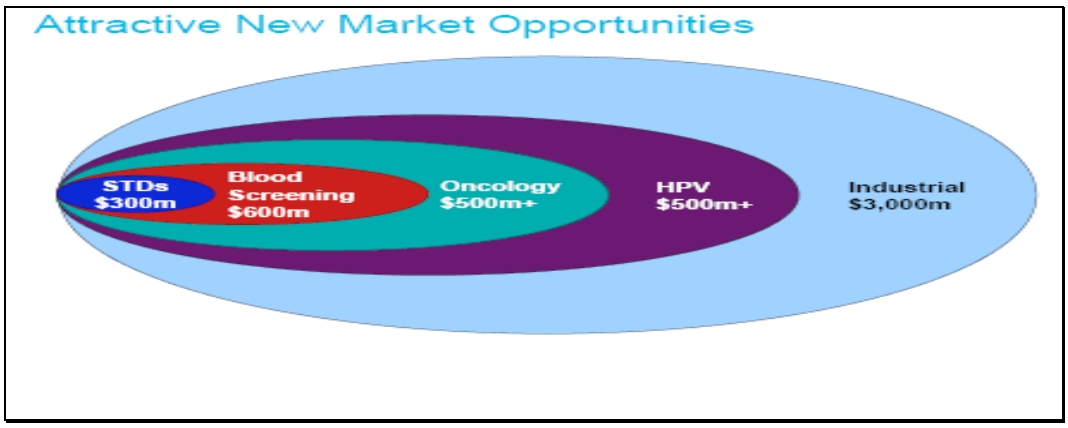


Although the exact figures of the magnetic particles market size are hard to determine with high accuracy. A market research report calculated the market size of paramagnetic beads to range about $1 billion for immunoassays and molecular diagnostics. An independent research report (by Adventus Research Inc.) funded by National Research council has estimated the current market for magnetic beads for immunoassays and molecular diagnostics to be about $1 billion (between 833 million to 1.3 billion).

According to Dynal, a leading manufacturer of magnetic beads, the largest part of its Molecular Systems' business is OEM sales of magnetic bead to IVD companies. Dynal stated that "the IVD market is very large, and still growing. However, the magnetic bead-based part of this market is growing at an even higher rate per year". According to Dynal, immunoassays make up more than USD 4 billion of the IVD market, and magnetic beads are now the golden standard, as opposed to older technologies. Nucleic acid testing makes up a smaller portion of the IVD, USD 2 billion, but is fast growing, magnetic beads also the most common solid phase employed in this market.

According to Dynal, end-user business goes to research and routine laboratories within Genomics, Expression Profiling and Proteomics. The market size for Genomics, including DNA and RNA extraction and purification products was USD 300 million in 2001 while the market size of Pharmacogenomics was estimated to be USD 2.3 billion.

Gen-Probe, a leading nucleic acid testing company, states that other markets that are employing magnetic beads are growing also. Further, magnetic particles are used for Separation of Microorganisms in Food and Water Testing and also for HLA Diagnostics.



Source: Gen-Probe presentation- May 2006

Several companies produce magnetic beads, both naked and finished product (linked to biological reagents). The top bead producers are Dynal, which was acquired by Invitrogen, Merck Estabor, Bang Laboratories, Seadyne and Qiagen.

A list of all global suppliers of magnetic beads is included.

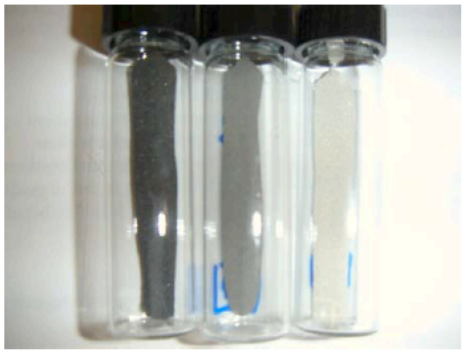
- Dynal Inc.(Lake Success, N.Y.);
- Merck Estabor, FR;
- Seradyn Inc. (Indianapolis, Ind.);
- Bangs Laboratories (Fishers, Ind.);
- Spherotech Inc. (Libertyville, Ill.).
- Advanced Magnetics Inc. (Surrey, U.K.);
- CPG Inc. (Lincoln Park, N.J.);
- Cortex Biochem (San Leandro, Calif.);
- Promega (Madison, Wis.);
- Ferrofluidics Corp. (Nashua, N.H.);
- FeRx Inc.; (San Diego, Calif.);
- Immunicon Corp. (Huntingdon Valley, Pa.);
- Magnetically Delivered Therapeutics Inc. (San Diego, Calif.);
- Micromod Partikeltechnologie GmbH
- Miltenyi Biotec GmbH;
- Microcaps GmbH (Rostock, Germany);
- PolyMicrospheres Inc. (Indianapolis, Ind.);
- PureBiotech, LLC; and
- Scigen Ltd. (Kent, U.K.).

CardioGenics Magnetic Beads

CardioGenics proprietary magnetic beads are targeted to improve testing sensitivity. The proprietary magnetic beads are light colored and are optimized for collecting light signals in binding tests. The light colored magnetic beads are covered with a thin layer of silver and are available in various sizes from 1 to 50 micron. The magnetic beads are then covered with a functionalized polymer shell for chemical drivitizaion. The polymer shell is needed for linking biological material to the metal core. A simplified process to manufacture these beads was developed.

A proprietary color conversion by silver-plating process was developed and adapted to magnetic beads of various sizes. Through proprietary electroless silver-plating, black magnetic beads are converted to silver-colored beads. As shown, the thickness of the silver layer is controlled and optimized in order to control the surface reflectivity and in the mean time not to impede the beads magnetic moment. Through know-how, the process was optimized to magnetic beads of various sizes.

With the support of several National Research Council (NRC) grants, the electroless silver plating process was optimized and adjusted to beads of various sizes. The batch size was scaled up to commercial lot sizes. Currently, the lot size is 300 grams of silver coated magnetic beads a day by a single technician. The lot size could also be scaled up to higher amounts, if required.



During a 24 months development process and 4 NRC grants, large amount of data and expertise on beads stability have been acquired. Although the developmental process was extended more than planned, the end results of testing have confirmed the quality of the developed beads and their value in increasing test sensitivity. CardioGenics magnetic beads are employed in its QL Care analyzer and also will be commercialized as a stand alone product.

The white colored magnetic beads are coated silver layer of thickness that has no effect on magnetic moment of the beads. The beads magnetic material is about 80% to ensure a quick magnetic response for ease of manipulation. The plated silver layer is very stable to various solutions of high salt. No deterioration, peeling or loss of either the silver or polymer layers in high salt solutions. The coated layers are stable in various buffers for up to 12 months with no evident ion leakage as assessed by various enzymes with different ion sensitivities.

Competitive advantage

Current commercial manufacturing processes are labor intensive, expensive and require sophisticated and specialized equipments. Due to the manufacturing costs, commercial beads range in prices from $900 – 1500 per gram of solids.

CardioGenics magnetic particles are offered in sizes, functional groups similar to other commercialize magnetic beads. Although similar in some aspects, CardioGenics

magnetic particles differ from the commercial magnetic particles in several fundamental aspects, which could be summarized as follows:

1. Light collection optimization.

CardioGenics magnetic beads are light in color and were developed specifically for light collection measurements. Due to the minimized adsorption of generated light, the collected signal is several folds improved in comparison to black beads coated with the same polymer using the same procedure. This is evident at various sizes as well as when the light is generated off the surface of the beads as occurs in binding tests or in the surrounding environment. Further, the signal collection improvements are consistent at various levels of light.

CardioGenics beads were tested along side commercial magnetic beads from various suppliers. Without correcting for size variances (surface area) or density of the functional surface groups, CardioGenics beads consistently showed improved signal. In comparison to commercial magnetic beads from the top 4 suppliers, CardioGenics beads showed several folds improvements of at least 4 folds in the collected light signal. Further, this improvement in collected light was not associated with an increase in the background signal.

2. Other improved characteristics include:

- High magnetic moment and easy manipulation
- Hydrophilic surface – optimal specific and very low background
- Chemically robust surface chemistry
- Simplified manufacturing process – less costly