

Medical Devices Sector
Core activities: Haemodynamic monitoring
Core area of activity: Global
Listing: London AIM (LID.L)

LiDCO Group plc



With the introduction of the 'easy to use', non-invasive LiDCORapid the company is poised to make a material assault on the global market for haemodynamic monitoring.

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I certify that this report represents my own opinions.

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Key Points

24 April 2008
Price: 7.75p

With the introduction of the 'easy to use', non-invasive LiDCOrapid haemodynamic monitor (HDM), the company is poised for a period of further rapid revenue growth which should lead it to profitability within the next 12 months. With it we believe that LiDCO can make a material assault on the global HDM market that we estimate at some £1.2 billion annually – and rising.

- **LiDCOrapid will be the driver for the next few years**

The introduction of this easy to use, non-invasive, continuous cardiac output device along with enabling disposable patient cards should drive the company's revenues for the coming years.

- **Competitive positioning of the new product is superb**

There is nothing else in the market to rival the ease of use, reliability and accuracy of the **LiDCOrapid** particularly as it pertains to the operating room before and during surgery.

- **Clinical validation of the underlying algorithm is what clinches it**

The wealth of clinical data and inherent reliability of measurements made with the underlying **PulseCO** software combined with a proprietary nomogram-based database should make this an easy sell where an accurate trend of cardiac output is required.

- **Operating Room (OR) use should be extensive**

The need for a device which can assist the anaesthetist in managing the patient pre- and intra-operatively is increasingly in demand as positive patient outcome and hospital cost data accumulates to say that such aggressive intervention and patient management is warranted; we see a further role for this device in driving therapy in the ICU.

- **LiDCOplus should continue to make inroads**

While its near-term growth rate may suffer from the introduction of **LiDCOrapid** we believe that in the medium to long term, this instrument should continue to make inroads in the market both in its own right but also spurred on by its presence in this market.

- **LiDCOlive networking product later in FY09 should complete the picture**

The addition of a remote monitoring capability through PC's, laptops and other portable devices from monitors operating in the ICU should become a longer term driver for LiDCO's product line.

- **Revenues projected to be up 24% and loss reduced by circa 33% in FY09**

We are projecting revenue growth acceleration and operating loss reduction based on the new product launch. In FY2010 and beyond, LiDCO should be profitable on our projections.

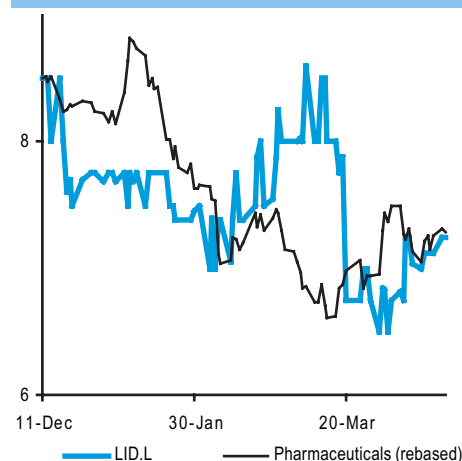
- **Clear upside to our numbers is evident**

Our core valuation at 13p is significantly higher than the current stock price. However, it is based on a 'minimum' execution scenario. Our more optimistic model yields a valuation at 26p based on more effective marketing execution and we think that there is considerable upside to this as well.

- **Execution, as always, is the key factor here**

Continued clinical and outcomes/cost benefit validation are key to modifying current hospital acute/critical care patient HDM practice and achieving upside in the longer run. In the short run, performance will be driven by the effectiveness of LiDCO's sales and marketing efforts. We believe that the network being put in place should be able to drive revenues in a way that makes our valuation objectives achievable.

Price chart (£)



Current fair value of equity

Core scenario	£18.7m
Value per share	13p
Optimistic scenario	£37.0m
Value per share	26p

Company details

Quote	
Shares	
-London AIM	LID
Hi-Lo last 12 mos. (p)	13.81 - 6.25
Shares issued (m)	141.9
Fully diluted (m)	150.6
Market Cap'n (£m)	11.0
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LiDCO Group plc is a UK-based medical device company specialised in instrumentation and associated disposables enabling the continuous measurement of cardiac output in critically ill patients. It has developed a proprietary, indicator dilution-based method (based on Lithium) for deriving an accurate measure of cardiac output. This measure is then used to calibrate a monitor that uses the arterial waveform derived from commonly used blood pressure monitors to measure cardiac output on a continuous basis.

This minimally invasive cardiac output technology uses signals that are generated through catheters that are routinely used in the critical care setting obviating the insertion of additional devices.

The company has just introduced a novel, proprietary, non-invasive continuous monitor that measures trends in cardiac output and other derived haemodynamic parameters. This device should find extensive use in pre- and intra- surgery, assisting the anaesthetist in making therapeutic adjustments to maintain the patient in an appropriate haemodynamic state. In the second half of fiscal year 2009, the company expects to release a server-based networked capability to enable remote viewing of live haemodynamic monitoring data by clinical personnel.

LiDCO markets and sells these products through the combination of a direct sales force in the UK and US and a network of distributors outside of the UK.

Together, these products provide LiDCO with a powerful platform to assist physicians in achieving better clinical outcomes (through the reduction of morbidity and mortality) and the hospital with lower costs (through less complications and a reduced length of stay). In an era, of fixed reimbursement healthcare, these are the ingredients required for a successful medtech product.

Launch of the LiDCOrapid™: the beginning of a new era for LiDCO

Having learned from earlier missed forecasts, the company has decided to offer a sobering, conservative view of its near term prospects. A significant shortfall in revenues was experienced in fiscal 2007 when sales were delayed in the US by the vigorous competitive actions of Edwards Lifesciences to prevent the company from making further inroads into the market with LiDCO*plus* and the inability of its Japanese distributor to progress in Japan absent reimbursement. This background, and the subsequent action of its stock, has made the company a bit gun shy and accounts for its conservative stance with the launch of LiDCO*rapid*. We believe that although the company is prepared to convey its excitement about the prospects of its products, the guidance that is being given to investors masks, to some degree, what is about to occur in the HDM market. The launch of this new product into the hospital surgery and ICU market has the potential to trigger a period of exceptional growth for LiDCO. It will also lead, in 2010, to the emergence of a profitable company after many years of red ink. The LiDCO*rapid* is the refined version of the company's technology, based on market needs, and the provisioning of proprietary, innovative, reliable and accurate technology.

Potential for market penetration enhanced by improved costs and outcomes

Our read of the medical literature and discussions with clinicians and distributors have convinced us that the need for technology that enables better outcomes and lower hospital costs is pervasive throughout healthcare systems globally. As a result, we believe that **LiDCOrapid** could make quick and deep inroads in the 'convenience' cardiac output market in acute and even critical care patients. The simplicity with which highly useful data can be generated and monitored fits 'hand in glove' with the current clinical view that better patient haemodynamic management leads to better outcomes and lower costs. This device enables this in an 'easy to use', 'plug in and get started' way.

LiDCOplus should continue to make inroads into the 'calibrated' market

It is likely that calibrated absolute cardiac output generated methods will not disappear that quickly. The Swan-Ganz catheter, an invasive, age-old technology for measuring absolute cardiac output, while declining, is still a significant presence in the market; old habits die hard. While in some hospitals it is getting increasingly difficult to learn how to use one of these, inertia keeps that market going until a better solution comes around. LiDCO's technologies based on the PulseCO software, offer a minimally or non-invasive option. The LiDCOplus, while it is training-intensive, offers an alternative. As positive clinical, outcome and cost data enhance its visibility it has continued to make significant inroads into the ICU market. With the advent of the LiDCOrapid it is possible to envision the latter as both a marketing and clinical stepping stone towards the LiDCOplus.

LiDCOview and LiDCOlive complete the product line in very useful ways

LiDCOview™ provides a data interface to export data for further analyses, to feed other algorithm-based protocols (diagnostic or therapeutic) and for training purposes. While still early stage, it could be the basis for future enhancements of LiDCO's monitor capabilities. The LiDCOlive™ is a networking and remote access capability, to be launched in the second half of fiscal year 2009. It provides treating physicians, nurses and ICU heads with the ability to keep abreast with what is going on with patients on an ICU ward through a PC, laptop or other portable devices at a remote location. We believe that this could be a significant future driver for the development of LiDCO's monitor business.

Positive peer comparison

A recent independent review from a Danish group has also favourably compared the LiDCOplus technology to other technologies tested for their usefulness in goal directed therapy.

It's all about execution stupid!

We believe that the key to this story will be in management's execution of a robust sales and marketing plan to drive penetration in these markets. The team has considerable experience and, arguably, benefits from historical disappointments and mishaps that it has experienced along the way. Under the able guidance of the CEO and Head of Marketing, we believe that the plan in place should enable a successful drive to greater inroads. The convergence of market dynamics and faltering competitive products, are increasingly opening doors for LiDCO that were previously closed. The addition of LiDCOrapid to that mix could turn a

small opening into a floodgate if the execution of the plan is competently carried out. By the end of fiscal 2009, LiDCO should have around 90 pairs of feet on the ground selling its technology into the hospital. While the sales to be booked in the remainder of this year are likely to remain modest, this will set the stage for a potential acceleration in placements and disposables from fiscal 2010 on.

The dynamics of the HDM market are changing

Although inertia is a fact of life in medical markets, we think that a confluence of factors could mean that we are in for a change. Much of hospital-delivered care is moving towards acute and critical care as more and more beds are dedicated to the services that cater to the critically ill. Unacceptable levels of mortality and morbidity continue to be experienced when the complications that are the trigger can often be avoided by better haemodynamic management of the patient.

The cost implications are evident in an era of fixed cost reimbursement where clinical outcomes and costs are increasingly taking a role in the choices of technology made by both hospitals and clinicians. Better haemodynamic monitoring has been pegged as a means to improve both outcomes and costs in various clinical settings. LiDCO's technology is enabling in this regard and assuming that our competitive analysis is correct, the company will have only execution to blame if it is unable to seize the opportunity.

LiDCO's competitive characteristics in guiding fluid administration in goal-directed therapy

	PAC	OD	MF	PiCCO	LiDCO	CVC(S _v O ₂)	NIRS	GT	MD	Imp	TOE
Strategy											
Challenge	✓	✓	✓	✓	✓	✓	✓	✗	✗	✓	✓
Responsiveness	(✓)	✗	✗	✓	✓	✗	✗	✗	✗	✗	✓
Practicability											
Precise	✓	✓	(✓)	✓	✓	?	?	✓	✓	?	✓
Safe	(✓)	✓	✓	(✓)	✓	(✓)	✓	✓	✓	✓	✓
Easy											
Interpretation	✓	✓	✓	✓	✓	✓	✓	✗	✗	✓	✗
Installation	✗	✓	✓	✗	✓	✓	✓	✗	✗	✓	✗
Minimal Skills	✗	✓	✓	✗	✓	✓	✓	✗	✗	✓	✗
Non-invasive	PAC	min	(✓)	fem.a./CVC	a.	CVC	✓	min	rec/s.c.	✓	min
Promptness of changes	✓	✓	?	✓	✓	?	?	✗	✗	?	✓
Stability of signal	✓	✗	(✓)	✓	✓	✓	✗	?	?	?	✗
Period											
Pre-op.	✗	✗	✓	✗	✓	(✓)	✓	✗	✗	✓	✗
Intra-op.	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Post-op.	✓	(✓)	✓	✓	✓	(✓)	✓	(✓)	(✓)	✓	(✓)

a., arterial line; Challenge, fluid challenge strategy; CVC, central venous catheter; fem. a., femoral arterial line; GT, gastric tonometer; Imp, thoracic impedance; Intra-op., intra-operative; LiDCO, Lithium dilution cardiac output method; MD, microdialysis; MF, Modelflow; min, minimally invasive; NIRS, near-infrared spectroscopy; OD, oesophageal Doppler; PAC, pulmonary artery catheter; PiCCO, pulse contour cardiac output method; Post-op., post-operative; pre-op., pre-operative; rec/s.c., placement of probe in rectal lumen or subcutaneous cannula; Responsiveness, fluid responsiveness strategy; S_vO₂, venous oxygen saturation; TOE, trans-oesophageal echocardiography; ✓ suitable; (✓), practicable with limitations; ✗, unsuitable; ?, evidence missing.

Source: ACTA Anaesthesiologica Scandinavica

The HDM market is a complex one to model. It encompasses three areas of the hospital where there are potential targets for the application for LiDCO's technology: the emergency room (ER), operating room (OR) and intensive care unit (ICU). We have not modeled any applications for the ER as these are not clear at this time. We have also not modeled the LiDCO*live* as the business model of this product has not been secured by the company itself and may ultimately be bundled with LiDCO*plus* and LiDCO*rapid*.

Our modeling, in all cases, begins with the US market where there is more reliable data from sources such as the Center for Disease Control (CDC), the Society of Critical Care Medicine (SCCM) as well as other sources in the medical literature. We have extrapolated to other regions of the world by assuming a relatively standard percentage for each region. We have assumed the US represents about 38% of the world market and Europe, with the emerging European countries and Russia, another 42%. For the purposes of this analysis, we have split out the UK (where LiDCO has a direct sales effort) which represents about 6.4% of the global market.

Our estimates for product revenue in the ICU market are based on what we believe to be conservative assumptions. As an example of our reasoning, we have assumed that around 3 LiDCO*rapid* disposable kits will be sold per month per monitor in each of ICU and surgery. We have kept this relatively constant in both the ICU and surgery model and have assumed a constant price and a plateauing number of salespeople after 2011. Our more aggressive model assumes the number of kits is around 4 per monitor per month, a slightly more realistic model. The effect of increasing the number of kits sold per month per monitor in the ICU and the OR by only one would be to increase the valuation by 13p. Given past disappointments, we prefer, at this juncture to err on the very conservative side and see how the market for this new product develops.

This conscious low-balling of the market potential must also be seen within the context that the overall market potential for LiDCO*rapid* is probably in the range of just under £1 billion. This potential market is unlikely to be achieved by any product but given that our 2019 projection for total LiDCO*rapid* is around £18 million in our core scenario and £24 million in our more aggressive one, we are not asking the company to take over the world in order to achieve our valuations (both core and optimistic). As indicated above, it is easily possible to envisage double or triple the potential in a scenario that more realistically reflects what we believe the uptake of such a product could be. In surgery, we believe that an uptake of disposables in the range of 2-3 a day (48-72 a month) is certainly possible if the use of HDM and GDT became more widespread in an effort to improve morbidity and mortality outcomes and lower hospital costs. If that were the case, the resulting disposables numbers are too big to contemplate. Either way, when compared to the total market, this all represents fairly modest market penetrations.

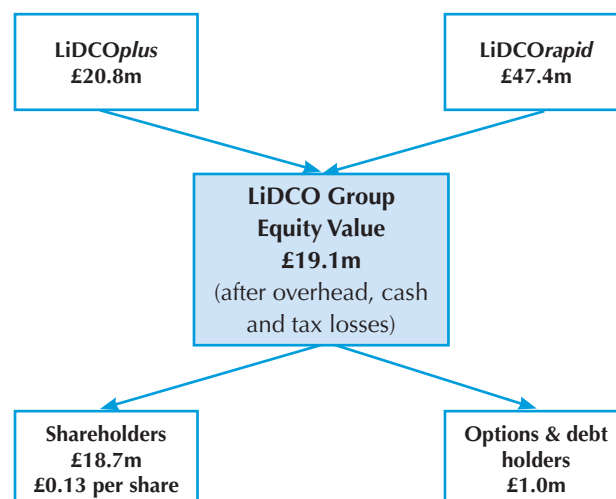
Based, *inter alia*, on these assumptions, our core and optimistic scenarios produce valuations of around 13p and 26p; a material premium to the recent share price. We attribute this discount to the historic lack of profitability, previous mis-steps in regard to milestones, the impression of its market position conveyed by its quoted competitors and, most of all in our view, the significant reduction in risk appetite by investors in general.

Our analysis suggests a turning point over the next 12-18 months based on the introduction of the new product (LiDCO*rapid*) added to a growing base of business (LiDCO*plus*) and leveraged by the disposables business. Furthermore, our projections of sales growth, which we view as very conservative in nature, assume only modest penetration into what is a potentially significant market (£1 billion). How much of this upside can be achieved will be driven by further clinical validation and outcomes/cost benefit studies, the ability to affect current hospital practices in HDM with acute and critical care patients and, last but definitely not least, the ability of LiDCO to create an effective marketing push.

Fair value summary (£m)

Product	Scenario	
	Core	Optimistic
LiDCOplus	20.8	27.9
LiDCOrapid	47.4	58.6
Less: overhead	53.8	53.8
Expected value of products	14.3	32.6
Add: other assets	3.2	3.2
Add: starting cash + new funds	2.2	2.2
Total current value for firm	19.7	38.0
Less: bank & other debt	0.6	0.6
Total value to equity claims	19.1	37.5
Less: warrants	0.4	0.4
Ordinary equity holders	18.7	37.0
Value per share (£)	0.13	0.26

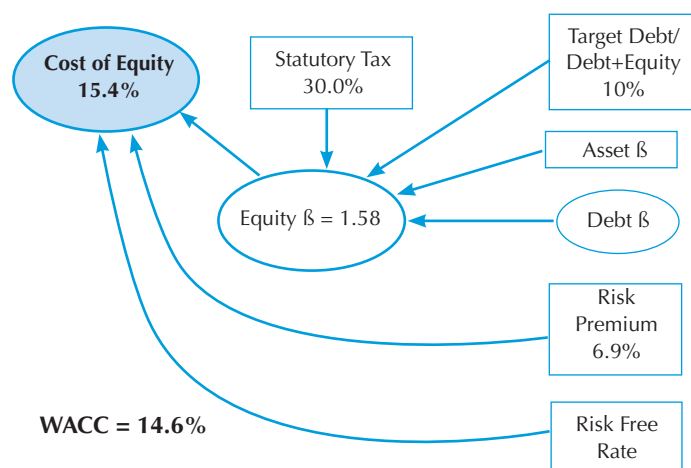
Components of LiDCO's entity value



Comparable companies

	Symbol	Market capitalisation (in millions)	Shares outstanding (in millions)	Price	Revenues latest (in millions)	Cash equivalent (in millions)	Cash/ share	Market Cap to sales
Edwards LifeSciences	EW:NYSE	\$2,733.0	56.7	48.21	\$1,090.0	\$191.2	3.37	2.5
Criticare Systems	CMD:AMEX	\$68.2	12.3	5.53	\$31.4	\$3.8	0.31	2.2
Enteromedics	ETRM:NASDAQ	\$61.2	16.3	3.76	\$0.0	\$57.0	3.50	NA
LiDCO	LID:AIM	£11.2	144.0	0.0775	£4.1	£2.0	0.01	2.8
Deltex	DEMG:AIM	£21.7	92.5	0.24	£4.2	£2.0	0.02	5.2
Lombard Medical	LMT:AIM	£111.2	643.0	0.17	£1.0	£2.7	0.00	110.1
Optos	OPTS:AIM	£96.4	69.4	1.39	£86.0	£21.0	0.30	1.1
Pulsion	PUS:FSE	€ 56.1	9.6	5.85	€ 28.3	€ 5.4	0.57	2.0
USCOM	UCM:ASX	\$7.7	38.6	0.20	\$1.2	\$3.1	0.08	6.5

Weighted cost of capital



Inability to build a successful distribution network to better access the global market

The company has already built a significant presence in the UK and US through a direct salesforce and continues to build its distribution in the US, Europe and the rest of the world. However, the key to achieving the deep market penetration that it has targeted, in a way that is affordable for a company of its size, requires the building of an effective distributor network. The company has already tried to do so but its distributors were acquired by a Japanese company. The success of this endeavour is crucial to our investment thesis.

LiDCO's capital constraints leave little room for error particularly if pitted against its main competitor

LiDCO's primary competitor in the acute/critical care market is Edwards Lifesciences, a company with over \$1 billion in sales. While LiDCO has been able to tap the market when necessary, it is operating (by choice) within a limited capital environment which leaves it open (as it was in fiscal year 2007) to frontal attack by Edwards. On a pure product basis, LiDCO's product is in our opinion vastly superior to Edward's competitive offering but it remains vulnerable to such attacks from its well capitalised competitor.

Fighting clinical practice inertia in hospitals can be a big mountain to climb

With the LiDCO*rapid*, the company needs to be able to persuade anaesthetists, intensivists, relevant nurses and other key hospital personnel that the clinical and economic rationale for this novel technology creates better clinical outcomes for the patient and lower costs for the hospital. The rationale for such a profile looks like it could be quite strong. Because the LiDCO*rapid* is based on the PulseCO algorithm (also the core of the LiDCO*plus*), the positive outcome data generated by this technology should be equally applicable. The measurements made by these two products are based on the same principles. From a therapeutic point of view, the goal of delivering fluids and drugs to optimise haemodynamic parameters should be the same as well. However, few if any prospective and comparative studies have been conducted with this new product and its effect on outcomes and costs is unknown at this time. Hence, convincing doctors and nurses to use the technology requires effective marketing and somewhat of a leap of faith.

Defining the best uses for its products remains unfinished business

While LiDCO has an excellent track record at generating quality clinical data on the best use of its technology, the business of building validation for its technology and making sure that it is implemented in appropriate subpopulations of patients is the key to its ultimate success. It continues to encourage opinion leaders to generate this kind of data. There remains much to do to achieve full penetration in these markets and our numbers only skim the surface of the potential for these products. More training and clinical data will be needed to overcome the perception that these products are for 'niche' applications.

In the final analysis, it is all about execution at this point

The biggest risk here remains execution. The management of LiDCO will have learned much in getting the company to where it is today. We believe that the company is on the cusp of a breakthrough with LiDCO*rapid* and has come up with a more convenient way of tackling its market through this new offering. However, previous execution issues have shown the company the path forward and, in a capital constrained environment, the ability to bring to fruition an effective marketing push is paramount. LiDCO's past experience should serve it well in achieving profitability in the coming 12-18 months and increases the chances of success.

LiDCO Group plc was co-founded in 1991 by entrepreneurs Terry O'Brien and Robert Linton along with Dr David Band and other scientists at St Thomas's Hospital, Kings College London. The company has developed innovative technology in minimally invasive haemodynamic monitoring of cardiac output, along with associated intellectual property, based on two platforms:

- LiDCO, a lithium dilution-calibrated measurement of absolute cardiac output and
- PulseCO, an algorithm that can calculate (amongst other parameters) absolute cardiac output based on a continuous measurement of arterial pressure waveform measured using standard arterial and venous catheters that are routinely inserted into high-risk, critical care, surgical patients.

Data is then displayed on user-friendly screens (which makes up the **LiDCOplus** monitor) for easy interpretation.

LiDCO's development has been driven by the perceived need to replace invasive monitoring systems (e.g., the Swan-Ganz pulmonary arterial catheter) with a less-invasive one. The monitoring of blood pressure, cardiac output and oxygen delivery is central to assessing the cardiac and metabolic state of high-risk surgical and other critical-care patients: it acts as an early warning system and can guide both fluid and drug therapy.

Traditionally, only highly invasive monitoring systems were available to monitor these parameters in critically ill patients. The invasiveness is part of the reason why physicians and skilled nurses have preferred not to use such systems to monitor patient status. In more recent times, the advent of less invasive monitoring systems, and the demonstrated efficacy of haemodynamic monitoring (or HDM), have been shown to improve clinical outcomes (lowering both morbidity and mortality) in peri-operative surgery patients.

Additionally it has been shown that such therapy can lower the overall cost of the patient and shorten the length of stay in the hospital. Based on these findings, there is renewed interest in employing HDM further enhanced by the advent of less-invasive technologies such as the ones developed by LiDCO.

The required criteria of accuracy combined with convenience and user-friendliness along with excellent outcomes data is clearly evident in the company's product line. To a significant extent, the **LiDCOplus** product fulfils required criteria although the need to draw blood while performing the indicator dilution measurement is training intensive and reduces the convenience factor.

Lithium sensor



Source: LiDCO

It also suffers partly from the commercial disadvantage of being compatible with existing, thermodilution devices in common use. While this triggers a user fee, it has lowered the throughput of disposable kits and the 'razor/razor blade' commercial potential of the platform to date. The new **LiDCOrapid**, based on the **PulseCO** algorithm combined with a proprietary database of normative patient data, generates what we view as a non-invasive platform¹ that is extremely convenient and very user-friendly. Although it does not measure absolute cardiac output (which in many cases is not needed anyway), its ability to estimate it and follow trends in haemodynamic parameters and fluid, makes it widely suitable for the surgical and acute care markets.

Two other products complete the overall product line. One is called **LiDCOview** that is a viewing and analysis tool that enables the use of **LiDCOplus** and **LiDCOrapid** data for further review, research and training. This has important ramifications for supportive clinical research and the potential to trigger other useful clinical applications. The final product, to be launched in the second half of 2008, is the **LiDCOlive** which enables the delivery of live data to PC's, laptops and other portable devices of treating physicians or attending nurses remotely within the hospital or in remote locations via existing networks.

LiDCO sales and marketing strategy

One of the major barriers to success is the ability to put enough marketing muscle on the ground. At clinical meetings, LiDCO has no problems generating marketing leads. The key objective for 2008 and beyond is to put enough feet on the ground to translate those and other leads into actual sales.

The second task is to translate the placement of instruments into sales of associated disposables. To achieve this, LiDCO is putting in place a 2-tier marketing effort with company-employed sales specialists to market directly and to train selected distributors. In calendar 2008, the company plans to have around 90 sales people on the ground in all relevant territories.

In FY 2008, the company strengthened its distribution in Canada, Turkey, Israel and Saudi Arabia. In the US, it employs a direct sales force of 4 selling to hospitals and is poised, along with training staff, to develop a network of distributors in FY 2009. With this nascent sales and marketing platform, the company is aiming to achieve significant market penetration particularly with the recently launched **LiDCOrapid** product.

¹ From a regulatory point of view this would be categorised as a minimally or less invasive technology. However, as it uses measurements into a blood pressure through venous and arterial lines that would be there anyway, no additional invasion is performed so we believe that it is fair to call this technology 'non-invasive'

In the UK, where it has an established direct sales force it has recently begun collaborating with Becton Dickinson to jointly market its products alongside BD's critical care range in selected NHS trusts.

In Europe, a network of distributors (with the exception of France, Germany and the Netherlands) has been created as it has in other regions of the world.

Following this strategy, LiDCO estimates that, in fiscal 2009, it will have around 90 sales people covering the globe. Of those it expects 10 to be direct (6 in the UK and 4 in the US) and the rest will be distributors. The ramping up of this distribution network will be the key driver to market penetration. In fact, we would say that any limitation on growth comes from the number of people on the ground that can be deployed to market and sell these products.

At two recent clinical conferences (the annual ISICEM meeting in Brussels and the WCA meeting in Cape Town), LiDCO's booth was buzzing with activity as the company displayed its new *LiDCOrapid* platform. In the end, the company came out of these meetings with over 500 marketing leads. Even with the current capacity, the company will have a hard time following up on all of these in the current fiscal year. These sales are highly technical and require demonstrations, leaving equipment behind for the physician to try out...etc.

While we expect that the sales cycle for the *LiDCOrapid* will likely be shorter than that for the *LiDCOplus*, it is based on a new concept and might require some missionary selling. However, because it is relatively non-invasive, it is also very easy to try out. We believe that the key to sales in this area will be in getting the user to understand the benefits of the HDM parameters in terms of outcomes and costs.

Manufacturing overview

Life could not be simpler when it comes to manufacturing. The company combines outsourced, customised hardware manufacturing with internal software inputting and the manufacturing of its proprietary lithium sensor.

The latter is manufactured in batches that are carefully quality controlled in house. The production of the sensor is highly automated in a process that is scaleable (multiple shifts and additional machines) at a relatively low cost. The monitors are manufactured in Taiwan and can be obtained with lead times of three months in any quantity desired. LiDCO tend to have six months of inventory on hand to ship to customers and distributors from its facility in Hoxton, London. In the US, LiDCO use a logistics company to warehouse and ship product to customers. The *LiDCOrapid* data card is manufactured in Cambridge. It can be obtained in any quantities required pretty much on demand.

Overview of HDM-relevant clinical sub-markets

The key market segments involve critically ill and high-risk patients for whom maintaining proper fluid balance and oxygenation of tissues is crucial to clinical outcomes. First it is important to know that although cardiac output monitoring has wide applicability within the context of high-risk patients, the main benefits of the technology are believed to be fundamental to the management of those patients who are being treated with inotropic and vasoactive drugs.

The concept of outcomes in clinical medicine is complex and generally adapted to the type of disease one is analysing. In critically ill patients a wide variety of complications have the ability to influence the degree of morbidity and mortality that is observed. As it is not the purpose of this report to teach a course in clinical medicine, we will focus on the salient issues that are relevant to the deployment of HDM technologies in peri-operative high-risk surgical patients, without attempting to be exhaustive.

How do patients get to the hospital and which ones are likely to be monitored for CO and other haemodynamic parameters? Often, patients can come through the emergency department as a result of trauma, pneumonia, or a cardiac/stroke event. They will receive whatever immediate treatment is required and are then sent to surgery, the ICU (intensive care unit), the CCU (cardiac care unit), the general ward or simply discharged from the hospital.

While in the ER, some patients may require resuscitation or stabilisation through fluid supplementation or vasoactive drug treatment but generally will only be put on standard blood pressure monitors, ECG, pulse oximetry and the like until stabilised and moved on to the next phase. While the ER could be a target for minimally or non-invasive HDM, those patients that go to surgery or to the ICU are the main target population at this time.

A recent study has shown improved survival, outcome and costs following an early aggressive resuscitation protocol, using a combination of fluid and vasoactive drug supplementation guided by central venous SO_2 (or $S_{cv}O_2$) and pulse oximetry in the emergency room in patients presenting with septic shock.² However, current practices in the ER appear not be open to such sophisticated GDT at this time.

The second, and most important population, are elective/scheduled surgical patients. As we shall see it is in this population that HDM and GDT have been shown to improve outcomes and overall patient cost.

Fixed reimbursement, outcomes and cost reductions

In an era of ever expanding healthcare costs based on the greying of the population driven by baby boom demographics, many countries (the US and Japan are prime examples) have capped the cost of treating a patient for a particular condition. Fixed reimbursement is limited to whatever the governmental health authorities have decided for each condition so that the hospital is incentivised to aim at a cost of treatment that is within or below these parameters.

² Rivers E et al. (2001) *New Engl. J Med.* **345**:1368-77

To increase its profitability (or simply to work within a budget and avoid losses), a hospital where such issues matter, will attempt to minimise complications (which require additional treatment and associated costs) and reduce the length of stay. It is within this context that any technology shown to improve clinical outcomes (e.g., reduction of complications) and reduce the length of stay in the hospital, is or should be welcome.

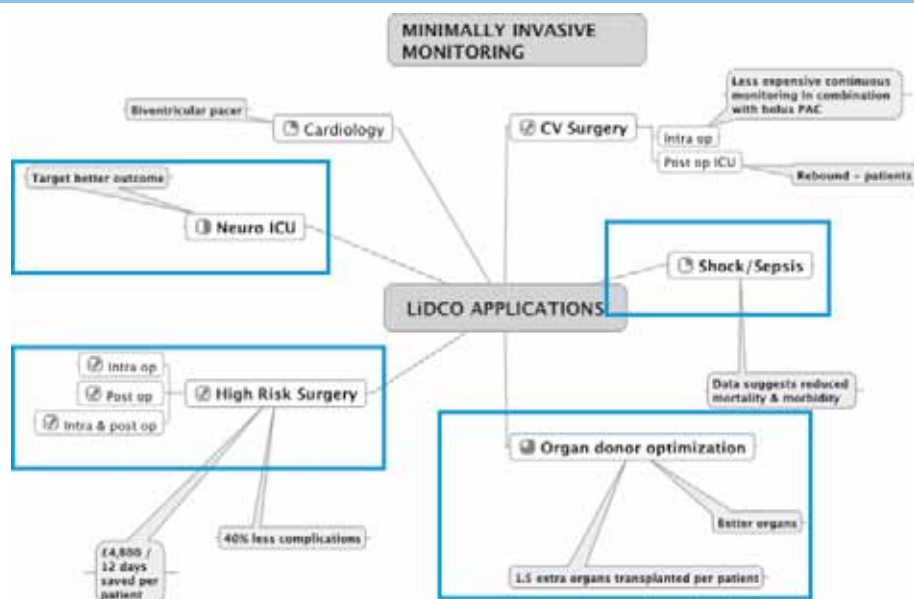
HDM and GDT: improved outcomes and lower costs

The main function of HDM is to monitor the flow of blood and enable therapies that enable the transport of adequate oxygen to tissues. The inability to do so is almost always the result of various forms of circulatory shock. These range from the above mentioned hypovolaemic shock, cardiogenic (heart dysfunction), obstructive (pulmonary embolism or cardiac tamponade) and distributive (septic, anaphylactic and neurogenic) shock.

The ability to determine when and how to treat these conditions through fluids or drug (inotropic, vasoactive or other) is the key objective. Hence defining the state of the patient through HDM provides a guide to the appropriate therapy. In surgery, a patient under anaesthetics will require careful monitoring to adjust the level of anaesthetic (regulating the depth of anaesthesia), the level of fluids or drugs required and the cardiovascular status of the patient.

In recent times, a considerable body of work has been directed at determining whether the traditional standardised fluid supplementation and medical treatment protocols result in optimised care of high-risk surgical patients. A recently applied protocol has been developed based on using cardiac output and similar parameters to guide intravenous fluid and inotropic/vasoactive³ therapy. Traditionally, patient-characteristics along with standardised fixed fluid and drug therapy have been employed to manage the cardiovascular well-being of high-risk patients in surgery and in the ICU.

Minimally invasive monitoring



Source: LiDCO

³ Inotropic drugs are used to increase the force of muscular contractions and vasoactive drugs focus on dilating or constricting blood vessels with a direct effect on blood flow.

It is now believed that the early use of CO targeting and maintenance through what is called Goal-Directed Therapy or GDT improves general outcomes for such patients and generally reduces the overall cost of major surgery through the reduction of complications and resultant morbidities.

Whether GDT adjustment of fluids and blood volumetric pressure is required at each stage of the patient's stay in a hospital (from arrival in the ED through to the ICU and step-down) is still open for debate in the clinical community⁴. Nevertheless, for high-risk surgical patients, it has been shown in various studies that haemodynamic optimisation of high-risk surgical patients can reduce complications and morbidity and reduces the length of hospital stay⁵.

A landmark single-centre study conducted by Professor Bennett (a consultant to LiDCO) and colleagues demonstrated that early; post-operative GDT in high-risk surgical patients resulted in reductions in complications and duration of hospital stay⁶. It is therefore fair to say that continuous cardiac output (CCO) monitoring of the type delivered by LiDCO (and doppler as well) has been shown to benefit patient outcome, hospital length of stay and leads to the reduction in the overall cost of major surgical intervention when targeted appropriately.

During the surgical intervention itself, the need for monitoring the haemodynamic status of a patient and the use of GDT during the intervention has been shown in multiple studies to improve gut function, reduce post-operative nausea and vomiting (PONV), morbidity and hospital stay⁷. Although these studies were primarily conducted using Oesophageal Doppler, the principle is likely to be the same for any comparable CCO technology that can accurately measure absolute CO or its trend. The recently introduced LiDCO*rapid*TM product is squarely aimed at exploiting this GDT opportunity with an easy to use 'trending' device which can also accept calibrated, absolute CO measurements from other devices where required.

In conclusion, early HDM monitoring and the tailored management of CO using patient-specific GDT-optimised fluid and drug therapeutics has been shown to improve outcomes and lower hospital costs⁸. With the advent of GP-directed care and outpatient procedures over the past 25 years, a steadily increasing proportion of hospital resources and beds are being dedicated to emergency, surgical, cardiac and intensive care for critically injured or ill patients. As a result, the market for equipment serving these markets has been very dynamic indeed.

⁴ see Harvey S. et al. (2006) *Health Technology Assess. Vol 10*, 29

⁵ for review see Bundgaard-Nielson, M, et al. (2007) *Acta Anaesthesiol. Scand.* 51 (3): p 331-340

⁶ Pearse R. et al. (2005) *Critical Care*, 9:R687-R693

⁷ Bundgaard-Nielson, M, et al as above

⁸ for review see Pinsky M. *Critical Care* 10:p117

Overall market dynamics

The HDM market is driven by a number of factors including:

- ageing population increasing demand for critical care;
- the rising number of ICU beds in hospitals;
- capped cost procedural reimbursement is increasingly adopted globally;
- the drive to lower the cost of hospital care and reduce length of stay;
- a focus on outcomes;
- the shift away from invasive technologies to less-invasive technologies.

These factors make for a very dynamic market situation and the market growth seen in 2007 is highly indicative of that. Despite the well documented weaknesses in the technology, Edward's *FloTrac/Vigileo* sales doubled (from circa \$15 million to over \$30 million). We believe that much of this growth has been built on the strength of Edward's reputation for product excellence rather than on the data behind the technology.

Our market intelligence, based on our own discussions with clinicians, indicates that they are beginning to look for alternatives. Even if this is the case, we doubt that it will show this early in the sales and growth figures. Deltex's CardioQ grew 20% in 2007, as did LiDCO's.

Clearly hospitals are buying this equipment but will there be follow-through in the sales of related disposables? It is one thing to sell the underlying equipment to a distributor or a hospital and book the sale; it is another to begin clocking a disposable revenue stream upon which the real dynamics of this business can be built. So, what is the size of the opportunity and how does it best get exploited?

Market size

The market for HDM is relatively hard to estimate. There are not any easily interpretable statistics (other than mortality statistics) to differentiate between surgical/ICU patients that will require HDM and those that are unlikely to need it. We would argue that most surgical procedures where total anaesthesia is used and where the patient is known to have cardiovascular risks and/or is of a certain age, would benefit from HDM.

However the reality is that at this stage, HDM is not commonly used, as there is no simple non-invasive way to do so. Enter the relatively non-invasive *LiDCOrapid™* which we believe has the potential to achieve a significant penetration of the OR market. The ICU market is a different matter – the *LiDCOplus* is training-intensive and therefore will require an expensive marketing effort to make significant in-roads.

We have estimated a potential US market size, based on US CDC⁹ surveys, and from there we have extrapolated to what the global market might look like. To achieve this we have made estimates of target sub-surgical markets and looked at the number of ICU's, beds and estimates of utilisation to arrive at an estimate for the global surgical and the ICU markets priced in LiDCO product terms. There is, of course overlap between the two because a percentage of surgical patients (non day surgery and non-critical) end up in the ICU post-op. We have extrapolated these US numbers to the global market.

These estimates show that the potential standalone surgical market for LiDCOrapid™, based on the number of OR's in the US and the number of procedures per day in the average OR, is just over US\$404 million which translates into a \$1.1 billion or a £540 million market. Even a modest market share could make a material difference to LiDCO.

Estimate of LiDCOrapid-relevant US surgical procedures

in 000's	2004	2008	2009	2010	2011	2012	2013	2014
Total number of surgical procedures	45,000	48,709	49,684	50,677	51,691	52,725	53,779	54,855
CABG	466	504	515	525	535	546	557	568
Other vascular bypass	160	173	177	180	184	187	191	195
Cerebrovascular procedures	150	162	166	169	172	176	179	183
GI surgery (ex-endoscopy)	2,629	2,846	2,903	2,961	3,020	3,080	3,142	3,205
Orthopaedic procedures	1,634	1,769	1,804	1,840	1,877	1,914	1,953	1,992
Total	5,039	5,454	5,563	5,675	5,788	5,904	6,022	6,143
As a % of total	11.2%	11.2%	11.2%	11.2%	11.2%	11.2%	11.2%	11.2%
Data from CDC NCHS data-2004 survey								
Number of hospitals	4,927							
Number of beds	802,000							
Average number of OR's	5							
Average beds/OR	40							
Number of operating rooms	24,635	25,635	25,892	26,151	26,412	26,676	26,943	27,212
Number of procedures/OR/day	5	5	5	5	5	5	5	5
Number of operating days/week	6	6	6	6	6	6	6	6
Number of OR's/instrument	2	2	2	2	2	2	2	2
Total number of procedures (in 000's)	38,431	39,991	40,391	40,795	41,203	41,615	42,031	42,451
Average cost per LiDCOrapid kit	\$120	\$120	\$120	\$120	\$120	\$120	\$120	\$120
Average cost of LiDCOrapid monitor	\$6,000	\$6,000	\$6,000	\$6,000	\$6,000	\$6,000	\$6,000	\$6,000
Total potential OR instrument market (monitors)	12,318	12,818	13,210	13,614	14,031	14,461	14,903	15,360
Total US market for LiDCOrapid monitor (in \$m)	\$74	\$77	\$79	\$82	\$84	\$87	\$89	\$92
Total est. US disposables market (in \$m)	\$302	\$327	\$334	\$340	\$347	\$354	\$361	\$369
Total US potential LiDCOrapid market (\$m)	\$376	\$404	\$413	\$422	\$431	\$441	\$451	\$461

Source: US CDC, LiDCO and Objective Capital estimates

⁹ Center for Disease Control

Potential LiDCOrapid global market									
(US\$m)	2008	2009	2010	2011	2012	2013	2014	2015	2016
Global LiDCOrapid monitor market									
US	\$77	\$79	\$82	\$84	\$87	\$89	\$92	\$95	\$98
UK	\$13	\$13	\$14	\$14	\$15	\$15	\$16	\$16	\$16
EU (ex-UK)	\$72	\$74	\$77	\$79	\$81	\$84	\$86	\$89	\$92
ROW	\$15	\$16	\$16	\$17	\$17	\$18	\$18	\$19	\$20
Global total	\$202	\$209	\$215	\$222	\$228	\$235	\$243	\$250	\$258
Global LiDCOrapid disposables market									
US	\$327	\$334	\$340	\$347	\$354	\$361	\$369	\$376	\$383
UK	\$55	\$56	\$57	\$58	\$60	\$61	\$62	\$63	\$65
EU (ex-UK)	\$307	\$313	\$319	\$325	\$332	\$339	\$345	\$352	\$359
ROW	\$172	\$176	\$179	\$183	\$186	\$190	\$194	\$198	\$202
Global total	\$861	\$878	\$896	\$914	\$932	\$951	\$970	\$989	\$1,009
Potential total global market	\$1,064	\$1,087	\$1,111	\$1,135	\$1,161	\$1,186	\$1,212	\$1,239	\$1,267
In £'s (at and exchange rate of £1=\$1.97)	£540	£552	£564	£576	£589	£602	£615	£629	£643

Source: US CDC, LiDCO and Objective Capital estimates

On the ICU side, the numbers are just as spectacular. We have split this market 20%/80% in favour of **LiDCOrapid™** versus **LiDCOplus™** as we believe from discussion with experts that a non-invasive HDM monitor will find favour in the ICU. Nevertheless, we believe that there are clinical situations (septic shock is one) where absolute CO measurements will be important; hence the split. On the basis of ICU beds, we estimate the total market for a **LiDCOplus™**-type market for monitors and associated disposable is around US\$505 million (£256 million) worldwide. Our estimated **LiDCOrapid™**-type total potential ICU market is approximately US\$723 million (£367 million).

Hence the overall market potential for both instruments and disposables in both the surgical and the ICU markets for LiDCO's products is £1.2 billion. We believe that these estimates are conservative because we have not taken into account the differences in utilisation between the US and Europe, for example, where the ratio of nurses to beds is close to 1:1 and the US where the ratio is closer to 4:1.

Also, clinical practices in emerging markets are less tied to age-old dogmas and more amenable to technologies of this kind. We have not estimated any serious penetration or growth here and have assigned a rather standard market share for those markets. We have also not taken into account the potential for ER applications.

Having said all of this, we believe that it is unlikely that either of these products will achieve such a potential in the near term. The reason has little to do with the usefulness or efficacy of the measurements being made and the improved outcomes and costs that are generated. Rather it is more to do with market inertia

related to clinical practice. The widespread penetration of this market is highly dependent on translating the data achieved in clinical trials into 'best medical practice' in the eyes of anaesthetists, surgeons and intensivists.

For that to occur, a whole new generation of clinicians needs to be taught the why's, when's and where's of HDM and the ensuing outcome and costs benefits that its use generates. To be sure, the market is already quite dynamic as witnessed by the significant growth rates of Edwards Lifesciences, Deltex, Pulsion and LiDCO with revenue growth rates in the 20%-50% range. With the advent of the **LiDCOrapid™** it is possible that the world of HDM is about to change.

Potential US ICU market for LiDCO products

	LiDCOplus		LiDCOrapid						
	in \$ 000's		in \$ 000's						
	2007		2008	2009	2010	2011	2012	2013	2014
Number of ICU's ⁽¹⁾	6,000		6,120	6,242	6,367	6,495	6,624	6,757	6,892
Number of ICU beds ⁽¹⁾	88,000		89,760	91,555	93,386	95,254	97,159	99,102	101,084
Number of pure ICU beds ⁽¹⁾	52,800		53,856	54,933	56,032	57,152	58,295	59,461	60,651
Number of beds per nurse	4		4	4	4	4	4	4	4
Beds per monitor	4		4	4	4	4	4	4	4
Total ICU monitors	13,200		13,464	13,733	14,008	14,288	14,574	14,865	15,163
LiDCOplus		2,640	5,386	5,493	5,603	5,715	5,830	5,946	6,065
LiDCOrapid			10,560	8,078	8,240	8,405	8,744	8,919	9,098
Average price LiDCOplus	\$20,000	\$52,800	\$107,712	\$109,866	\$112,064	\$114,305	\$116,591	\$118,923	\$121,301
Average price LiDCOrapid	\$8,000		\$84,480	\$64,627	\$65,920	\$67,238	\$68,583	\$69,955	\$71,354
Frequency of use/monitor/week									
LiDCOplus		2	2	2	2	2	2	2	2
LiDCOrapid			5	5	5	5	5	5	5
Yearly usage									
LiDCOplus		104	104	104	104	104	104	104	104
LiDCOrapid			260	260	260	260	260	260	260
Total usage per annum (000's)									
LiDCOplus		275	560	571	583	594	606	618	631
LiDCOrapid			2,746	2,100	2,142	2,185	2,229	2,274	2,365
Average cost per LiDCO kit									
LiDCOplus		\$150	\$150	\$150	\$150	\$150	\$150	\$150	\$150
LiDCOrapid			\$100	\$100	\$100	\$100	\$100	\$100	\$100
Total potential market/disposables (\$m)									
LiDCOplus		\$41	\$84	\$86	\$87	\$89	\$91	\$93	\$95
LiDCOrapid			\$275	\$210	\$214	\$219	\$223	\$227	\$232
Total potential US market		\$94	\$359	\$294	\$300	\$306	\$312	\$318	\$331

⁽¹⁾ SCCM

Source: SCCM, LiDCO data and OC estimates

Estimate of the potential global LiDCOplus and rapid ICU markets

Monitors (\$m)		2008	2009	2010	2011	2012	2013	2014	2015	2016
LiDCOplus										
US	38%	\$108	\$110	\$112	\$114	\$117	\$119	\$121	\$124	\$126
UK	6%	\$18	\$19	\$19	\$19	\$20	\$20	\$20	\$21	\$21
EU (ex-UK)	36%	\$101	\$103	\$105	\$107	\$109	\$111	\$114	\$116	\$118
ROW	20%	\$57	\$58	\$59	\$60	\$61	\$63	\$64	\$65	\$66
Total	100%	\$283	\$289	\$295	\$301	\$307	\$313	\$319	\$326	\$332
LiDCOrapid										
US	38%	\$65	\$66	\$67	\$69	\$70	\$71	\$73	\$74	\$76
UK	6%	\$11	\$11	\$11	\$12	\$12	\$12	\$12	\$13	\$13
EU (ex-UK)	36%	\$61	\$62	\$63	\$64	\$66	\$67	\$68	\$70	\$71
ROW	20%	\$34	\$35	\$35	\$36	\$37	\$38	\$38	\$39	\$40
Total	100%	\$170	\$173	\$177	\$180	\$184	\$188	\$192	\$195	\$199
Disposables (in \$m's)										
LiDCOplus										
US	38%	\$84	\$86	\$87	\$89	\$91	\$93	\$95	\$97	\$98
UK	6%	\$14	\$14	\$15	\$15	\$15	\$16	\$16	\$16	\$17
EU (ex-UK)	36%	\$79	\$80	\$82	\$84	\$85	\$87	\$89	\$90	\$92
ROW	20%	\$44	\$45	\$46	\$47	\$48	\$49	\$50	\$51	\$52
Total	100%	\$221	\$226	\$230	\$235	\$239	\$244	\$249	\$254	\$259
LiDCOrapid										
US	38%	\$210	\$214	\$219	\$223	\$227	\$232	\$237	\$241	\$246
UK	6%	\$35	\$36	\$37	\$38	\$38	\$39	\$40	\$41	\$41
EU (ex-UK)	36%	\$197	\$201	\$205	\$209	\$213	\$217	\$222	\$226	\$231
ROW	20%	\$111	\$113	\$115	\$117	\$120	\$122	\$124	\$127	\$130
Total	100%	\$553	\$564	\$575	\$587	\$598	\$610	\$622	\$635	\$648
Global Markets										
LiDCOplus monitors & disposables		\$505	\$515	\$525	\$535	\$546	\$557	\$568	\$580	\$591
LiDCOrapid monitors & disposables		\$723	\$737	\$752	\$767	\$782	\$798	\$814	\$830	\$847
Grand total		\$1,227	\$1,252	\$1,277	\$1,302	\$1,329	\$1,355	\$1,382	\$1,410	\$1,438
Global market in £'s (at £1=\$1.97)		£623	£635	£648	£661	£674	£688	£702	£716	£730

Source: company data and Objective Capital estimates

Products and Technologies

Haemodynamic Monitoring: a key to better hospital care outcomes

The basics

The amount of oxygen delivered to organs in the human body is fundamental to life itself. In humans, oxygen is delivered to organs via a protein called haemoglobin in the blood.

The amount of oxygen that can be delivered to organs is thus a function of the volume of blood circulating through our bodies. Hence, the reduced circulation of blood volume in the body, also known as hypovolaemia, can result in oxygen insufficiency, trigger tissue damage, and a whole host of complications leading to extensive morbidity and, in some cases, a significantly increased level of mortality.

In the acute hospital setting, where critically ill patients are treated, the management of fluids (to counteract dehydration) and the volume of blood flowing to organs in the body using pharmacological management (through vasoconstrictor/vasodilators for example), is central to the management, treatment and well-being of such patients.

Haemodynamics is the study of forces that drive the circulation of blood. Haemodynamic monitoring, or HDM, originated in the cardiac catheterisation experiments of Dr Werner Forssmann in the 1920's (which he performed on himself!). Those were followed by the development of haemodynamic monitoring itself in the 1940's by Dr Dickinson W Richards and Dr Andre Cornand enabling the use of catheterisation to measure blood pressure inside the veins, arteries and in the heart. For this work, all three physicians were awarded the 1956 Nobel Prize for Medicine.

Through the quantification of cardiac output, haemodynamic measurements are crucial to the management of critically ill patients. Any severe fluctuation in blood flow can have devastating effects on the patient's ability to survive the necessary treatments to overcome the short-term (acute) conditions that afflict them.

In critical care patients, sporadic and spontaneous increases in demand for oxygen (or vice versa, the presence of excess oxygen) require medically driven adjustments that are essential to successful patient outcomes. The response to increased oxygen demand somewhere in the body is usually met through arterial oxygen and requires increased cardiac output. Many critically ill patients may have disorders that prevent the heart's ability to respond which would then trigger a secondary reserve of venous oxygen.

However, when oxygen supply becomes inadequate, even briefly, tissue damage may arise. Hence one of the primary objectives in the management of critically ill patients is to prevent such tissue hypoxia. Multi-parameter HDM enables the prophylactic management of oxygen flow to prevent organ hypoxia, which in turn has a direct impact on the success of critical care therapeutics. Often, critically ill patients are also patients that undergo surgery. As we shall see, HDM is particularly important in the management of patients intra- and post-operatively.

Invasive to minimally invasive monitoring: what to measure?

The current standard for haemodynamic monitoring, against which any new technology is measured, involves the invasive insertion of a pulmonary artery catheter into a major vein (either the internal jugular or subclavian) via an introducing sheath. A Californian-based cardiologist called H.J.C. Swan developed this balloon-tipped catheter in the 1970's.

When combined with the work of William Ganz, who had worked out a thermodilution method (using a cold saline solution at a defined temperature) for measuring cardiac output, the Pulmonary Artery Catheter (PAC) or Swan-Ganz catheter (SGC) was born and is extensively used to this day.

However, the use of this type of catheter, and its more modern version, is in decline. SGC's suffer from complications such as infection, cardiac tamponade, (where fluid accumulates in the pericardium and elevates pressure) embolism (occlusion) and arterial rupture. The latest version, involving the use of heating

coils, was developed to enable continuous cardiac output monitoring but its design has triggered further potential complications. In one case the patient required a cardiac transplant to repair the damage.

This SGC and its associated monitoring system, developed and sold by Edward Lifesciences, was the subject of a recent lawsuit against the company based on the damage inflicted in the above patient. It has become evident from this episode that faulty software was able to trigger an overheating of the coils and damage the tissue with which it came into contact. While the software problem has been fixed and the instrument upgraded, this product (called Vigilance) is in decline as doctors seek to replace it with less invasive and more truly continuous cardiac output monitoring techniques.

The emergence of less invasive HDM

Despite the position of SGC as a 'gold standard' for cardiac output measurement, the aforementioned potential complications of this type of procedure has triggered the emergence of a series of less invasive techniques for measuring CO. We will deal with each technology as relevant to a full analysis of the competitive market situation confronting LiDCO in its objective to attain a dominant position in the HDM market.

Doppler ultrasound

The oesophageal insertion (through the mouth) of an ultrasound-tipped catheter to measure real-time continuous cardiac output is a relatively common invasive technique. Oesophageal doppler combines doppler measurements (which measures blood velocity) with a nomogram¹⁰ to derive a measure of cardiac output.

This technique (of which Deltex's CardioQ is a prominent example) has a number of reported shortcomings:

- in order to obtain a reliable signal, it requires a skilled operator to position it so as to get a precise maintenance of the angle of alignment with the Descending Thoracic Artery (DTA) to which it is proximal. That can be difficult to achieve in a breathing/moving (non-ventilated) patient hence its applicability tends to be limited to surgical patients under total anaesthetic;
- while its proximity to the blood flow of the DTA makes for a highly validated measurement, it does not represent the true Q, i.e., the true CO;
- it is susceptible to signal interruption in surgical procedures where (rather commonly) electrocautery is used;
- it loses accuracy in patients who have received an epidural for pain management, fairly common in high-risk abdominal surgery;
- its use tends to be limited to anaesthetised surgical patients where a rapid temporal evaluation of a validated measurement such as this is useful;

¹⁰ A nomogram is a specially designed formula that uses a database of age, gender, size, weight data characteristics to calculate cardiac parameters in a particular patient

- as patients age the space for insertion of such a probe into the oesophagus becomes more and more restricted to the degree that in roughly 20% of the patients, a signal cannot be obtained¹¹. This has implications for the propensity to use this technology with the attendant risk that the measurement might fail, the need for a backup technology and the cost implications that ensue from a wasted procedure.

CardioQ is also able to measure extravascular lung water although the usefulness of this measurement from a diagnostic point of view is subject to debate and controversial at this time.

Partial Carbon Dioxide (CO₂) rebreathing

In this technology, the patient inhales his or her own exhaled carbon dioxide through the mouth. From the carbon dioxide produced by the body, and using a form of Fick calculation, it is possible to calculate an absolute value cardiac output in a totally non-invasive fashion.

However, this technique is impractical in critically ill patients, as it requires a skilled operator and the co-operation of the patient for reliable results. In a surgical situation, where a ventilator tube has been inserted, it is possible to calculate absolute CO values and to observe its trend (although every 3 minutes) which can be useful particularly in unstable patients. We have witnessed this technology being used in conjunction with LiDCO*rapid*TM in a relatively routine peripheral vascular bypass operation by an anaesthetist.

The combined measurement (along with depth of anaesthesia and cerebral blood oxygenation measurements) assisted him in anticipating the patient's needs for neuromuscular blockers, vasoactive drugs and analgesics while keeping the patient anaesthetised at a desired level aid in an haemodynamically acceptable state.

Partial Carbon Dioxide re-breathing technology is embodied in the NICO system sold by Respironics (recently acquired by Covidian). We believe that this device has achieved limited market penetration. Furthermore, we are not convinced that the additional calibration from this technique is commonly necessary.

Calibrated Pressure Waveform technologies

PiCCO (Pulsion Medical Systems AG, Munich Germany)

This technology uses arterial pulse pressure waveform analysis to calculate continuous cardiac output. It requires calibration using a transpulmonary saline thermodilution method measuring temperature differences from a central venous to a central arterial line and a modified Stewart-Hamilton calculation to generate the Q (Cardiac Output) required to calibrate the Arterial PP contour for continuous Q analysis.

While less invasive, it is not considered to be as accurate as the PAC methodology (it overstates CO versus the latter) and does usually require the additional placement of an invasive femoral or axial arterial catheter. However, the main problem is that the equipment used is complex to operate, given the need for a femoral arterial catheter, and so requires an expert operative (usually a doctor). In Germany, Austria and Switzerland, where the doctor is intimately involved in the management of the patient, this technology has found extensive usage.

¹¹ Personal communication from an anaesthetist

LiDCOplus (LiDCO Ltd, London, England)

The Lithium dilution technology requires peripheral or central venous and arterial lines that are usually already in place. This technology uses a sensor to measure the lithium concentration which, using a modified Stewart-Hamilton calculation, can be converted into Q. This Q measurement can then be used as calibration for LiDCO's PulseCO software that calculates continuous cardiac output through the analysis of the arterial waveform derived from the arterial blood pressure trace.

These two technologies have been combined into a product called the **LiDCOplus™** monitor as a minimally invasive replacement for PAC/thermodilution measurements. The LiDCO/PulseCO instrument embodied in the **LiDCOplus™** configuration has been shown to correlate well with intermittent and continuous CO measurements using PAC and thermodilution.

This is the only pressure waveform technology to have shown a demonstrable improvement in patient outcomes and a reduction in hospital length of stay.

Uncalibrated Pulse Pressure technology

FloTrac/Vigileo (Edwards Lifesciences Inc, USA)

This technique uses a standard arterial catheter that is placed in the mid-flow portion of either the radial or femoral artery. The catheter connects to a pressure sensor (called a FloTrac pressure transducer) that measures the arterial pressure waveform, which it relays both to the main blood pressure monitor and separately to the Vigileo.

Arterial Pressure Cardiac Output (APCO) measurements are based on the principle that aortic pulse pressure is proportional to stroke volume (SV) and inversely proportional to aortic compliance (a measure of arterial wall stiffness). However, for this to be accurate, changes of both a natural and pharmacological nature resulting from variability within a patient and from patient to patient must be taken into consideration.

The FloTrac sensor measurements are fed into an algorithm combined with patient-specific parameters (age, gender, height and weight) to compensate for these differences. However, studies published in the medical literature suggest a lack of correlation between this type of measurement and those derived from PAC/thermodilution, particularly with changes in vascular tone¹².

LiDCOrapid (LiDCO Ltd, London, England)

LiDCO has recently introduced a new technology aimed primarily at the acute care market (e.g., OR). The **LiDCOrapid™** is an uncalibrated 'plug in and measure' instrument that captures the arterial waveform via a simple cable connection to the vital signs monitor (itself connected to a pressure transducer catheter that is standard in all operations).

¹² There is considerable medical literature on this product but *Lorsomradee S et al (2007) Anaesthesia* 62: 979-983 is pretty representative of these studies

Using the PulseCO algorithm, this pressure measurement is then converted into a measure of stroke volume (SV) and Heart Rate (HR) that can then be converted in CO. That in turn is scaled to the patient's own characteristics (gender, age, height and weight) using a proprietary database constructed from extensive analyses using the calibrated LiDCO-based instruments.

By measuring the trend in CO (rather than the absolute CO value), the **LiDCOrapid™** can then act as an early warning sign for additional fluid or drugs to achieve optimal haemodynamic status.

Non-Invasive technologies

This includes a whole set of other technologies which use **Near-Infrared Spectroscopy (NIRS)**, changes in electrical impedance (**Impedance Cardiography** or **ICG**) and MRI amongst others. While all of these are valid methods of CO measurement, they often lack practicality (as in the case of MRI) or consistency and accuracy as in the case of NIRS and Impedance Cardiography.

A new technology has emerged which uses a novel form of monitoring related to ICG. A company called **Cheetah Medical Inc.** out of Israel has devised a novel technique combining traditional impedance with measurements of amplitude and frequency of electrical impulses. Bioreactance technology yields a signal to noise ratio some 100-fold greater than the older bioimpedance measurements. NICOM as it is called¹³ has been tested in a variety of settings (peri-operative, ICU, CCU, step-down, doctor's office...etc). In the peri-operative/ICU setting, it has been shown to correlate well with a CCO measurement with PAC/thermodilution as a reference and using the +/-30% range of limits of acceptability (LOA) empirically proposed¹⁴ for cardiac output.

The technique, when operating correctly seem to be more precise than thermodilution and haemodynamic changes were tracked faster than the latter. The sensitivity of the technology to detect significant directional changes was 93% and the specificity 95%. Overall, the technology seems to display the accuracy, responsiveness, and reliability in detection of CO directional changes that could make it a useful non-invasive technology. However, to date it has undergone only limited testing in a particular type of cardiac surgery patient in the ICU/CCU setting and will require much more robust data to achieve wide clinical acceptance.

Conclusion

In conclusion, our analysis of the available technologies suggests LiDCO's technology are highly competitive. A further independent analysis was published by a group in Denmark which looked at the use of HDM technology to drive GDT. Most of the available technologies were reviewed and the conclusions were summarised in a table that we have reproduced on page 6.

¹³ Non-Invasive Cardiac Output Monitoring

¹⁴ Critchley L.A. and Critchley J.A. (1999) A meta-analysis of studies using bias and precision statistics to compare cardiac output measurement techniques. *J. Clin. Monit. Comput.*, 15:85-91

LiDCO's product offering is based on two distinct technology platforms:

- a lithium dilution-calibrated measurement of absolute cardiac output and
- an algorithm that can calculate (amongst other parameters) absolute cardiac output based on a continuous measurement of arterial pressure waveform measured using standard arterial and venous catheters that are routinely inserted into high-risk, critical care, surgical patients.

To grasp the relative merits of this technology versus its competitors, it is important to understand the:

- clinical context within which these technologies are used;
- ease of use and integration into current clinical practice;
- value it has in driving therapy and the potential it has to improve patient outcomes and lowering hospital costs.

Clinical context

There are three areas where HDM monitoring has been shown to be useful in the monitoring and treatment of critical care patients:

- early intervention/resuscitation in the ER;
- early use in major, high-risk surgery;
- post-operatively following such surgery¹⁵.

While not universally proven in each clinical situation, the use of cardiac output and other haemodynamic parameters (such as central venous saturation oxygen concentration or $S_{cv}O_2$ and arterial pressure¹⁶) is deemed to be the essential data required to make goal-directed therapy or GDT effective.

Positive effects on outcomes (morbidity and mortality) and costs have been demonstrated in multiple studies using multiple HDM technologies⁸.

The ability to further demonstrate the correlation between the use of HDM measures and outcomes and costs is a powerful driver leading to even wider use of the technology. In this regard, the **LiDCOplus** instrument performs to spec and measures up well against the PAC/thermodilution gold standard while offering a much less invasive CO measurement. Its use is essentially targeted to the ICU where absolute CO measures might be required in certain patients.

The **LiDCOrapid** instrument is an easy to use, rapid 'plug and use' device connected to the standard blood pressure monitor. It can measure the trend in CO and various other parameters to assist the anaesthetist to maintain a surgical patient in an optimised haemodynamic state through fluid and pharmacological dosing during the operation.

¹⁵ for review see Pinsky MR. *Critical Care* (2006) 10:p117

¹⁶ along with total body oxygen delivery- DO_2 -and consumption- VO_2 which can be measured from non-invasive pulse oximetry data

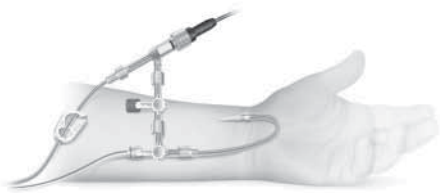
Ease of use and integration into clinical practice

Another important element leading to the greater adoption of HDM in general, and LiDCO's technologies in particular, is the ease with which they can be set up. Using the routinely present arterial and central venous lines in this category of patient or by plugging into routinely used catheters, no additional non-routine steps (other than lithium calibration with the **LiDCOplus**) need to be made.

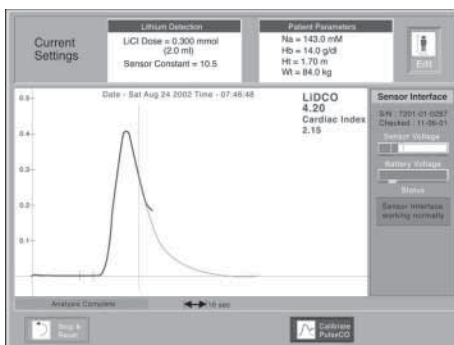
Injecting lithium intra-venously and drawing blood from a peripheral arterial line to make the sensor-based measurement is needed to calibrate the **LiDCOplus** instrument. This does require training and adds an additional step in ICU/CCU settings where the ratio of nurses to beds might be anywhere from 1:1-3.

In the operating theatre, the **LiDCOrapid** is simply plugged into the anaesthetist's routine blood pressure monitor. It adjusts for the characteristics of the patient, estimates a level of CO and begins to monitor. The trend will then detect any significant changes in haemodynamic status and guide the anaesthetist's actions as regards the supplementation of fluids and vasoactive drugs.

The LiDCO System™



Lithium sensor placed on the arterial line



Lithium dilution curve on LiDCOplus screen



Central/peripheral LiCl injection

Source: LiDCO

Value in driving therapy and outcomes

Several recently published reviews⁸ find it increasingly evident that GDT can result in better outcomes and lower overall hospital costs for certain types of critical care patients and situations.

The ability to measure absolute HDM parameters within a range of accuracy compared to the gold standard of PAC/thermodilution using the less invasive **LiDCOplus** enables early GDT in the major, post-operative, surgical setting and has been shown to reduce complications and the duration of stay in the hospital¹⁷. The advent of the **LiDCOrapid**, enables haemodynamic optimisation using a simple device that also takes advantage of the arterial pressure waveform available from arterial catheters already in place.

LiDCO products

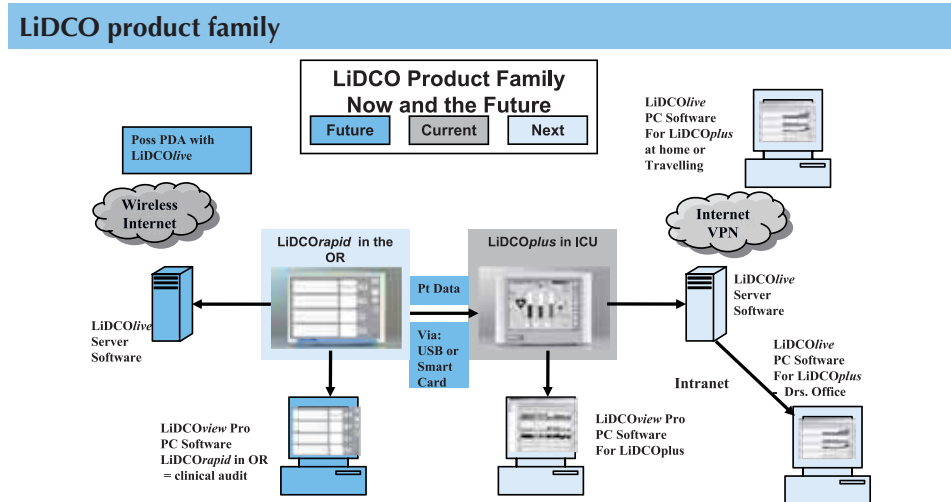
LiDCOplus™ monitor

Product technology

This product combines the company's two technology platforms: LiDCO and PulseCO. The reference voltage measurements derived from the LiDCO system generate a 'wash out' lithium concentration curve which is converted into an absolute Cardiac Output level in the LiDCO monitor software. This calibrated level is then used by the **PulseCO™** algorithm, in the **LiDCOplus™** monitor, as a base CO so as to yield a continuous CO derived from the arterial waveform analysis.

The **PulseCO™** software uses the arterial blood pressure trace, following calibration, to calculate a continuous 'beat-to-beat' measure of CO. This software derives a nominal stroke volume and heartbeat duration which, when calibrated with the LiDCO measurement, yields actual stroke volume and absolute CO value.

The screen presents a user-friendly graphical display of all pertinent data. This display combines all of the key parameters (CO, DO₂I, Left Ventricular Stroke Volume or SV, etc) required for monitoring at a distance by the nurse.

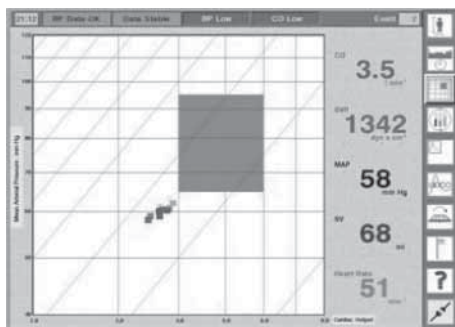


Source: LiDCO

¹⁷ Pearse R. et al. (2005) *Critical Care* 9:R687-R693

LiDCO graphical interface

Graph Screens



Depicts a screen where the user set haemodynamic targets for flow and pressure are compared against actual patient values that are graphically displayed

Trend Screens

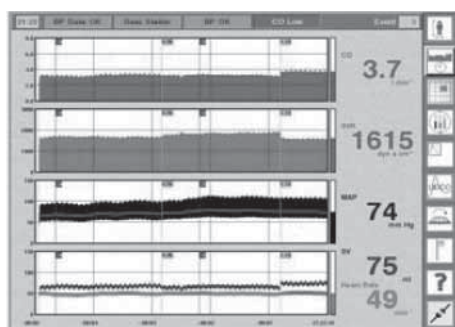
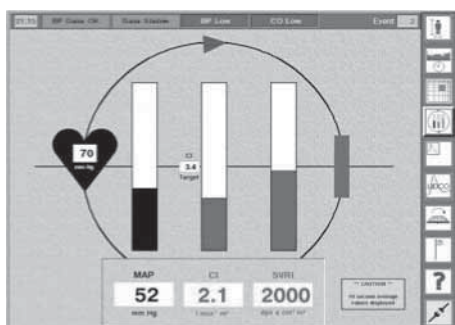


Chart Screens



Depicts the midline target and measures patients actual pressure flow and resistance measures while looking at the interrelation between these

Source: LiDCO

It is also possible to look at a historical trend for all parameters (CO, CI, Systemic Vascular Resistance or SVRI, SV, etc) over several hours or minutes. This allows an assessment of responses to medical therapy (fluid challenge, drugs or other interventions). The **LiDCOplus™** can be combined with CO from thermodilution catheters to calibrate the PulseCO.

All of this equipment can be integrated to deliver a continuum of information to monitor the progress of the patient during a hospital stay. LiDCO's vision of how this would work is depicted in the accompanying diagramme.

Clinical usage and data

The **LiDCOplus** instrument has been tested extensively in different settings (peri- and intra- operative) and in a wide variety of critically ill patients. It has been rigorously measured against the gold standard of PAC/thermodilution against which it performs well within the Limits of Agreement parameters (LoA at +/- 30%) set empirically using what is called a Bland-Altman analysis (statistical analysis within +/- 2 standard deviation of the mean) of an instrument against a referenced one.

These studies conclude that this instrument provides an acceptable method of continuous CO. It not only compared favourably to the PAC/thermodilution method (which requires the introduction of a central SG-type pulmonary catheter) but also to the PiCCO system which employs a form of arterial pulse contour analysis for calibration but requires femoral/axial artery catheterisation.

While the **LiDCOplus** instrument requires calibration, it has been shown to provide continuous accurate CO measurements for up to 24 hours. However clinical views from opinion leaders collected by Objective Capital suggest that prudent clinical practice indicates recalibration should be looked at every 8 hours or if a significant change in the arterial waveform prompts a change in the medical management of the patient.

Calibration with lithium is contra-indicated in patients on lithium therapy but also within 15-30 minutes of receiving a neuromuscular blocker because these drugs react with the lithium sensor. Arrhythmias may make this sort of analysis unreliable as demonstrated in a study¹⁸ where atrial fibrillation made the arterial pressure signal too unstable for analysis. However, it appears that although arterial dampening may occur¹⁹, this does not seem to affect the relative accuracy of the technique versus its reference.

¹⁸ see for example Pittman J. et al (2005) *Crit. Care Med.* 33 (9): 2015-2021

¹⁹ this effect is triggered by the physical bending of the catheter when inserted. See ref 12 for its lack of effect on absolute CO

A retrospective study of 256 patients diagnosed with shock, from a database of close to 7000 patients admitted to an ICU at a tertiary academic hospital, compared the effects of no monitoring, a central venous pressure line, PAC (static monitoring) and **LiDCOplus** (dynamic) on outcomes.

In mechanically ventilated patients, the use of the **LiDCOplus** monitor was associated with a significant reduction of both ICU and 28-day mortality in these patients versus the other 'static' modalities. Mortality in the **LiDCOplus** group was 12% versus 32% in the PAC group or 31% in the group without HDM²⁰.

In the organ transplantation setting, work carried out prospectively at the University of Pittsburgh has demonstrated that the use of **LiDCOplus** to monitor patients who are potential organ donors, enabled improved organ harvesting in this setting (3.7 per donor versus 2). Inadequate volume resuscitation was associated with a higher level of inflammation leading to lower harvesting yields²¹.

The body of evidence emanating from these and other studies points to the clear contribution of **LiDCOplus**-driven improvements in outcomes in various settings. It has also shown a clear propensity to reduce the overall cost of treatment in critically ill patients and to reduce the length of stay in the hospital.

While other technologies have also demonstrated the benefits of HDM monitoring on outcomes, they suffer from the various disadvantages that we have outlined above and below. Ergo, we believe that LiDCO's platform is uniquely positioned to benefit from the data that demonstrates its role as a driver for better outcomes and its impact on costs, a factor that will not be lost on both payors and hospital management.

Revenue model for LiDCOplus ICU products (£000's)

LiDCOplus ICU monitor revenues	2008	2009	2010	2011	2012	2013	2014
UK	336	232	232	232	232	232	232
US direct	396	109	109	109	109	109	109
US via distributors	0	130	149	162	162	162	162
ROE	533	292	303	314	314	314	314
ROW	114	342	353	375	375	375	375
Total (in 000's)	£1,379	£1,105	£1,146	£1,191	£1,191	£1,191	£1,191
LiDCOplus ICU disposable revenues	2008	2009	2010	2011	2012	2013	2014
UK	1,199	847	906	966	1,025	1,085	1,145
US direct	420	447	458	468	479	489	500
US via distributors	0	43	41	79	119	159	199
ROE	327	463	533	605	679	754	828
ROW	40	298	397	500	608	715	823
Total (in 000's)	£1,986	£2,097	£2,335	£2,618	£2,910	£3,202	£3,494
LiDCOplus ICU total (without MedOne)	£3,365	£3,202	£3,481	£3,809	£4,101	£4,393	£4,685

Source: Objective Capital

²⁰ Hata J et al, *ISICEM 2007 and Abstract and Poster at SCCM 2008*

²¹ Kellum et al, (2008) *SCCM Abstract*

The revenue model for the *LiDCOplus* monitor demonstrates that despite its lack of immediate convenience, and the requirement for training to breed familiarity and ease of use, we believe that the revenue potential remains significant. On our estimates, monitors and disposables can, on a very conservative basis, represent a business that is almost double the size of the current business by 2019 (just under £8million) implying an overall growth rate in the high single digits per annum.

Strengths and weaknesses

The main strengths of the *LiDCOplus* are:

- its measurement accuracy;
- the fact that it takes advantage of catheter lines that are routinely present in the type of critical care patients where HDM is performed;
- its user-friendly graphical interface for ease of monitoring, analyses and graphic display;
- its proven ability in certain settings to improve outcomes and lower costs.

The main weaknesses appear to be:

- training intensive to achieve ease of calibration;
- the perceived need, by some, for re-calibration when major dynamic changes occur;
- the potential need for recalibration with time (8-24 hours);
- the ability to use PAC and thermodilution as a calibration method.

These weaknesses have not been and are not, in our view, major obstacles to adoption. They may lengthen the sales cycle and increase the cost of marketing, but the value of the instrument in the ICU setting is demonstrable.

It is however more cumbersome to use this equipment in the surgical suite and the measurement of absolute CO in that setting may not be necessary for the most part. It is possible that, through patient sub-population identification, this technology could segregate itself to particular clinical situations where its use would be optimal to achieve better outcomes and lower costs. However, the emergence of the *LiDCOrapid* based on similar technology creates a significant market opportunity and ability to leverage this platform into significant, easy to access usage.

LiDCO*rapid*TM monitor

Prompted by the demand for a product in the surgical setting that embodies the ease of use of the LiDCO*plus*TM monitor without the need for lithium dilution calibration, LiDCO set about building a monitor based on the PulseCO software. This new monitor should be used to monitor trends in CO and other haemodynamic measures without the need for cumbersome lithium dilution measurements pre- and intra-operatively.

The LiDCO*rapid*TM provides the anaesthetist with an easy-to-read, simultaneous viewing of pressure and stroke volume, event responses, measures of CO all in a trending fashion to guide the provision of fluid and drug therapy during an operation. The resultant screen is easy to use with the ability to be simply plugged into a standard vital signs/blood pressure monitor (which generates the arterial waveform that is used to convert into these measures).

By combining all of these measures into an easy to view trending fashion, the anaesthetist has all that is needed to optimise therapy during the operation. The history can be viewed instantaneously and the entire dataset can be downloaded via a USB port for subsequent analysis or use.

We witnessed the use of this monitor during a peripheral bypass operation in a London hospital and are convinced that this type of technology could gain widespread acceptance in the anaesthesiology community. Its versatility and ease of use could, in our view, make this a standard piece of kit during any moderate to high risk operation. Further more, we believe that this monitor will find significant uses in the ER and for the ICU itself where the assessment of HD status does not require a measurement of absolute CO. As regards the ICU, we believe that a segregation of the market will occur between the LiDCO*plus* and *rapid* depending on the application and type of patient.

The main commercial difference between the *plus* and the *rapid* is that the *plus* can use other means of calibration along with the monitor; by contrast the *rapid* only operates when a patient-specific card is inserted along with patient specific data. This opens the door for a potentially lucrative disposables business, where the placement of the monitor, automatically translates into a disposables revenue stream. The only variable then becomes frequency of use.

We believe that the LiDCO*rapid* could be significant for LiDCO. In our core model we are forecasting, conservatively we believe, that revenues for the LiDCO*rapid* monitors and disposables could reach over £22 million by 2014. Our more aggressive model leads to a substantial market and even the latter model may be conservative.

LiDCO*rapid* screen

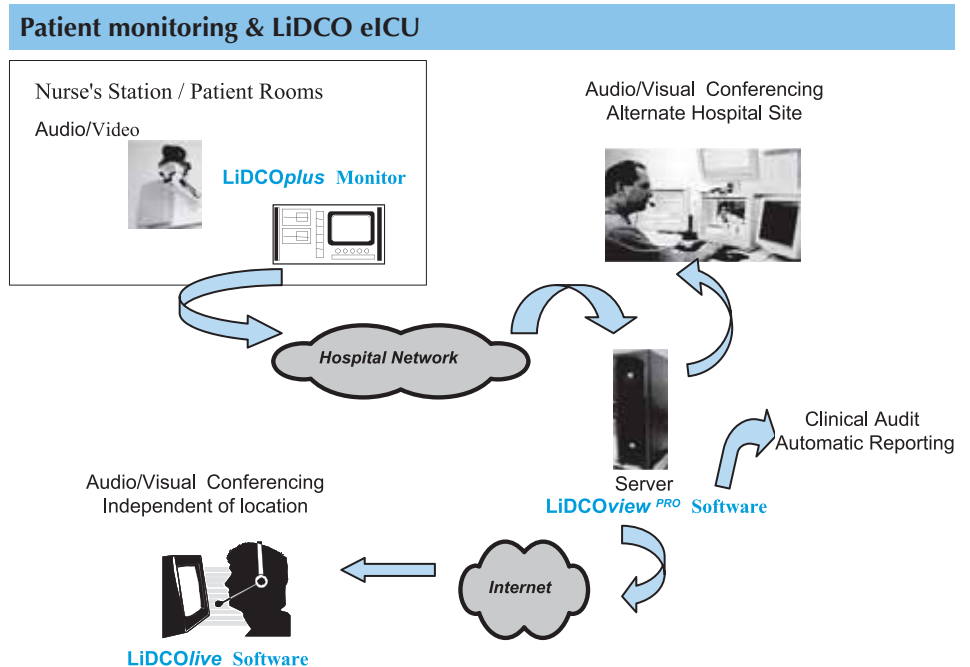


Source: LiDCO

LiDCOview™ and LiDCOlive™ to complete the offering

Two other products are on offer to complete what LiDCO has to offer. The LiDCOview™ is a software interface that can offload data to a computer for further analysis or to use in training in a medical school setting. It also holds the potential of being used to create a link to therapeutic driven protocols. The LiDCOlive product is a remote networking product driven off a server and using both wired and wireless communication of live data so that both doctors and nurses can continue to monitor critical patients from whatever location they are in. Data can be delivered live via the hospital network, by wireless or via the internet to various interested parties. The resultant data can be stored on a server and is available for further clinical audits and reporting purposes.

We have not modelled these products as their business model has not yet been determined by the company and they are likely to be bundled with the LiDCOrapid and plus.



Source: LiDCO

LiDCOrapid ICU and surgical product model (£000's)

Total LiDCOrapid ICU monitor revenues	2009	2010	2011	2012	2013	2014
ROE	18	37	37	38	39	39
US (direct)	20	54	57	58	59	58
US (distributors)	26	57	61	62	63	62
ROW	12	24	25	25	26	26
Total	36	76	82	84	85	84
	£112	£247	£261	£267	£272	£269
Total LiDCOrapid ICU disposable revenues	2009	2010	2011	2012	2013	2014
UK (direct)	19	119	203	290	381	472
ROE (distributors)	36	268	479	698	925	1,155
US (direct)	27	91	162	235	309	382
US (distributors)	24	166	298	436	579	723
ROW (distributors)	65	406	711	1,028	1,358	1,691
Total	£172	£1,051	£1,853	£2,687	£3,551	£4,423
Total LiDCOrapid surgery monitor revenues	2009	2010	2011	2012	2013	2014
UK (direct)	40	79	86	88	90	88
ROE (distributors)	165	474	563	574	585	574
US (direct)	26	119	205	293	383	471
US (distributors)	334	693	783	799	815	798
ROW (distributors)	396	817	945	964	983	964
Total	£961	£2,182	£2,582	£2,718	£2,856	£2,895
Total LiDCOrapid surgery disposable revenues	2009	2010	2011	2012	2013	2014
UK (direct)	29	171	295	422	552	679
ROE (distributors)	30	230	433	639	850	1056
US (direct)	14	57	62	63	65	63
US (distributors)	60	249	282	288	293	287
ROW (distributors)	71	370	652	939	1232	1520
Total	£204	£1,078	£1,724	£2,352	£2,992	£3,606
Total LiDCOrapid monitor revenues	2009	2010	2011	2012	2013	2014
UK (direct)	58	116	124	126	129	127
ROE (distributors)	185	528	619	631	644	632
US (direct)	52	175	266	355	446	534
US (distributors)	346	717	808	824	841	824
ROW (distributors)	432	892	1,027	1,047	1,068	1,048
Total	£1,073	£2,429	£2,844	£2,984	£3,128	£3,164
Total LiDCOrapid disposable revenues	2009	2010	2011	2012	2013	2014
UK (direct)	48	290	499	713	932	1,151
ROE (distributors)	66	499	911	1,337	1,775	2,211
US (direct)	41	148	225	298	374	446
US (distributors)	84	415	580	723	872	1,010
ROW (distributors)	136	776	1,363	1,967	2,590	3,211
Total	£376	£2,128	£3,577	£5,038	£6,543	£8,028
Total LiDCOrapid Revenues	£1,449	£4,558	£6,421	£8,023	£9,671	£11,193

Source: Objective Capital

Competitive position in clinical use

The **LiDCOplus** and **LiDCOrapid** run up against a number of competitive barriers in their target markets. Arguably the most important is inertia: the segment of the market that obstinately hangs on to historical methods of measuring CO such as the PAC/thermodilution technology and its more modern form using Edwards' **Vigilance** Swan-Ganz PAC catheter with associated software and monitor.

The recent judgement against Edwards, related to significant injury caused by software malfunction, may have depressed further an already declining market within the ICU. However, inertia in these markets cannot be underestimated. The software problem that triggered this event has been fixed and the instrument upgraded.

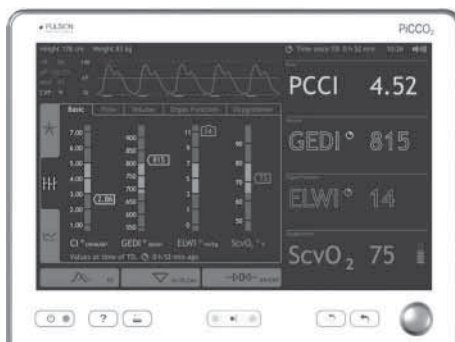
The second threat is posed by Edwards Lifescience's **FloTrac/Vigileo** uncalibrated arterial pressure waveform analysis instrument and, to a much lesser extent, Pulsion's **PiCCO** instrument. In distant third place would be the oesophageal doppler technology of Deltex and others. In the longer run, it is possible that the emerging NICOM technology may also pose a threat post-operatively but it will require significantly more data to be convincing.

FloTrac/Vigileo

We have noted earlier the lack of correlation, as reported in the scientific press, between the FloTrac/ Vigileo and PAC/thermodilution systems. This lack of correlation could pave the way for LiDCO to make serious in-roads into the surgical market, where many Vigileo monitors have been placed. We know of several hospitals that have already opted replace their Vigileo monitors and replace them with the **LiDCOrapid**.

It is too early to tell whether this can be viewed as a generalised movement away from the Vigileo but early signs (and feedback) are rather positive in this regard. In any case with a market estimated in the \$400-800 million range, there is room for several players. None of these technologies have made a serious dent into this market to date.

PiCCO



Source: Pulsion Medical Systems AG

Pulsion's PiCCO System

The **PiCCO** is also a calibrated arterial waveform measurement system. The calibration is made via thermodilution through an axial or femoral catheter. This system may not provide a true measure of CO in a continuous format and measures many other parameters as well.

However, the need to insert an additional, invasive, femoral catheter narrows the applicability of the technology to settings where a skilled individual can insert the catheter and operate a rather complex instrument that is not very user-friendly. The graphics are minimal and not as visually indicative of the patient's status from afar as the **LiDCOplus** which uses a graphical display to show where the target CO is for the patient and where the actual haemodynamic measurements are situation versus the target.

In Germany, Switzerland and Austria where the doctor is the primary caregiver in the ICU and the nurse performs an unskilled role, the **PiCCO** has made significant in-roads in the HDM market. It has attempted to do the same in the UK and in the US, so far without much success. With the advent of the **LiDCOrapid** its ability to make in-roads in the surgical suite are, we believe, even less likely. If anything, the latter may be able to make in-roads in the markets where the PiCCO already has significant market share.

Oesophageal Doppler (such as Deltex's CardiacQ)

The oral insertion of a oesophageal doppler catheter and estimation of absolute CO is a technique that has been around from some time. Other products in this market include the Hemosonic from Arrow International (now part of Teleflex) and the USCOM doppler probe and monitor. All suffer from the same issues:

- they are impractical to use in patients that are awake;
- in the surgical suite the need for an absolute CO measure is questionable;
- only accurate in the hands of experienced operators;
- susceptible to electronic interference (particularly where electrocautery is used).

As noted earlier, in up to 20% of older patients, we have been told that this probe does not get a signal at all due to the space for the probe to be positioned versus the DTA (Descending Thoracic Artery) being significantly reduced making achieving the desired angle difficult. Additionally, once the probe is inserted, if it does not work, it becomes a wasted cost item to the hospital.

With the advent of the **LiDCOrapid** "plug and use" trend monitor the need for such a probe becomes significantly reduced. If an absolute measure of CO is really needed, a partial re-breathing CO₂ test using Respironics NICO instrument is much easier to perform. This suggests significant opportunity to displace doppler based techniques in the OR setting, an issue for both USCOM (ASX :UCM) and Deltex (AIM: DEMG).

Impedance technologies

Impedance technologies such as Cardiogenics (NASDAQ:CDIC) are not particularly accurate in measuring cardiac output. Additional fluids in the lungs, such as in pneumonia and bleeding, can skew this type of measurement. Furthermore, these measurements are susceptible to external interference from the myriad of other electrical apparatus that are present in the ICU and has generally not gained much traction.

As indicated earlier, a new technology (**NICOM**) developed by **Cheetah Medical Inc.** out of Israel uses a combination of impedance and amplitude/frequency fluctuations (Bioreactance) to measure CO which increases the signal to noise ratio 100-fold. However, this technology has limited clinical validation to date so it is unclear what its ultimate impact will be. It is however not directed at the surgical suite in any case and may be a more appropriate technology (if validated) to measure CO non-invasively pre-operatively or in the ER.

Financial & Marketing Overview

With fiscal 2008 just reported, we can see that the dynamics of the business are relatively healthy. Overall revenues were up 18% to around £4 million with administrative and distribution costs reduced by 6%. While the company lost around £2 million for the full year, that loss was down 23% from the previous year. The cash balance was £2.2 million at year-end and should, combined with a rolling debt facility of around £500k, be enough to take the company to profitability. Margins that reflect the inherent margins on these products are being achieved.

Gross margins of around 65% (versus 67% the previous year), reflect a blend of the product gross margin (which is around 75%) and margins achieved on the MedOne business. MedOne is a relatively unique medical equipment leasing company who place instruments on behalf of the company and are paid a 50% premium that is charged on disposables sold under this model for a period of 3 years. This premium is then remitted to MedOne and is booked as a cost of goods sold. LiDCO are not planning to carry out any more MedOne placements at this time. The jump in our forecasted gross margins (from 64.4% to 70%) in fiscal 2009 is partly based on the premise that the true product margins will begin to be reflected as the MedOne business transitions to more traditional distribution (where the products are sold outright at a discount).

The MedOne model was used as a means to kick start the US business. With the LiDCO*plus*, as the cross-use of lower cost calibration methods reduced the degree to which LiDCO's kits were utilised, this made the MedOne business less attractive. With the advent of the LiDCO*rapid*, the utilisation of disposables becomes unavoidable so the leverage of this model is expected to operate fully as the only variable becomes the frequency of use within the clinical settings to which it is sold (OR, ICU and perhaps ER).

The current strengthening of the sales and distribution network has driven export sales by 63% to £2.32 million which now represents over half of the overall sales of the company. The UK was down in monitors (43%) while sensor sales were up 10%. This is related to the capital budget cycles in the NHS that are expected to recover in FY2009 after several years in which the focus of many NHS Trusts has been on debt reduction and achieving balanced budgets. As a result, the company expects a resurgence of this market and has made appropriate adjustments to its sales efforts in anticipation of this and the launch of the **LiDCO*rapid***. LiDCO is committed to continuing to build its market penetration through the active building of further distribution in all regions.

What is apparent throughout these numbers is that sensor sales (in the US and EU and ROW in particular) are not tracking **LiDCO*plus*** monitor sales in ways one would expect them to. This can mostly be traced to two main reasons. The lack of sensor sales follow-through is partly attributable to the compatibility of other

systems with the **LiDCOplus**. While there is additional income generated from the use of the monitors (through an internal procedure counting system), disposable kit sales are still lagging monitor sales by a relatively large margin.

The other main reason is that once a monitor goes to a distributor, LiDCO has little control over what happens to it. It can book the revenues from the instrument's sales but it has no ability to push the distributor to buy disposables. With the advent of the **LiDCOrapid** that is all about to change as the latter does not work unless the patient card is inserted. Despite the introduction of the **LiDCOrapid** we expect that the sales of the **LiDCOplus** monitor to continue a pace and believe that as training becomes more pervasive, and nurses, particularly in the US, become more skilled in the art of doing lithium measurements, sensor sales will follow through. Nevertheless, we also expect some weakening in growth in fiscal 2009 as the sales effort concentrates on the launch of the **LiDCOrapid**.

The **LiDCOrapid** should be an 'easy sell' to anaesthetists in the OR setting and immediately begin to generate the card sales that are needed for the use of the system. With the latter, the product will not work without the card so there is no point in buying one if one is not going to use it.

At the end of FY08, the company reported that it had an installed base of 1,184 **LiDCOplus** monitors installed out of a potential ICU monitor market that we estimate to be around 35,000 units. Clearly, there is a long way to go to achieve any semblance of significant market penetration. As the company adds definition and colour to the applications where it believes this instrument adds to both the clinical and value proposition (along with application-driven protocols), we think that the company can turn the lag of sensor sales to monitors around.

In the Surgery market, we estimate that there is a putative market of around 34,000 HDM monitors worldwide. We think that our estimate of around 590 sold in fiscal 2009 (only 6 months of sales) rising to around 1,503 in 2014 is not unrealistic given the size of the market (this represents a 4.7% penetration). In our core model, on a salesforce of around 100, with other discount factors applied, this represents about 15 monitors per salesperson per year or between 1-2 monitors per salesperson per month: not a stretch in our view. To put this within context, an average hospital with 6-8 OR's alone should order between 3-4 monitors for its OR's and probably some additional units for the ICU and ER.

We have also constructed a more aggressive model based on what we think are realistic numbers. In that model, the number of monitors sold in fiscal 2009 would be 323 and reach around 1,500 in fiscal 2013. In this model, the leverage to revenues, triggered by the sale/placement of each instrument is very high indeed. In our more optimistic scenario, the number of monitors of **LiDCOrapid** sold is pegged at 630 in fiscal 2009 rising to roughly 1,750 in fiscal 2014. Again, the

leverage of disposables on this at 4 per unit per monitor per month is significant but the numbers we arrive at are reasonable. We need to see how the business develops before turning on the disposable spigot, with inevitable valuation consequences. Again, to put this in perspective, there are about 30 operations a week in the OR which translates into 1200 operations a year. If we assume that only 25% of these would use HDM (in a new outcomes/cost world, this would be low in our view), that would translate into 360 operations requiring HDM. Our 48 disposable units per annum needs to be measured against this potential

The **LiDCOview** is unlikely to be anything more than a useful tool for research-orientated applications and training in the near-term. This use is mostly relevant to teaching hospitals and research physicians. However, there are possible ways of integrating this technology into therapeutic-driven protocols and this may very well represent its future potential. The soon to be introduced **LiDCOlive** will, in our view, represent another driver for the **LiDCOplus** business (both monitors and disposables) as well as the **LiDCOrapid**. We believe that the company might use this as a means of encouraging hospitals to use more lithium dilution with the **LiDCOplus** as part of a package deal to drive further penetration of the disposables market. At the very least though, the potential convenience factor offered by such a networking product should be a very valuable sales driver for LiDCO's products. So, watch this space.

All in all, we think that FY 2010 should be a pivotal year for the company. As the **LiDCOrapid** begins to generate a volume of disposables, along with the installed base of **LiDCOplus** instruments, the company should reach profitability. With a cost base (G&A and manufacturing) largely fixed, the operating leverage is significant. Our projections suggest that 2011 should generate a substantial profit for shareholders and with close to £8 million in tax losses the company will not have to pay any taxes for some time to come.

Profit & Loss					
(£000's)	2007A	2008A	2009E	2010E	2011E
Revenues from monitors/isposables	3,443	3,365	4,651	8,038	10,230
MedOne		467	0	0	0
Other revenues		218	200	200	200
Net revenues	3,443	4,050	4,851	8,238	10,430
Cost of sales					
Monitors/Disposables	811	998	1,131	1,783	2,059
MedOne	316	444	300	300	300
Gross profits	2,316	2,608	3,420	6,156	8,072
Gross margins	67%	64.4%	70%	75%	77%
Distribution costs	69	93	129	222	283
Administrative expenses	4,870	4,526	4,957	5,407	5,901
Depreciation	321	235	250	260	270
Amortisation	227	376	400	410	420
Wages and staff costs	2,552	2,281	2,509	2,760	3,036
Other admin	1,770	1,634	1,797	1,977	2,175
Operating Profit (Loss)	(2,623)	(2,011)	(1,665)	526	1,888
Interest income	69	49	22	12	44
Interest expenses	(35)	(25)	(25)	(25)	(25)
Pretax income (loss)	(2,589)	(1,987)	(1,668)	513	1,907
Taxes	(204)	(120)	(120)	(120)	(120)
Rate	NA	NA	NA	NA	NA
Net income (loss)	(2,385)	(1,867)	(1,548)	633	2,027
Average shares outstanding (m)	114	122	142	142	142
EPS (p)	(2.1)	(1.5)	(1.1)	0.5	1.4

Balance Sheet					
(£000's)	2007A	2008A	2009E	2010E	2011E
Current Assets					
Inventory	1,080	839	658	1,093	1,248
Trade and other receivables	1,279	1,329	965	1,752	2,254
Current tax	142	120	120	120	120
Cash & equivalents	1,474	2,234	1,005	541	2,029
Total	3,975	4,522	2,748	3,506	5,651
Non-current assets					
Property plant & equipment	854	833	753	663	563
Intangible assets	656	747	814	871	918
Total	1,510	1,580	1,567	1,534	1,481
Current Liabilities					
Trade & Other Payables	(778)	(707)	(472)	(564)	(628)
Trade	(415)	(364)	(94)	(149)	(172)
Other payables	(363)	(343)	(377)	(415)	(457)
Deferred Income	(68)	(41)	(38)	(38)	(38)
Short term Debt	0	(563)	(563)	(563)	(563)
Total	(846)	(1,311)	(1,072)	(1,164)	(1,229)
Net Current Assets	3,129	3,211	1,676	2,342	4,423
Net Assets	4,639	4,791	3,243	3,876	5,904
Non-Current Liabilities					
Finance Lease Liability	51	34	34	34	34
Total	51	34	34	34	34
Shareholder's Equity					
Share capital and premium	21,315	23,260	23,260	23,260	23,260
Merger Reserve	8,513	8,513	8,513	8,513	8,513
Retained Earnings		(27,016)		(27,931)	(25,903)
Total Equity	4,588	4,757	3,209	3,842	5,869
Shareholder's Equity and Non-Current Liabilities	4,639	4,791	3,243	3,876	5,903

Cashflow					
(£000's)	2007A	2008A	2009E	2010E	2011E
Operating Loss	(2,623)	(2,011)	(1,665)	526	1,888
Depreciation and Amortisation charges	412	611	650	670	690
Share-based Payments	66	88	0	0	0
Inventories	196	241	181	(436)	(155)
Receivables	495	(50)	364	(787)	(502)
Payables	88	(96)	(239)	92	64
Finance Expenses	(35)	(25)	(25)	(25)	(25)
Income Tax Credit Received	283	142	120	120	120
Net Cash from Operations	(1,118)	(1,100)	(614)	161	2,080
Cashflow from Investing					
Property plant & Equipment	(137)	(170)	(170)	(170)	(170)
Purchase of Intangible fixed Assets	(410)	(467)	(467)	(467)	(467)
Interest Received	69	49	22	12	44
Net cash from investing activities	(478)	(588)	(615)	(625)	(593)
Net Cash before financing	(1,596)	(1,688)	(1,229)	(464)	1,488
Cash Flow from Financing Activities					
Issue of Ordinary shares	3,245	1,943	0	0	0
Convertible Debt Drawdown (Repayment)	(1,126)	502	0	0	0
Net Cash from Financing	2,119	2,445	0	0	0
Net Increase (Decrease) in Cash Flow	523	757	(1,229)	(464)	1,488
Closing Cash Equivalents	1,474	2,234	1,005	541	2,029

Source: Objective Capital

APPENDIX: MANAGEMENT

Theresa Wallis – Non-Executive Chairperson

Ms Wallis formerly worked for the London Stock Exchange where she became the COO of the AIM market. Previously she was a principal executive of Angle plc and currently also serves as a non-executive Director of Noble Income and Growth VCT.

Dr Terence O'Brien – Co-Founder, CEO

Dr O'Brien co-founded the company with Dr Band in 1991. Prior to that he held senior positions at a number of biomedical companies including Sandoz SA, Pharmacia AB, Meadox Medical Inc., Novamedix and Enzymatix which eventually became Chiroscience Plc.

Dr David Band – Scientific Director

Co-founded the group with Dr O'Brien in 1991 and is the co-inventor of the LiDCO system. Trained as an MD (Medicine and Surgery), he is a specialist in the fields of respiratory physiology, electrochemistry, and ion-selective electrodes. He is a former reader in Applied Physiology, Kings College London.

John Barry – Sales and Marketing Director

He joined the group in 2001 and was formerly with Baxter Healthcare where he was the Director of Critical Care products for Europe when Baxter spun off Edwards Lifesciences. At Edwards he was the EMEA Director for their cardiac surgery products business.

Paul Clifford – Finance Director

Paul Clifford recently joined LiDCO as its Finance Director. Previously he was the FD for Civica UK Ltd, a subsidiary of AIM-quoted Civica plc, specialising in software-based solutions for the public sector. Prior to that he was the Group FD and Company Secretary for Comino Ltd (1996 – 2006) which was acquired by Civica in February 2006.

Eric Mills – Product Development Manager

Joined the group in 2004 with over 13 years of experience in pharma and medical device development notably with Eli Lilly. In 1998, he joined MedVenture Technology where he was Director of Quality and Regulatory while continuing to work on product development in the areas of cardiovascular, neurological and general surgical disposable devices.

Jon Pepper – Operations Manager

Jon Pepper was previously the Operations & Manufacturing Director for VideoLogic Limited, a company specialising in the development and marketing of multimedia computer products. He was responsible for all product engineering, procurement, supplier management, quality, test, packaging and distribution.

Greg Speller – Quality & Regulatory Manager

Greg Speller has been with LiDCO for 9 years. Previously he spent 5 years as the Quality Manager for Expanded Optics Ltd (part of Johnson and Johnson), a company providing the design, manufacturer and service of medical endoscopes and accessories.

Rick Alberts – US Sales Manager

Rick Alberts has been with LiDCO for 7 years. Previously he has worked with Oximetrix, Abbott Labs, Baxter and 3M Healthcare.

Adrian Thomas – UK and Southern Europe Sales Manager

Adrian has been with LiDCO for 7 years. He was previously a European Product manager for haemofiltration in the Critical Care Division of Edwards LifeSciences. He began his career in Critical Care at Baxter Healthcare where his prime responsibility was with the Swan-Ganz catheter and other related products.

We are pleased to bring you this report on **LiDCO Group plc**.



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As always, I welcome your comments and feedback on our research!

Gabriel Didham, CFA
Objective Capital

Steven Zimmer, M. Sc. (Molecular Biology)

Steven has more than 25 years experience in analysis, corporate finance and as a portfolio manager in biotech and pharma including working for DLJ, CSFB and Robert Fleming in London, NY and Switzerland.

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Objective Capital has been sponsored by the company to provide research coverage of LiDCO Group plc.

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