Medical Devices Faraday Partnership

Regulatory Affairs Bulletin

Summer 2003
Issue No. 2

Welcome to the second edition of the Medilink Regulatory Affairs bulletin produced in conjunction with Medical Devices Faraday Partnership. The bulletin aims to keep you up to date with current issues and is produced from contributions provided by Medilink members. If you would like to see specific topics covered in future issues or would like to become a contributor please contact Medilink, see rear of bulletin for details.

Clinical trials of medical devices

In order to meet the essential requirements of the Medical Device Directive and obtain the CE mark, manufacturers must provide clinical data that demonstrates the safety and performance of their device. There are two methods that can be used to gather the evidence: -

Clinical evaluation is basically a compilation of relevant scientific literature that can include any of the following;

- Results of clinical investigations of similar devices
- Pre-clinical data; in vitro results, animal testing & assessment of compliance with relevant standards
- Technical data (e.g. design, manufacturing, risk analysis)
- Clinical/medical data & reports
- Review of marketing history, adverse events, post marketing surveillance results
- Risk/benefit analyses

If the Clinical Evaluation route is used the data must be relevant to the product, clearly demonstrate the safety and performance of the device and is often used when safety and performance data is already available for similar devices.

A clinical investigation is any systemic study in human subjects. If this route is necessary, the main objective of the clinical investigation should be related to establishing or verifying the safety and the performance of the device when used for its intended purpose and according to the documented instructions.

Circumstances under which clinical investigations are normally necessary include :-

- When it is a new (novel) device for which there is no established history or performance and safety information
- When safety and performance can not be satisfactorily demonstrated by the literature route
- When a device incorporates new (novel) material, components or features for which there is no prior clinical experience
- Generally for Class III and implantable long term invasive Class II a and II b devices (devices considered to be high risk)
- When there is a modification that significantly affects the safety and performance of an existing device

For any clinical investigation it is essential to understand the procedures, obtain the necessary approvals and to follow the scientific standards and in accordance with the Declaration of Helsinki[1].

If the study is of a non CE marked product then this must be approved by the appropriate Ethics Committee and Competent Authority (e.g.Medical Devices Agency) before it can begin. Studies being conducted with CE Marked products do not usually require Competent Authority approval, but do normally require Ethics Committee approval. The documentation includes an Investigator Brochure, Clinical Investigation Plan (protocol) Case Report Forms, Patient Consent Documents, Indemnity, Clinical Trial Insurance, Investigator Agreement, a Trial Master File, an Investigator Site file and much more.

The accepted standard to be used when conducting medical device studies is the ISO14155[2] (recently replaced the standard EN540) that provides a framework for conducting a device study.

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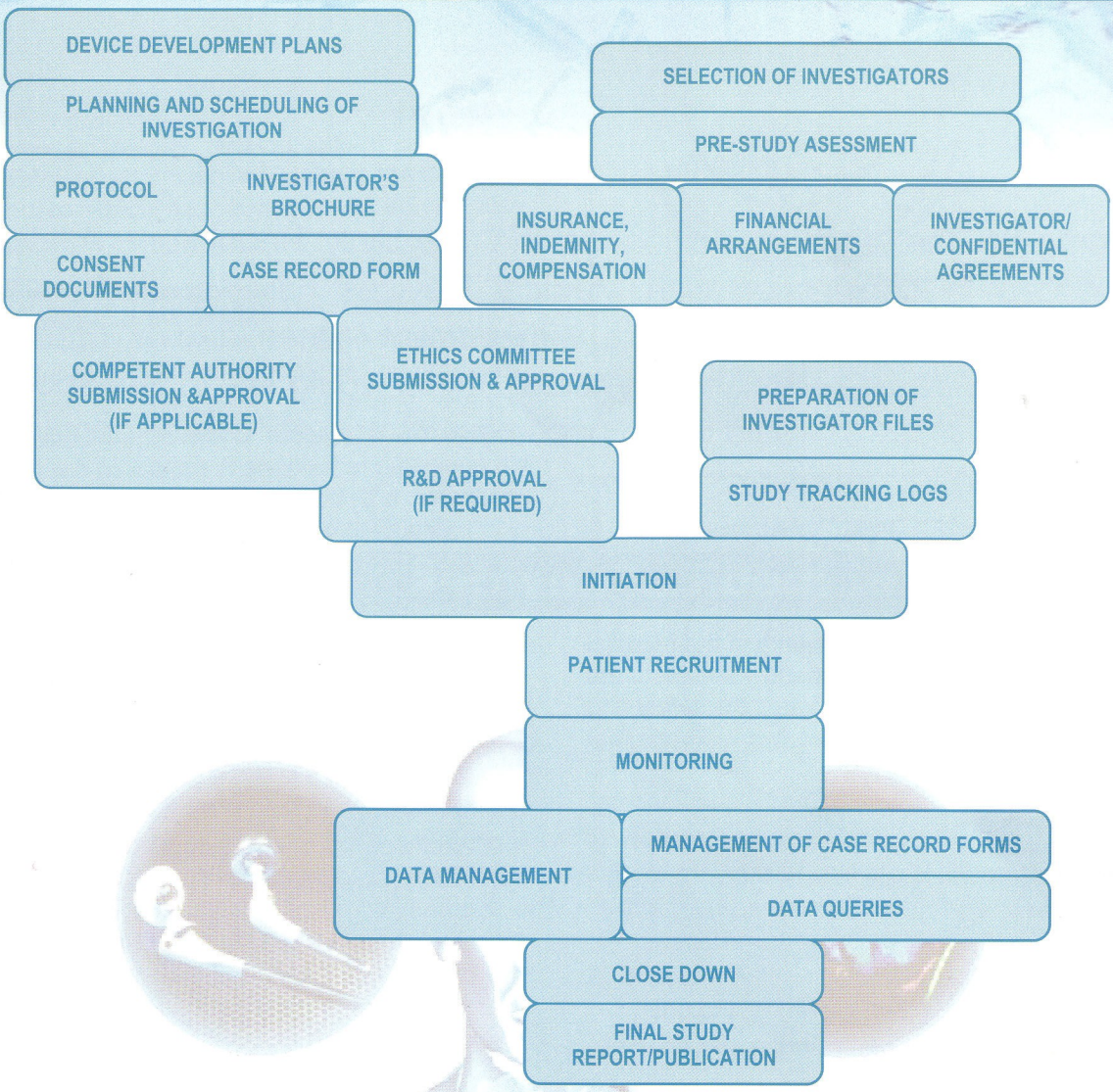
See next page - Fig 1 Critical Path of Clinical Investigation

[1] World medical Association Declaration of Helsinki, Ethical principles for medical research involving human subjects

[2] ISO 14155 Clinical investigation of medical devices for human subjects - Part 1: General Requirements, Part 2: Clinical Investigation Plan

Fig 1 Critical Path of Clinical Investigation



ISO 9001: 2000 - The soft side

It is interesting that many organisations seem content to operate quality systems that are less than ideal for them, but are easy to define for example ISO 9000: 1994 series. If one could tick off each 'element' listed in the standard, then the system was deemed to comply and the company could call itself "ISO 9000 registered".

It is no wonder, then, that many are now struggling with the new ISO 9001:2000 standard. Not only must the system be appropriate for **your** business, it must be monitored and measured against policies, objectives and targets..

What does this mean in practical terms, then? What does a company actually need to **DO**? Well, if one goes on a journey, a 'destination' and a 'route' are needed. So the company's 'destination' should be described in the **Quality Policy** statement, and the 'route' set out by a series of Objectives. The alone doesn't ensure that one gets to the destination though. A method of checking current progress is also required. This is where the '**Measurement**' part of ISO 9001: 2000 comes in.

Policy Does your current Quality Policy say things like "we aim to meet and exceed our customers' expectations...", or "we aim to be the best..."? These sound like worthy aims, but exactly how do you know if you have achieved 'exceeding customers' expectations...', or 'being the best...'? The answer is - you don't know and it is necessary to clarify such statements, and back up any claims with auditable evidence. In other words, define what it is that you are setting out to do. Then define how you will do it - 'objectives'.

Objectives An objective can be top-level, strategic, department-based, and, if appropriate, some may be individual.

Ask yourselves "what is the company here for?" Here are a few obvious ideas...

- To make money?
  - An objective may be expressed in terms of turnover or profitability (increase by 'x'% over 'y' time period)
- To develop market 'B' or tackle new markets?
  - Express objective in terms of market penetration, for example (increase market share by 'x'% by date 'y')

Then ask "What else is needed for these things to happen?"

- To satisfy customers? Nice aim but how would you quantify that? Market share, perhaps? Some sort of feedback initiative? Reduction in complaints? This is completely individual to each company - there is no single answer.
- To develop the company quality system to comply with ISO 9001: 2000 or implementing Investors in People? Good 'starter for ten' objective!

Setting quality objectives should support the company's quality policy, have a quantifiable end-point, and be capable of being **MEASURED**.

Measurement

How far have we progressed on our journey? How does that compare with where we expected to be?

Management must have information in order to make informed decisions, but it is not a simple matter if the data is not available. Here are a couple of recent examples: How can I show that I achieve on-time delivery, if my system doesn't record when my telephone customer asked for the order? How can I show a reduction in material costs for a given department, if the finance department don't segregate costs by department? How can I fully analyse customer complaints, if only certain types of complaint (the ones where the customer is screaming!) are logged?

To summarise, ask yourselves "what information will enable me to manage my company better?" or "what information tells me that we are better, worse or the same as this time last quarter/year"? If you answer these questions, rather than "what data do I have available to me at the moment?" then you will have identified the 'measures' that should be included in your system.

And then ensure that you have systems in place to collect all the right data! Which leads us on to "Process Mapping" - but that's another article...

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ISO 13485:2003 - Why Bother?

Twenty years ago I became enthused about the Revolution in Quality emanating from Japan, put away a lot of my conventional engineering training and set about understanding why Japanese companies could reach levels of quality we could not. Five years later, I had boiled this down to two factors: a **clear concept** and a **universality of application**. Dramatic changes were affected by explaining a very simple quality message and allowing people find their own ways of applying that message to any particular area of the business.

Hence while I can praise the standards-makers for producing ISO 13485:2003, the new quality management standard for the medical device industry, I wish they had not bothered! It is a skilled compromise that balances the old-fashioned inspection-based requirements of the regulators (led by the US) with lip-service to the Total Quality (TQ) principles in ISO 9001:2000. Furthermore, most SME's are not solely in the device industry, they also manufacture non-medical products where ISO 9001:2000 is the required standard.

Let me ask a question to make the point: "can you recite your quality manual word for word?" No, of course not, but you understand the concept in your Quality Policy and can apply it to any area of your business. With ISO 13485:2003 you need to understand three concepts: old-fashioned regulation/inspection based quality, Total Quality and which one the standards-makers have decided applies to a particular operation. If that operation is for an item that may or may not be (used in) a medical device, then you will end up crafting your own clever compromise.

So how did we get here?

In the late 80's and early 90's, with ISO 9001, it seemed like we had finally found a common Quality Management System for all industries. During the early 90's FDA moved away from voluntary standards such as ISO 9001 into a mandatory regulation, Good Manufacturing Practice (GMP) Quality System Regulation (QSR). Europe adopted a similar approach through EN 46001, which simply added some special requirements for medical devices (for example: sterilization) and was later adopted almost unchanged as ISO 13485:1996, see fig. 1. This was the heyday of systems harmonization!

To Total Quality (TQ) exponents, like me, the adoption of TQ philosophy, a systems approach and the restructuring of ISO 9000 in 2000 gave us the potential for much better Quality Systems, with a different but consistent philosophy. The World seemed finally set to make seed-change in quality systems and the effectiveness of business.

Alas, the regulators were not prepared to let the device industry move into this "Brave New World" where rigorous policing was replaced by co-operation to build a better society. The TQ principles were seen as too open and too soft: you could not pass a law saying, "You must ensure your customers are satisfied" ... and of course you needed laws to enforce it. Despite sticking with their existing GMP's, the FDA was a dominant influence in the design of the new standard which has emerged as an unhappy hybrid, see fig.2.

So what does it all mean? The dichotomy of the quality world still exists, device-makers have been handed one particular solution, but a solution based on pragmatic compromise not a consistent philosophy. Hence, application will be fraught, minor violations will multiply and many of us will be locked in an internal balancing act between the device requirements and the relentless march of the rest of the world towards Total Quality.

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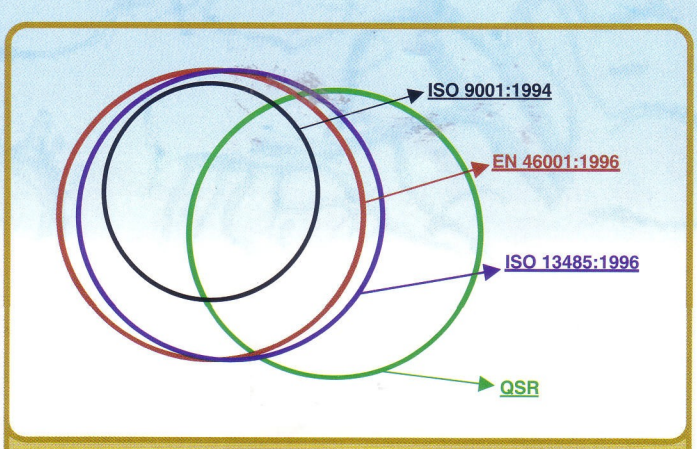

Fig. 1 - The Old Model ("Concentric Circles"): ISO 9001 is a subset of all systems

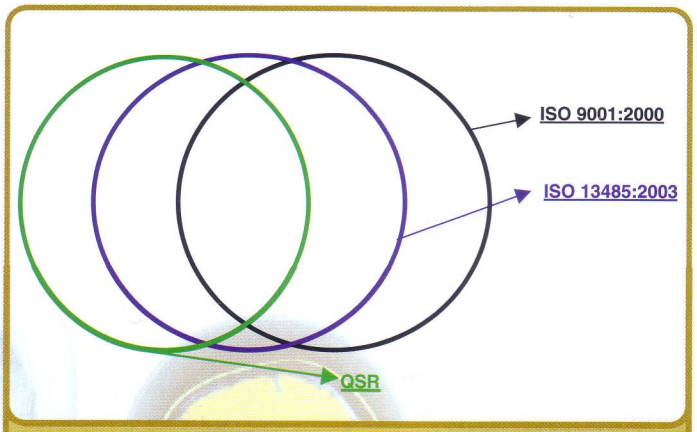

Fig. 2 - The New Model ("Translated Circles"): Nothing is necessarily contradictory, but nothing is centred on the same "philosophy"

Are you up to date with medical standards?

A comprehensive list of medical standards can be found on ACSL website **http://www.amtac.co.uk/supp/s0.htm** and the good news is that as a Medilink member or Medical Devices Faraday member you can order via the Amtac website and by quoting Medilink Member you will receive a **10% discount**.

Contacts

For further information on the issues raised or on how Medilink or Medical Devices Faraday Partnership can help your company contact:-

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