ISO 13485 – Implementation, Registration and Beyond

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Agenda

1. Medical Device Quality Systems and ISO 13485
2. Quality System Planning
3. Documentation Requirements
4. Implementation
5. Certification/Registration
6. Beyond Registration
7. ISO 13485 Future
8. Medical Device Single Audit Program

Company Background

- OptumInsight Canada, Inc – formerly CanReg Inc. – regulatory consulting drugs, medical devices, natural health products; medical information, pharmacovigilance etc
- Medical device consulting – product and establishment registration, quality systems; strategy, assessments, regulatory inspection preparation
  - Canadian, US, EU
  - ISO 13485:2003 CMDCAS (Canadian Medical Device Conformity Assessment System); FDA QS Regulation; EN ISO 13485:2003 CE mark
  - Regulatory strength, quality system experience

1. Medical Device Quality Systems and ISO 13485

- Quality System: The organizational structure, processes, responsibilities, procedures, and resources for implementing quality management.

US:

- Quality System Regulation – 21 CFR 820
- ISO 13485:1996 elements
- FDA inspected
- Third Party accredited auditors

Canada:

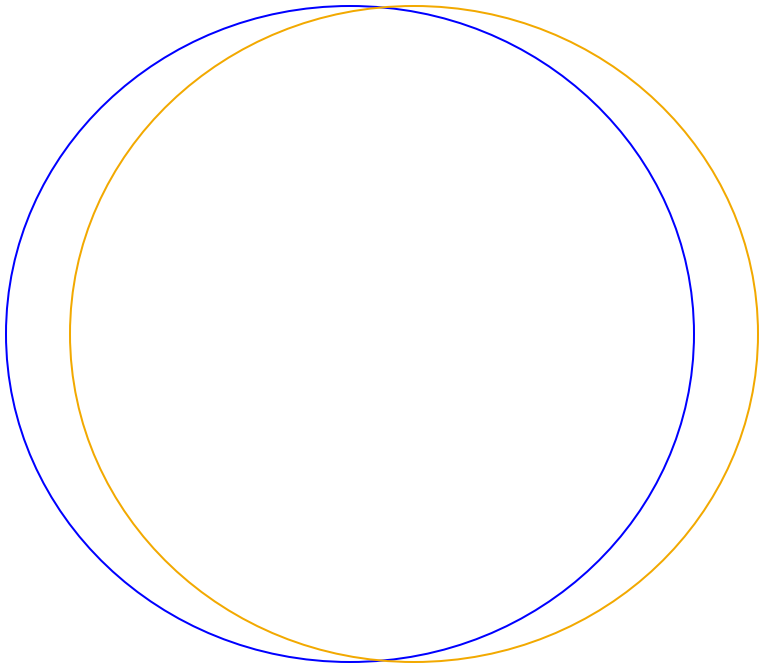
- ISO 13485:2003 CMDCAS certification – Class II, III IV devices
- Third party audit program with registrars

EU:

- CE marking
- Conformity assessment to Medical Devices Directive
- Routes to conformity – quality system assessment
  - EN ISO 13485:2003
  - Audit by Notified Body – third party

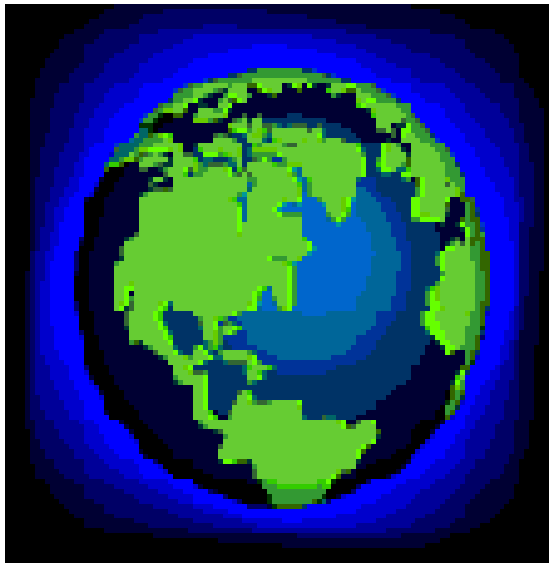
1. Medical Device Quality Systems and ISO 13485

- ISO 13485:2003 and QS Reg
- Very similar
- Complementary
  – Control of documents, facility, personnel, management, design, manufacturing, storage, delivery, improvement
  - Regulatory requirements



1. Medical Device Quality Systems and ISO 13485

- Other jurisdictions also require medical device QS
  - China, Japan, Australia
  - Emerging markets



1. Medical Device Quality Systems and ISO 13485

Overview of main sections that detail requirements:

- **Section 4** – Quality Management System - basic structure and key elements
- Documented policy and measurable objectives
  - Relevant at all levels - challenge
- Top Management support and commitment.
- Documentation, documentation

and more documentation.

1. Medical Device Quality Systems and ISO 13485

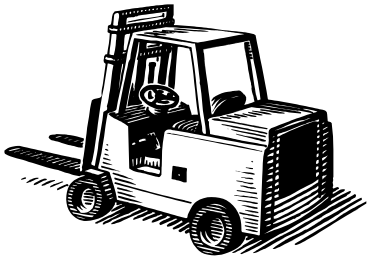
- **Section 5** – Management Responsibility
- Outlines Management roles in quality system – ensure effectiveness.
- Management Commitment.
  - Management leads the way

1. Medical Device Quality Systems and ISO 13485

- **Section 6** – Resource Management
- Identifies resources necessary to maintain an effective quality system
- Staff training, competence evaluation
- Work area resources

1. Medical Device Quality Systems and ISO 13485

- Section 7 – Product Realization
- Risk Management
- Customer and Regulatory Requirements
- Design and Development
- Purchasing
- Production and Service Provisions
- Process Validation
- Product Identification
- Conformity, Control, Measuring Devices



1. Medical Device Quality Systems and ISO 13485

- **Section 8** – Measurement, Analysis and Improvement
- Monitoring information to meet the customer's requirements –complaints, feedback, post market
- Auditing
- CAPA (Corrective Action/Preventive Action)
  - Root Cause Analysis
  - Analyzing Data to prevent occurrences
- Process Measurements – product tests
- Control of Non-conforming Product
- Improvement – effectiveness of the QS

2. Quality System Planning

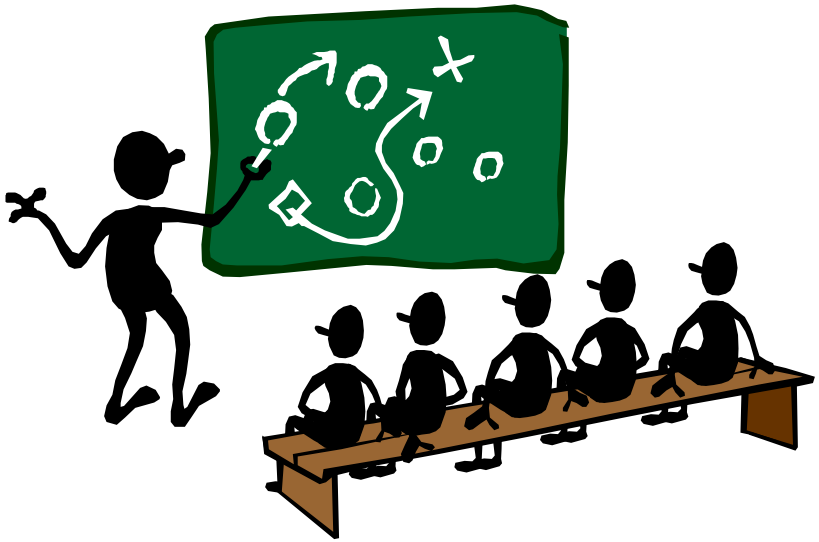
- When to start planning
  - New company
  - Expanding market to additional jurisdictions
  - New product(s) – new medical device, or adding medical device lines
  - Risk management, design controls, supplier controls
    - Never too soon

2. Quality System Planning

- Scope of quality system
  - Regulations for target market(s)
    - Device classification, regulatory pathway
    - Requirements, exclusions eg design
  - Where company lines include other product types (drugs, supplements, natural health products, cosmetics)
    - May have existing quality documents
    - Integrate into one system
    - Include other requirements for specific product types
    - Avoid duplication, gaps

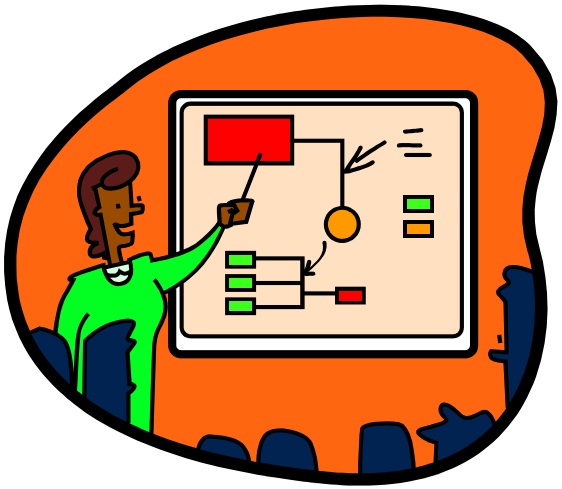
2. Quality System Planning

- Team
  - Critical
  - In house – ownership, action
  - Quality Representative, operations, management
  - Training, experience
  - Outside expertise
  - Not a last-man-in-the-door job!



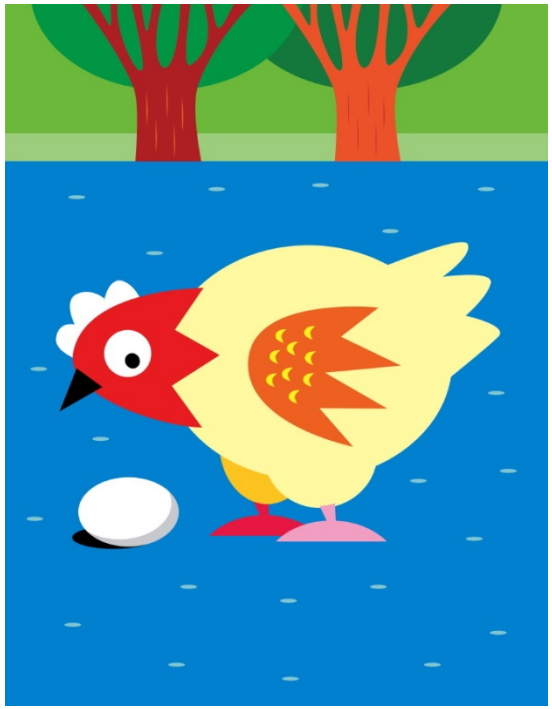
2. Quality System Planning

- Quality plan
  - Document it – flow chart, table, list, spreadsheet, project management tool
  - Define responsibilities, timelines, progress review



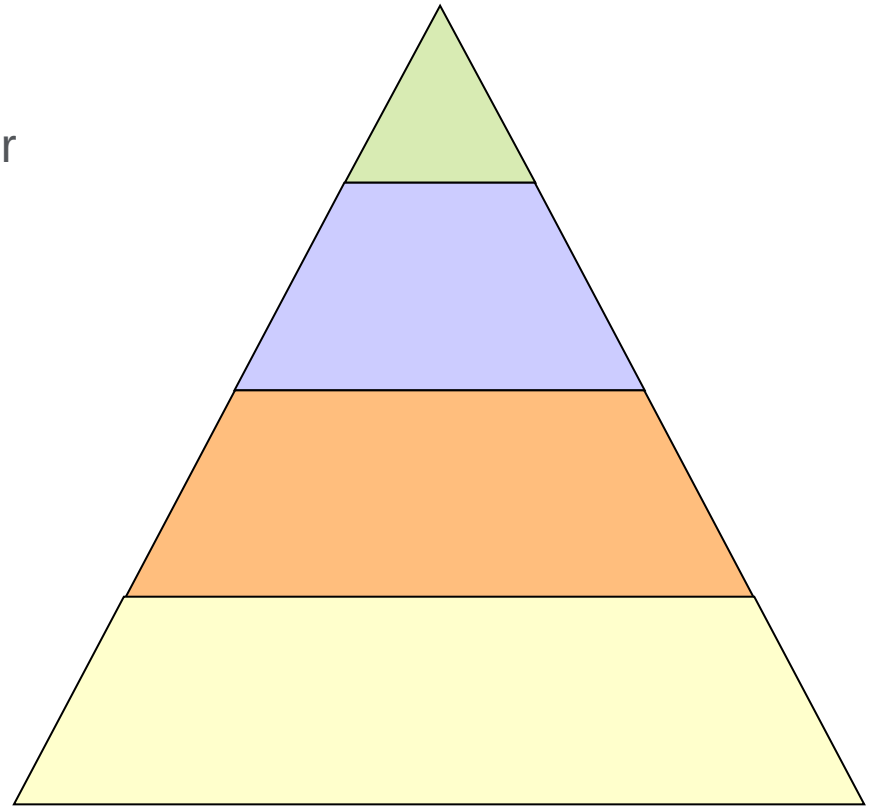
2. Quality System Planning

- Timeline to audit
  - Target for product launch or new market introduction?
  - Time to develop, implement, gather evidence of compliance
    - Product/certificate/licence
  - Registrar/auditor booking



3. Documentation Requirements

- Quality policy, quality objectives
  - Company thinking
  - Goals/targets –measureable, monitor
  - Must be relevant at all levels
- Quality manual – high level
- Standard operating procedures
  - process maps, forms
  - work instructions
- Records – evidence that the system complies with the plans



3. Documentation Requirements

- Include references to regulatory requirements, standards, guidance
  - Canadian Medical Devices Regulations, guidance documents/policies for recall, mandatory problem reports, complaint handling, labelling
  - FDA QS Regulation 21CFR820, guidance documents
  - EU Medical Devices Directive 93/42/EEC, MEDDEV guidances
  - ISO 14971 (Risk Management), other ISO standards as applicable to the product(s)
    - Recognized standards – vary per jurisdiction

3. Documentation Requirements

- Ensure the documents meet requirements of the standard, regulations
- Reflect actual practice
- Paper or electronic system
- List of controlled external documents
  - copies of standards, regulations, manuals etc
    - Paper or electronic format
  - Have a documented process to keep current
    - Specify interval to verify the latest versions are on hand, who is responsible

3. Documentation Requirements

- Strategy without existing QS documents:
  - Number them to follow the standard or the QS Reg sections
  - Logical, easy to find where requirements are addressed

List of Controlled Documents		
Number	Title	Effective Date
QMM rev 2	Quality Management Manual	Sept 1/13
401.01	Document Control	Aug 9/12
402.01	Records	Jul 31/12
501.03	Management Review	Sep1/13
601.01	Training	Jan 4/12
701.02	Purchasing	May15/ 13
702.01	Risk Management	June 9/12
801.01	Internal audit	May16/12

3. Documentation Requirements

- Strategy with existing QS documents – adding medical devices for Canada - cross reference, add additional procedures – customize approach –"knit" the system together
  - Drug Establishment Licence – GMP
  - ISO 9001
  - US FDA OTC
  - CE marked for EU
  - Corporate policies/procedures

3. Documentation Requirements

- Commercially available QS system templates
  - Caveats
  - Generic may address standard requirements:
  - May not capture:
    - company specific practices, responsibilities
    - regulatory requirements
  - Initial registration ? – maybe ok
  - Evidence of implementation, effectiveness – downstream audits? – maybe not
  - Custom system – in house expertise or outside help

4. Implementation

- Documents reviewed, approved, ready for use!
  - Training first
    - all involved staff, all levels, relevant, tailored
    - Matrix – correlates responsibilities to documents
    - Training records – evidence
    - Effectiveness
    - Use examples that relate to your business
      - Comparisons with life scenarios helpful

  - One complete internal audit, one full management review before registration audit required

5. Certification/Registration

- “Registration”
- Required for Canada, EU
- Not required if marketing only in US
  - May desire if supplying products/mfg service to customers
- Registrar
  - recognized by Health Canada and SCC
  - Notified Body for EU if CE marking
  - FDA Third Party
- Partner
  - registration, on-going commitment
- Provide a service – business
  - caveat emptor – value for investment
  - “good fit” – registrar, auditor

5. Certification/Registration

- Standardized program, registrar training
  - Difference in contracts, service delivery, interpretation, audit scheduling, costs
- Quotations
  - recommend obtain several – compare
    - Deposit, annual fee, charge for certificate and changes, per diem rate, number of audit days/auditors, surveillance audit charges etc
- Auditors
  - request CV – appropriate experience for

    company operation, product type(s)

5. Certification/Registration

- Documentation study (Stage 1)
  - review QS documents in advance - on site preferred by the registrars – exceptions possible (off site review – where experience with implementation – some conditions)
    - compliance with standard– quality manual, procedures
    - Auditor preference – e-copy, paper
  - As complete as possible
    - make auditor's job easy
    - good foundation for relationship
  - Report – time to address deficiencies

5. Certification/Registration

- On site audit (Stage 2)
  - Company practice vs written policies procedures?
  - Review documented evidence
    - records
  - Impressions important
  - Organized, clean, tidy, efficient
  - Management presence, key personnel briefed, available
  - Documents available

5. Certification/Registration

- Audit findings
  - Non-conformances/non-conformities/non-compliances – communicated as audit progresses
    - Major
    - Minor
  - Observations
    - Positive comments
    - Opportunities for improvement, recommendations
    - May evolve to nonconformances downstream
  - Corrections during audit – possible
    - Caution – hasty vs well planned

5. Certification/Registration

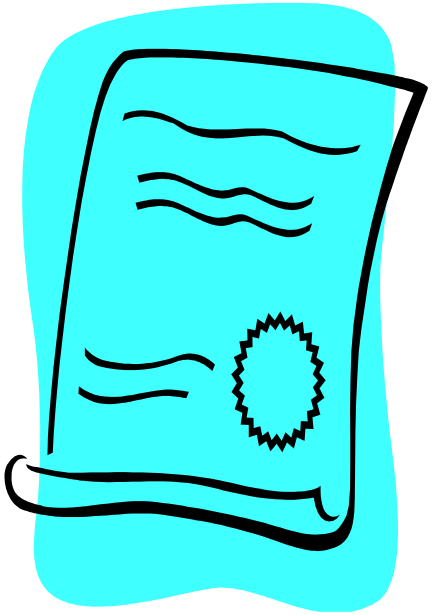
- Audit Report
  - Closing meeting – summarize findings
  - Report- draft at closing meeting or may follow
    - Internal process at registrar for review/approval
  - Non-conformances, conditions for responses/actions/timelines

5. Certification/Registration

- Audit follow up
  - Respond to non-conformances – propose actions, timelines
  - Auditor
    - approves plan, follow up determined – off site, next visit
- Registrar – review/approval of corrective actions - certificate issued

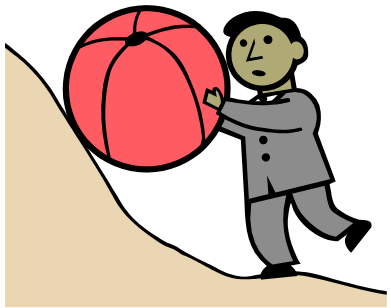
5. Certification/Registration

- Certificate
  - Content important – Health Canada guidance, scope templates, “effective” date
    - Difference from EU certificates
  - Auditor should discuss details during audit (scope, activities, products, company name and address etc)
  - May provide draft
  - Cost to change certificate – varies
  - Unacceptable certificate
    - rejected by Health Canada
    - Delay in licensing
    - Effect on product launch



6. Beyond Registration

- Registration – big achievement
- End of beginning
- Ongoing commitment – management, quality personnel
- 3 yr cycle – minimum annual surveillance audit
  - Shorter than full registration
  - follow up non-conformances, regulatory compliance, half of quality system elements
- FDA inspections
  - QSIT (Quality System Inspection Technique) method
  - PMA (preapproval inspection), 510(k) manufacturers
  - cyclic; directed



6. Beyond Registration

- Challenges
  - Staff with multiple responsibilities- conflicting priorities
  - Inexperience
  - Resources, training
  - Problem areas:
    - CAPA, complaint follow up, root cause, investigations, verify effectiveness of action
    - internal audit and follow up, management review
    - documentation/records

6. Beyond registration

- Notifications to registrar of changes
  - Changes to quality system eg manufacturing site, critical supplier of product, scope – products, activities
    - may need audit before implementation
    - auditor preparation for next scheduled audit
  - Change of address, contact
  - Advice from registrar – partner – valuable to keep in touch
- Notifications/submissions to regulator

7. ISO 13485 - Future

- Expected changes to ISO 13485:2003 – next iteration of the standard drafted, finalization 2014, 2015?
- If already certified, prepare for changes
- If planning certification before the new version, plan for the changes

7. ISO 13485 - Future

Proposed Changes to ISO 13485:

- More specific requirements included throughout the device life-cycle:
  - Design and development
  - Production
  - Storage and distribution
  - Installation
  - Servicing
- Clearly identify organization's role under applicable regulatory requirements.
- New definitions:
  - Medical device software
  - Post market surveillance
  - Performance evaluation
  - Risk management

7. ISO 13485 - Future

Proposed Changes (cont'd)

- New detailed requirements identified in subsections:
  - Design and development planning
  - Design and development verification
  - Design and development validation
  - Review of changes affecting the design of the device
  - Supplier selection, evaluation and approval
  - Verification of purchased product
  - Complaint handling
  - Response to nonconforming product

7. ISO 13485 - Future

Proposed Changes - Timeline

- Plan to revise/publish before the next version of ISO 9001 (suggested ISO 9001:2015)
- Comments to the “Committee Draft” by August 10, 2013
- Comments discussed by International Committee by October, 2013
- Prepare “Draft International Standard” for circulation and wider international public comment by October, 2013
- Target date for publishing late 2014 or early 2015

8. Medical Device Single Audit Program (MDSAP)

- Under development by a Work Group of IMDRF (International Medical Device Regulators Forum -formerly GHTF – Global Harmonization Task Force)

- IMDRF Mission:
  - accelerate international medical device regulatory convergence
  - promote efficient and effective regulatory model for medical devices that is responsive to emerging challenges in the sector while protective/maximizing public health/safety

- Work Group (WG(PD1)/N3R3 developing standard set of requirements for auditing organizations doing quality system regulatory audits of medical device manufacturers

- Will apply to competent authority auditing groups and inspectorates + third party auditing organizations

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8. Medical Device Single Audit Program (MDSAP)

Objectives:

- Single audit program with confidence in outcomes;
- Appropriate regulatory oversight of manufacturers' quality systems, minimize regulatory burden on industry;
- Promote more efficient and flexible use of regulatory resources through work-sharing and mutual acceptance among Participants, while respecting the sovereignty of each country;
- Promote greater global alignment of regulatory approaches, technical requirements based on international standards and best practices;
- Promote consistency, predictability, transparency of regulatory programs by standardizing oversight over third party auditing organizations
- Leverage, where appropriate, existing conformity assessment structures.

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8. Medical Device Single Audit Program (MDSAP)

- Expected program outputs/benefits: develop, manage and oversee a single audit program that will allow a single regulatory audit to satisfy the needs of multiple regulatory jurisdictions.
  - Less burdensome for Medical Device Manufacturers
  - Based on a three year cycle
  - International Coalition of Countries
    - Currently US, Canada, Brazil, Australia
    - Working group includes EU, Asia, Japan
  - More efficient
  - Pooled technology expertise, resources
  - Improved safety
  - Modelled after Health Canada's CMDCAS third party programs
  - Best Practices of Canadian and American systems
  - Unannounced Audits
  - 4 documents target end of 2013
  - Comment period
  - Pilot program will follow

8. Medical Device Single Audit Program (MDSAP)

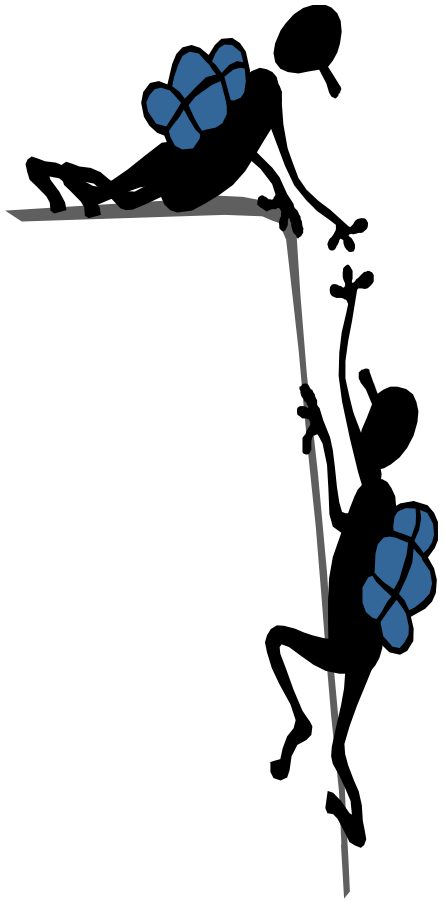
Audit Facilitators

- Code of Conduct
- Initial, Surveillance and Re-recognition Criteria
- Standard Requirements for Auditing Organizations
- Auditor Competency Assessments
- Regulatory Authority Assessed
- Standardized Rating System for audit findings

- Source Documents
  - WG(PD2)/N3R5 – Recognition and Monitoring of Organizations undertaking Audits of Medical Device Manufactures
  - ISO/IEC 17021:2011
  - EU Draft Legislation of Requirements for Notified Bodies
  - EU MEDEV 2.10-2 Rev 1:2001 – Designation and Monitoring of Notified Bodies within the Framework of EC Directives on Medical Devices

Summary

- Planning
  - Training, experience, help within/outside
- Good quality documents
  - Cover requirements, current practice
- Preparation for audit
  - Organized, impressions
  - Post certification - keep momentum
  - Don’t get behind
  - Document, document, document
- Future changes
  - Awareness, impact, planning
- Teamwork
  - Shared responsibility



Thank you!

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