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SOFTWARE AS MEDICAL DEVICE
SaMD, MDSW

An overview & strategic options

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Content

Introduction

Disclaimer

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Global iOS & Android
- >165'000 mHealth apps
- 500 m users
- CAGR > 40%
- Certified ~10%

MOBILE

FDA Will Not Review Low-Risk Wellness Apps or Wearables

Posted by
Sarah Morgan
January 30, 2015

Like 0 G+1
S» share»send»save

EXECUTIVE SUMMARY

Apple's updated App Store guidelines place added scrutiny on health, medical apps

By **Heather Mack** | September 06, 2016

Developers of health and medical apps will now have strict rules to abide by with Apple's new **App Store Guidelines** that establish a high bar for any app aimed at health and wellness.

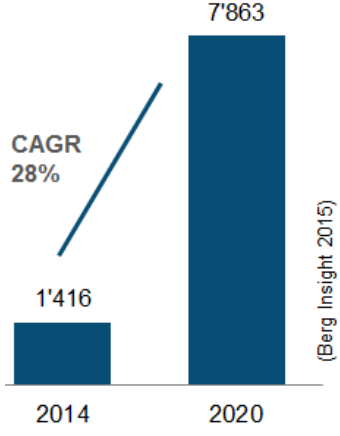
Previous **iterations of the guidelines** already laid out the proper protocol for human research subjects and avoiding physical harm, but the new rules carry much more detailed

Fitness-Tracker

Kunden reichen Sammelklage gegen Fitbit ein

Messen die Fitness-Armbänder des US-Unternehmens Fitbit zu ungenau, bringen damit die Benutz

Remote patient monitoring revenues
Europe (mHealth), € Millions



7. **Medizinprodukte: Bestimmte Software ist Medizinprodukt – Urteil des Europäischen Gerichtshofs vom 7. Dezember 2017**

Der französische Staatsrat hat sich an den Europäischen Gerichtshof mit der Frage gewandt, ob Art.1 Abs.1 und Abs.2 Buchst. a der Richtlinie 93/42/EWG dahingehend auszule-

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Various (so far separated) disciplines are converging (IT, mHealth, Medical Devices, HIS etc.)

Chaos! says the pessimists

- Confusion all over (safety, privacy, efficacy???)
- Non regulated
- Dangerous for patients
- Transparent patient

Chance! says the optimist

- Potential for prevention, monitoring…
- Simplified processes
- Cost saving possibilities
- Creates jobs

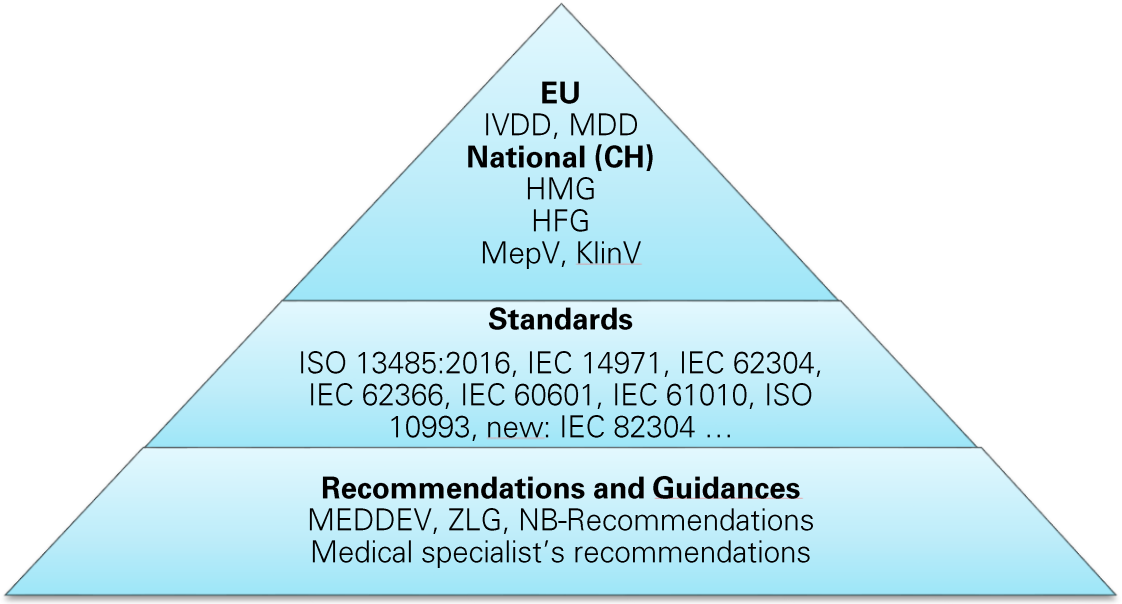
Regulatory Framework of Medical Devices

Objectives of the regulation of medical devices

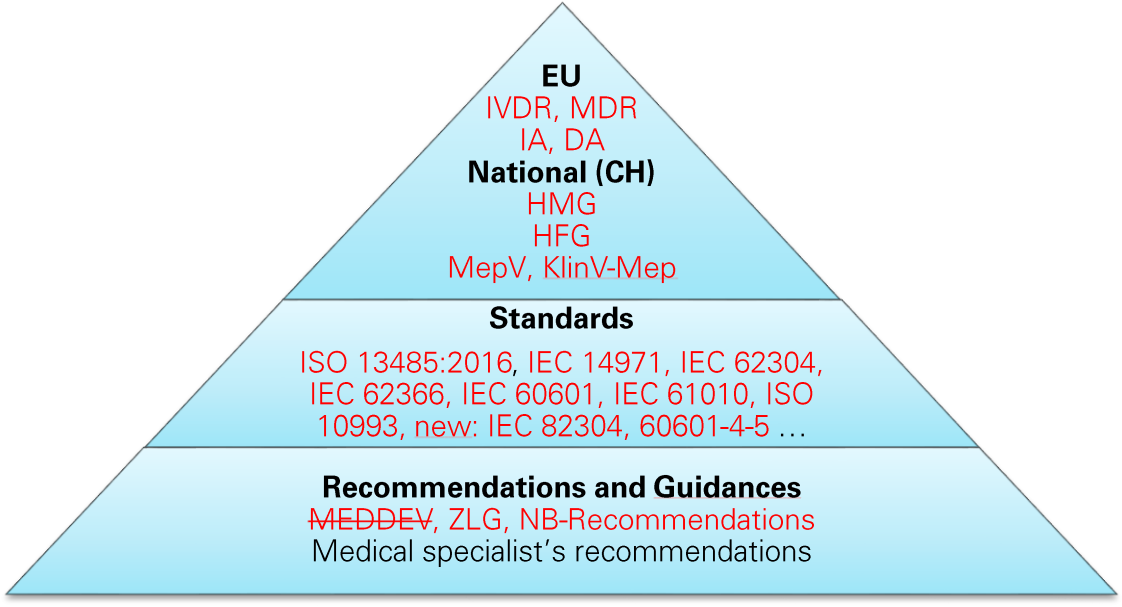
– To ensure that medical devices meet essential requirements with respect to **safety and effectiveness**;
– To protect patients and third parties from hazards and deception.

The regulations are based on various documents, e.g., the Code of Federal Regulations (CFR) in the USA, the EU Regulations, interpretations of the regulations, standards and international consensus documents.

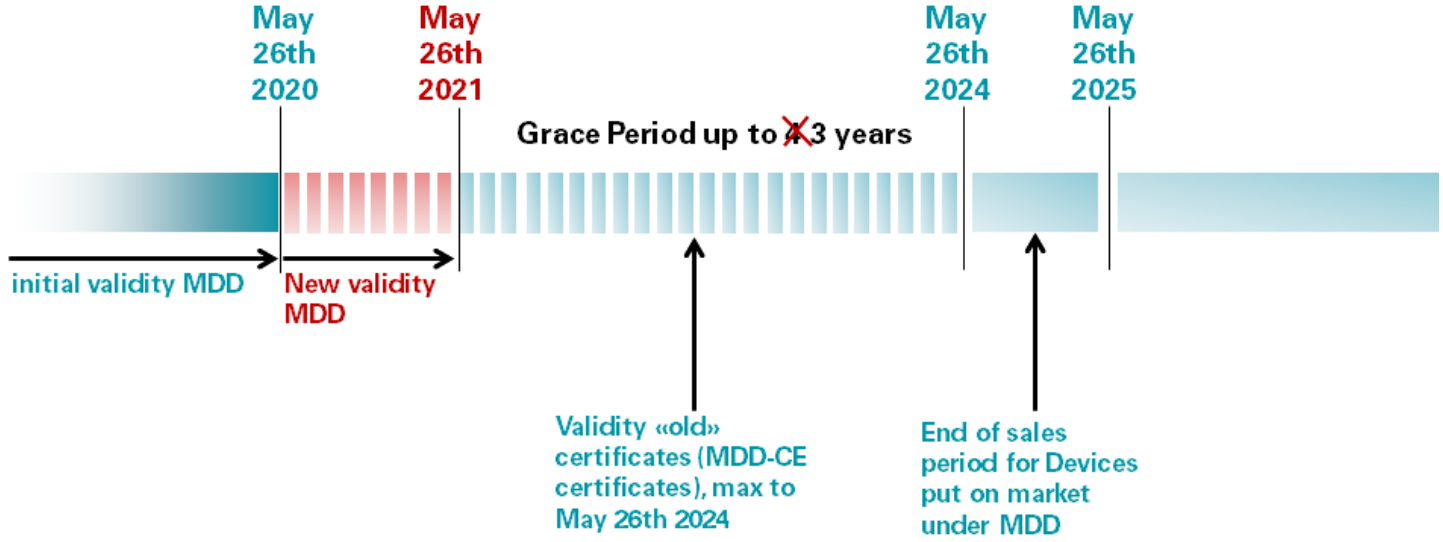
EU Regulatory Framework today…



and tomorrow (in 61 days)…



Roadmap introduction new regulation MDR



Definition I: What is a Medical Device

We focus on the definitions and requirements of the new regulation:

Definition of a „medical device" according to Article 2 of MDR (EU) 2017/745

'medical device' means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:

- diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,
- investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,
- providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations,

and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.

The following products shall also be deemed to be medical devices:

- devices for the control or support of conception;
- products specifically intended for the cleaning, disinfection or sterilisation of devices as referred to in Article 1(4) and of those referred to in the first paragraph of this point.

Definition II, MDSW, SaMD

SaMD: Software as Medical Device: introduced by IMDRF years ago and used in the MDD specific MEDDEV
"Software as a Medical Device" (SaMD) is defined as software intended to be used for one or more medical purposes that perform these purposes ***without being part of a hardware*** *medical device"*

MDSW: MDR does not mention SaMD anymore but only Medical Device Software.
Related MDCG Document states: *"Medical device software is software that is intended to be used,* ***alone or in combination****, for a purpose as specified in the definition of a "medical device" in the medical devices regulation or in vitro diagnostic medical devices regulation"*

In this presentation I focus on standalone MDSW

Definition III: SOUP

SOUP: (**S**oftware **o**f **U**nknown **P**rovenance)

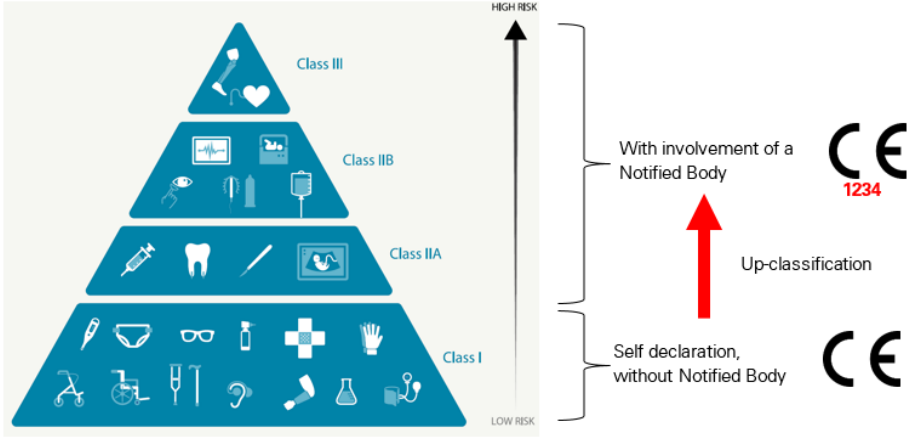
- Software item that is already developed and generally available and that has not been developed for the purpose of being incorporated into the medical device (also known as "off-the-shelf-software" or "3rd party component").
- Software item previously developed for which adequate records of the development processes are not available
  - ➔ Usually integrated into a product to reduce development time and cost and/or not to re-invent the wheel.
  - ➔ IEC 62304 defines requirements and activities regarding the use of SOUP, adding SOUP thus also incurs some effort and costs.

Qualification and classification of Software (introduction)

Qualification: is it a Medical Device Y/N

Classification: if yes, what risk class is the SW?

More details about this topic in session 4 (13.00)



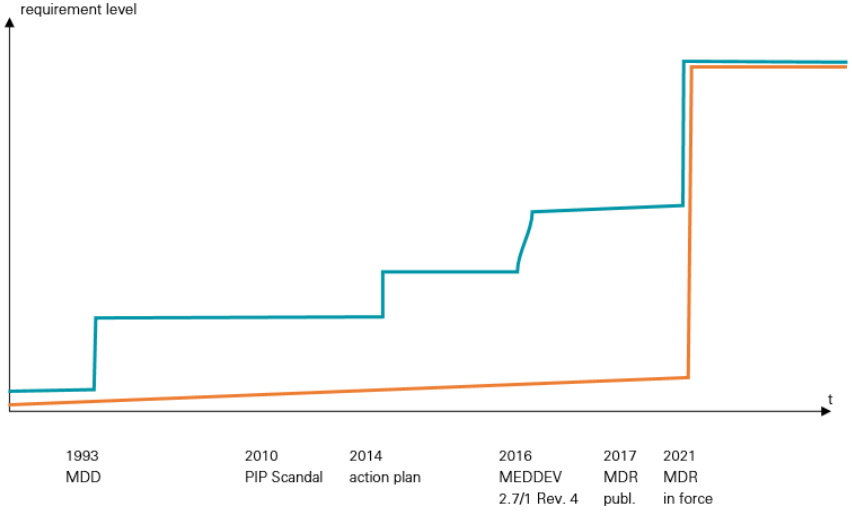
Source: MedTech Europe

Bottom line of classification under MDR:
Most Software will be up-classified under MDR to Class IIa or higher

More details about this topic in session 4 (13.00)

SW-developers: mind the “class I trap”

The leap regarding regulatory requirements for MDSW products becoming Class IIa (or higher) under MDR is very big:



Classification: example AVA woman

The Ava Fertility Tracker is a non-invasive device intended to measure and display physiological parameters to aid women in ovulation prediction to facilitate conception. ... This, in combination with historical menstrual cycle data, is the basis for the Fertility Tracker technology and the intended use of the device. (source: ava App Guide)

The MDCG Guidance says:

MDSW app intended to support conception by calculating the user's fertility status based on a validated statistical algorithm. The user inputs health data including basal body temperature (BBT) and menstruation days to track and predict ovulation. The fertility status of the current day is reflected by one of three indicator lights: red (fertile), green (infertile) or yellow (learning phase/cycle fluctuation). This MDSW app should be classified as ***class I*** *per Rule 11c.*


Abtreibungen in der Schweiz

Trendwende bei Schwangerschafts-abbrüchen

Lange gingen die Abtreibungen hierzulande zurück. Doch nun steigen die Zahlen wieder. Sind unzuverlässige Zyklus-Apps schuld?

Iwan Städler, Simone Rau
Aktualisiert: 26.06.2020, 08:08

60 Kommentare

Trend reversal in abortions (…) Are unreliable cycle apps to blame?

Q: What happens if the same Device is used for contraception?

A: it becomes a class IIb, since the risk profile completely changes (risk of unwanted pregnancy is different from the risk of not becoming pregnant)

Means:
Intended Purpose (Zweckbestimmung) **is crucial** and should be defined at the beginning of a project

What the Legal Manufacturer of a MDSW has to fulfill

Basically

- The legal manufacturer is liable for the medical device in terms of safety and effectiveness.
- The legal manufacturer has to fulfill manifold requirements given by the MDR.

Quality Management System (ISO 13485 certification)

Manufacturer have to maintain a Quality Management System, in most cases ISO 13485 is the best choice

Introducing a QMS according to ISO 13485 is quite a project.

It normally takes > 9 months

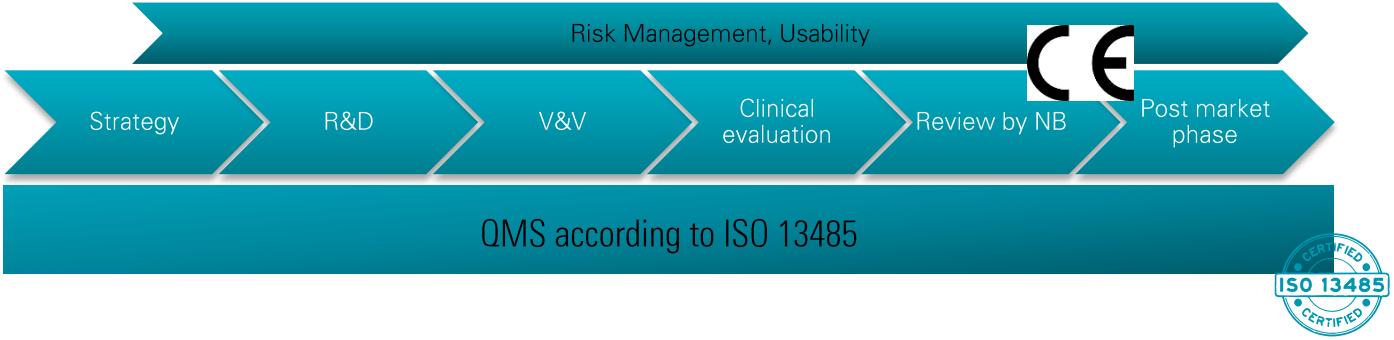
CE-Marking

- Each Medical Device needs a **CE mark**.
- The CE Mark is (if not class I) to be approved by the Notified Body
- For obtaining the CE mark, a set of standards have to be applied during the Lifecycle of the product.

Following information is relevant if the concerned SW is a Medical Device in Europe (including Switzerland)

Impact of new MDR requirements

Simplified CE-process so far



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CE process under MDR

Good news: the basic process does not change

Risk Management, Usability, **Cyber Security, PRRC** CE

Strategy, **CEP** → R&D → V&V → Clinical evaluation → Review by NB → Post market phase

QMS according to ISO 13485 **+ MDR req. not covered by ISO 13485**

ISO 13485 CERTIFIED

- What products to go for MDR?
- Where to go first?
- V&V options
- Clinical Eval. Plan

- Documentation according new rules/structure

- V&V will be of higher importance for RA approval

- more clinical data required
- adaptive study design

- less NB available
- stricter reviews
- longer lead-time
- scrutiny process in some cases

- More PMS work
- more resp. for distributors
- EC-Rep?
- CH-Rep?
- UK-Rep?

Concept of harmonized standards

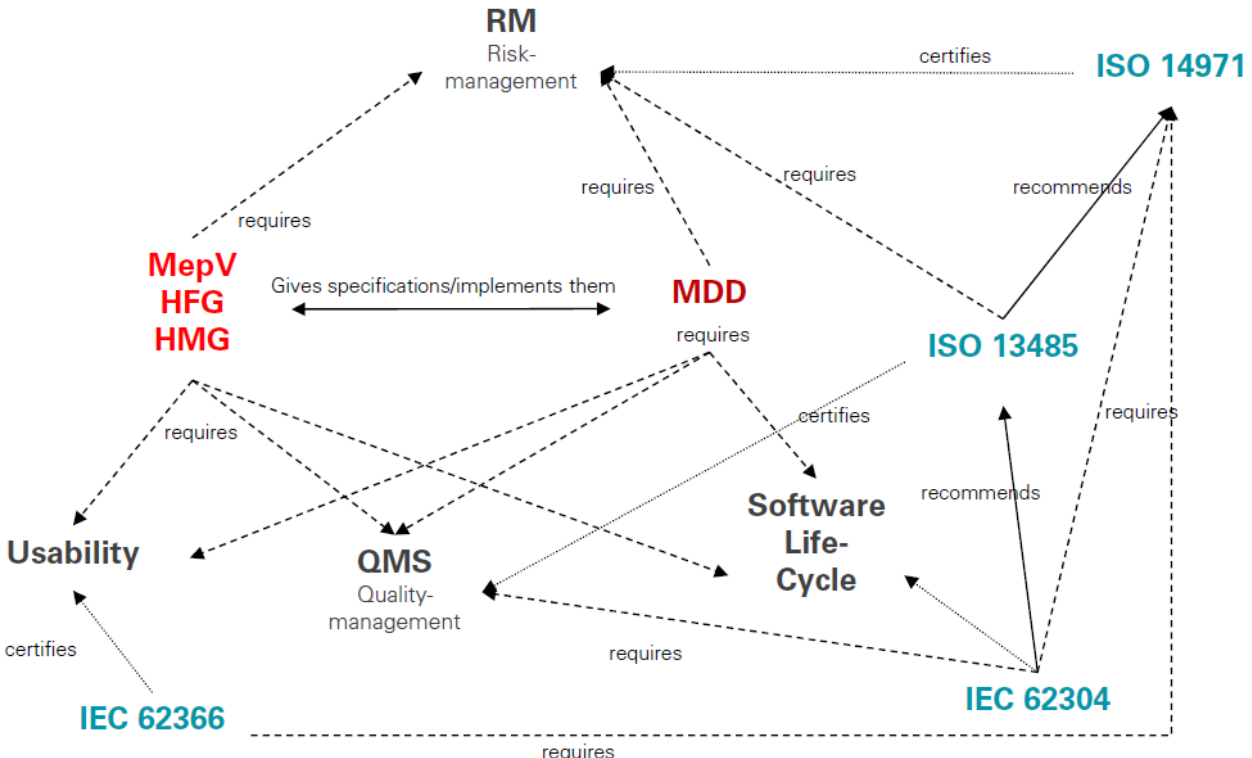
Harmonized standards are deemed to offer the „presumption of conformity“ to specific Essential Principles of Safety and Performance laid down in MDR EU 2017/745 Annex I.

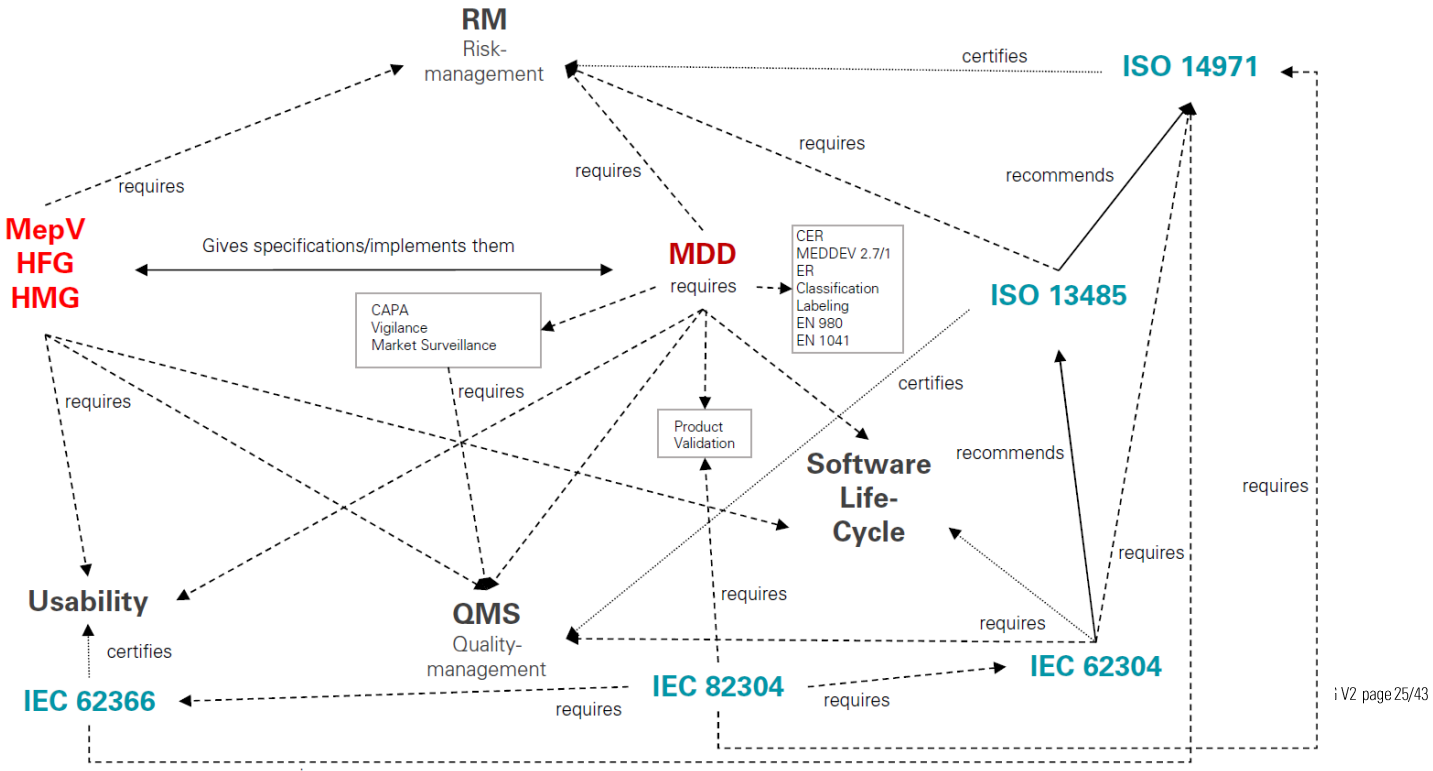
Means: each Annex I Requirement you can address with a Standard, is considered as “fulfilled”

Means: Standards are our friends, not our enemies

Remark: at the moment, the standards are not yet harmonized with the MDR (but only the MDD). However, standards are considered as part of the “state of the art” and still very important under MDR.

Standards to be considered:


RM
Risk-
management
certifies
ISO 14971
requires
requires
recommends
requires
MepV
HFG
HMG
Gives specifications/implements them
MDD
requires
ISO 13485
requires
certifies
requires
recommends
Software
Life-
Cycle
Usability
QMS
Quality-
management
certifies
requires
IEC 62366
IEC 62304
requires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HFG
HMG
Gives specifications/implements them
MDD
requires
CER
MEDDEV 2.7/1
ER
Classification
Labeling
EN 980
EN 1041
ISO 13485
CAPA
Vigilance
Market Surveillance
requires
certifies
requires
Product
Validation
Software
Life-
Cycle
recommends
requires
requires
Usability
QMS
Quality-
management
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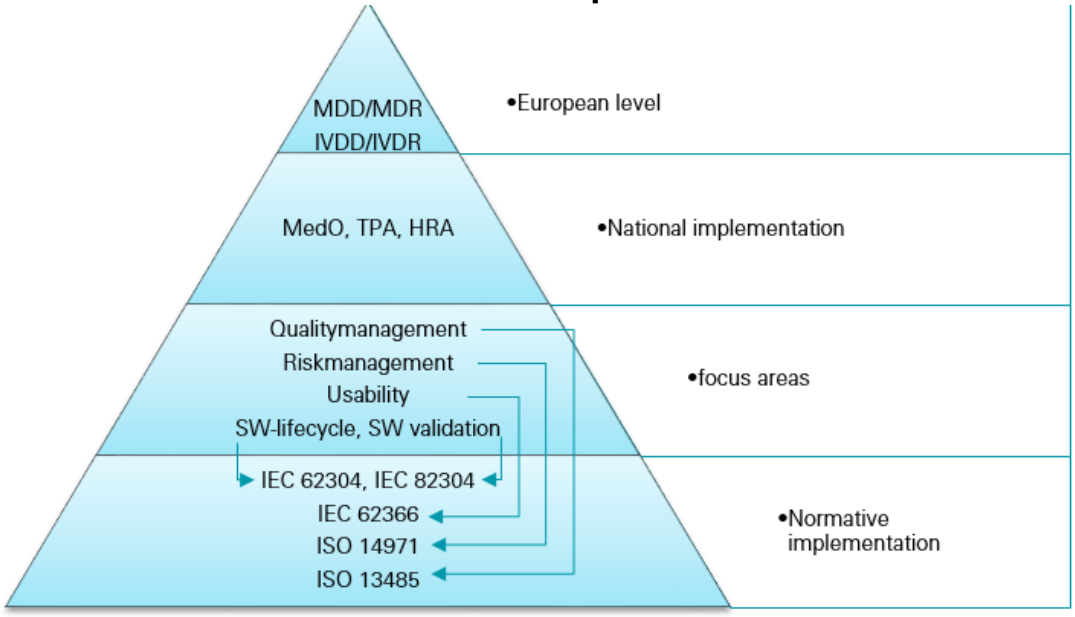
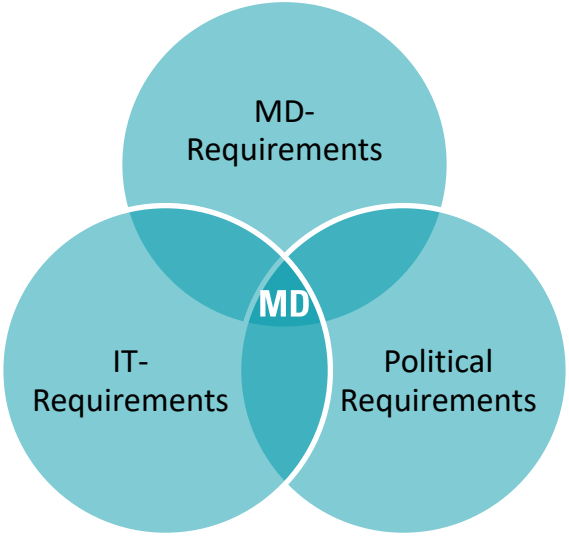
requires
certifies
IEC 62304
IEC 62366
IEC 82304
requires
requires

Standard-Stack for SaMD/MDSW-Development



It's getting even worse. Convergence of IT & MedTech leads to additional requirements…

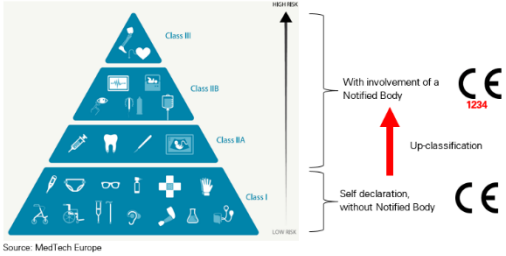


…including different Standards

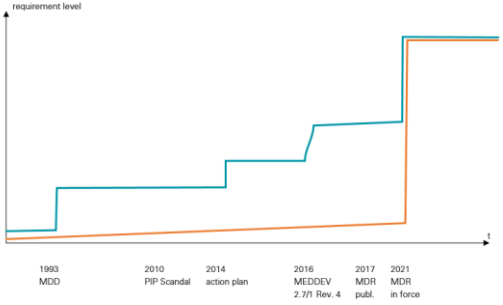
Medical world	IT world	Political world
ISO 13485:2016	IEC 80001-1	Data Protection Legislation (CH)
IEC 62304	ISO 270xx	GDPR
IEC 82304	ISO 20000	MDR
ISO 14971	ISO 9001	HIPAA
IEC 62366	…	Upcoming AI regulations

Potential strategic options for Legal Manufacturing

Considering the higher hurdles for MDSW, what options does Legal Manufacturers have?



Source: MedTech Europe



Option 1: DiYS (Do it yourself), the classic way

- Set-up and maintain your own ISO 13485
- Build-up own Q/RA organization, PRRC can be outsourced
- Search a NB, CE-certify your device
- Go to the market

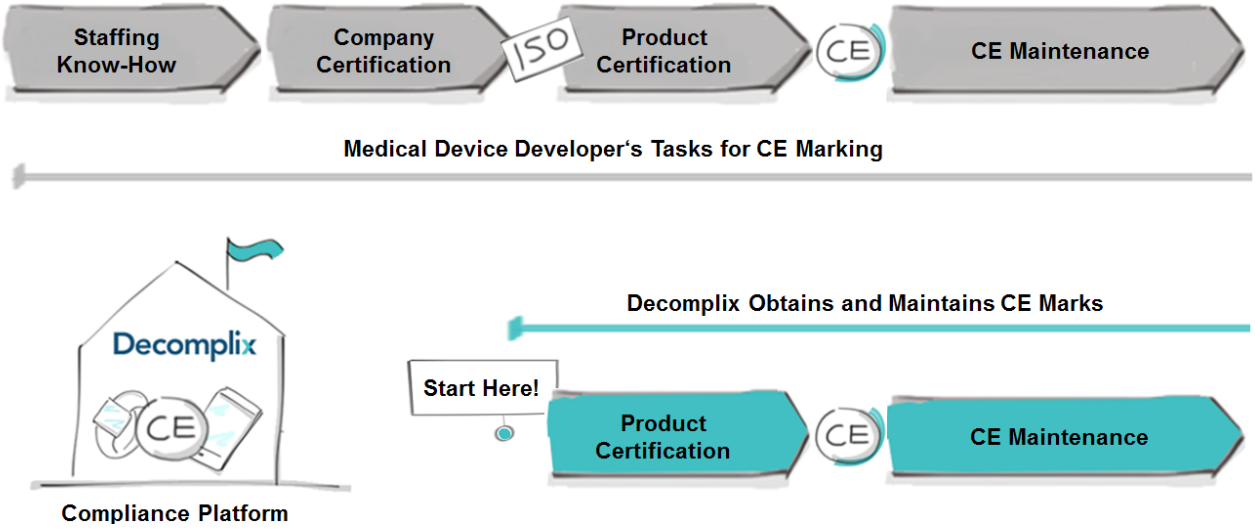
So far the "normal way"

Quite high investment in terms of time & money

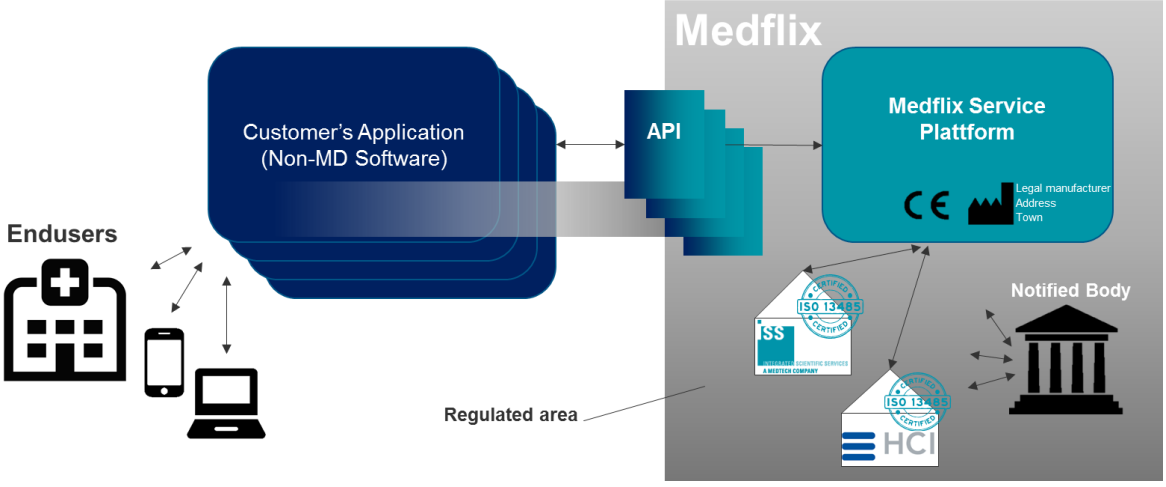
Option 2: forget about Europe

- Go “America first”
- FDA has significant lower hurdles for SaMD
    - No ISO certification needed (but a QMS according to CFR 820)
    - In many cases no 510(k) needed
- You can build-up experience, reputation, clinical data etc. quite fast
- But, be careful: Market access is not market success -> US market can be very expensive in terms of M&S

Option 3: outsource the legal manufacturing



Option 4: segregate your MD functionality and outsource the LM



Option 5, for health Institutions only: Article 5 of MDR gives some flexibility

Article 5 of MDR gives health institution the right to put Medical Devices on the market for internal use without the whole CE marking process but with the obligation to maintain technical documentation and fulfill the requirements of the Annex I (general safety and performance requirements)

Original Text:

5. With the exception of the relevant general safety and performance requirements set out in Annex I, the requirements of this Regulation shall not apply to devices, manufactured and used only within health institutions established in the Union, provided that **all of the following conditions** are met:

(a) the devices are **not transferred** to another legal entity,
(b) manufacture and use of the devices occur under **appropriate quality management systems**,
(c) the health institution justifies in its documentation that the target patient group's specific needs cannot be met, or cannot be met at the appropriate level of performance by an **equivalent device available on the market**,
(d) the health institution provides information upon request on the use of such devices to its competent authority, which shall include a justification of their manufacturing, modification and use;
(e) the health institution draws up a **declaration** which it shall make publicly available, including:

(i) the name and address of the manufacturing health institution;
(ii) the details necessary to identify the devices;
(iii) a declaration that the devices meet the general safety and performance requirements set out in Annex I to this Regulation and, where applicable, information on which requirements are not fully met with a reasoned justification therefor,

(f) the health institution draws up **documentation** that makes it possible to have an understanding of the **manufacturing** facility, the manufacturing process, the design and performance data of the devices, including the intended purpose, and that is sufficiently detailed to enable the competent authority to ascertain that the general safety and performance requirements set out in Annex I to this Regulation are met;
(g) the health institution takes all necessary measures to ensure that all **devices are manufactured in accordance with the documentation** referred to in point (f), and
(h) the health institution reviews experience gained from clinical use of the devices and takes all necessary **corrective actions**.

Member States may require that such health institutions submit to the competent authority any further relevant information about such devices which have been manufactured and used on their territory.
Member States shall retain the right to restrict the manufacture and the use of any specific type of such devices and shall be permitted access to inspect the activities of the health institutions.

This paragraph shall not apply to devices that are manufactured on an industrial scale.

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Tips and Tricks from our experience

General

- **System boundaries** are changing. Risk Management has to cover the Deployment (via shops), Updates via Shops etc.
- **IT-security**, privacy, product liability has to be taken into account -> not “automatically” covered by IEC 62304 -> see separate session about cyber security
- **Operating systems**: everything is possible, with respective pros and cons per OS. Remark: a FDA or CE-validated Operating Systems for Medical Software does not exist, even though it is promised in some advertisements. Validation has always to be done in the respective context.
- Independent from the strategic option for LM you chose: there is **homework** to do in the **RA/Q** area
- Define a trained and experienced **responsible Q/documentation** person

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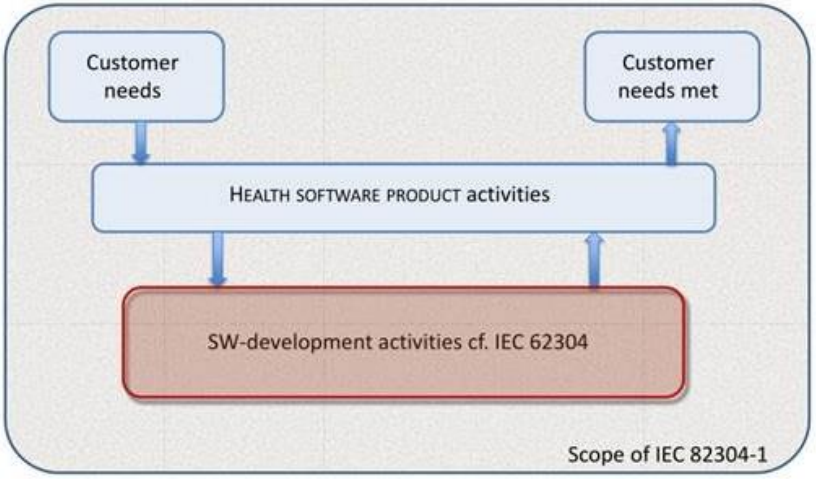
Validation of Stand-Alone-Software

- Validation against the intended use (inclusive clinical evaluation) is a requirement of EN ISO 13485 (chapter 7.3.6) and 21CFR820 chapter 820.3(z)(2) and 820.30(g).
- SW-validation is required in IEC 62304**,** but not really covered (SW-verification only)
- Actually, one has to create an own validation strategy (e.g. in the style of the strategies proposed in IEC 60601-1)
- Standard IEC 82304 **closes** this gap. IEC 82304 is on the list of the FDA consensus standards.

Clause 4 – HEALTH SOFTWARE PRODUCT requirements

For product safety standards, it is common practice that use requirements for a product are defined upfront and that criteria to validate the final product are based on these customer or use requirements. The phase in between defining initial system requirements and VALIDATION of the final product is the product development process. Such a development process is schematically given in Figure A.2. The actual process of HEALTH SOFTWARE development can follow various schemes, such as the waterfall model, the "V-model, or more iterative or incremental development schemes.



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Validation can be quite extensive (and expensive): example of a glucose monitoring app from dexcom

	Australia, Austria, Bahrain, Belgium, Canada, Czech Republic, Denmark, Finland, France, Germany, Hong Kong, Ireland, Israel, Italy, Jordan, Kuwait, Lebanon, Luxembourg, Netherlands, New Zealand, Norway, Oman, Poland, Qatar, Saudi Arabia, South Africa, Spain, Sweden, Switzerland, United Arab Emirates, United Kingdom
Dexcom G5 Mobile App	iPhone 5, iPhone 5C, iPhone 5S, iPhone 6, iPhone 6 Plus, iPhone 6S, iPhone 6S Plus, iPhone 7, iPhone 7 Plus, iPhone SE, iPhone 8, iPhone 8 Plus, iPhone X, iPhone XS, iPhone XS Max, iPhone XR iPod touch 6th Gen iPad 4, iPad 5, iPad Air, iPad Air 2, iPad Mini 2, iPad Mini 3, iPad Mini 4, iPad Pro, iPad (6th Generation) Apple Watch (1st Generation), Apple Watch Series 1, Apple Watch Series 2, Apple Watch Series 3 (watches require compatible smart device to use app) watchOS 3.0.0, 3.1.0, 3.1.3, 3.2.0, 3.2.2, 4.0.0, 4.1.0, 4.2.0, 4.2.3, 4.3.0, 4.3.1, 4.3.2, 5.0.0, 5.0.1, 5.1.0, 5.1.1, 5.1.2, 5.1.3 iOS 10.0.1, 10.0.2, 10.0.3, 10.1.0, 10.1.1, 10.2.0, 10.2.1, 10.3.0, 10.3.1, 10.3.2, 10.3.3, 11.0.0, 11.0.1, 11.0.2, 11.0.3, 11.1.0, 11.1.1, 11.1.2, 11.2.0, 11.2.1, 11.2.2, 11.2.5, 11.2.6, 11.3.0, 11.3.1, 11.4.0, 11.4.1, 12.0.0, 12.0.1, 12.1.0, 12.1.1, 12.1.2, 12.1.3, 12.1.4, 12.2 Samsung Galaxy S5 (Android 6.0.0, 6.0.1), Samsung Galaxy S6 (Android 6.0.1, 7.0.0), Samsung Galaxy S6 Edge (Android 5.1.1, 6.0.0, 6.0.1), Samsung Galaxy S7 (Android 6.0.1, 7.0.0), Samsung Galaxy S7 Edge (Android 6.0.1, 7.0.0), Samsung Galaxy S8 (Android 7.0.0, 7.1.1, 8.0.0), Samsung Galaxy S8 Plus (Android 7.0.0, 7.1.1, 8.0.0), Samsung Galaxy S9 (Android 8.0.0), Samsung Galaxy S9 Plus (Android 8.0.0), Samsung Galaxy Note 5 (Android 6.0.0, 6.0.1, 7.0.0), Samsung Galaxy Note 8 (Android 7.1.1, 8.0.0), Samsung Galaxy Note 9 (Android 8.1.0), Samsung Galaxy J3 [Models SM-J237, SM-J330 and SM-J337] (6.0.1, 7.0.0, 8.0.0), Samsung A5 [SM-A520 Model Only](7.0.0) LG G4 (Android 5.0.0, 5.1.0, 5.1.1, 6.0.0), LG G5 (Android 6.0.1, 7.0.0), LG G6 (Android 7.0.0), LG G7 (ThinQ) (Android 8.0.0), Google Pixel (Android 7.1.2, 8.0.0, 8.1.0), Google Pixel 2 (Android 8.0.0, 8.1.0), Google Pixel XL (Android 8.0.0, 8.1.0), Google Pixel 2 XL (Android 8.0.0, 8.1.0), Google Pixel 3, Google Pixel 3 XL, Huawei P20(8.1.0), Huawei P20 Pro(8.1.0)

Source: https://www.dexcom.com/dexcom-international-compatibility

Take home Message

- Yes, your SW can become a Medical Device -> double check early
- If the SW is a Medical Device, a CE marking is needed
- Clarify the intended purpose of your MDSW early
- Most MDWS will be Class IIa or higher -> mind the gap
- Consider strategic options for legal manufacturing and markets
- MDSW Development and certification is a very specific topic with a lot of traps: work with professionals

Helpful Links

Guidance on Qualification and Classification of Software in Regulation (EU) 2017/745 – MDR and Regulation (EU) 2017/746 – IVDR:
https://ec.europa.eu/docsroom/documents/37581

European Commission, Green Paper on mobile Health (mHealth), 10. April 2014,
http://ec.europa.eu/digital-agenda/en/news/green-paper-mobile-health-mhealth

MHRA Guidance on medical device stand-alone software (including apps), 25. August 2016,
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/548313/Software_flow_chart_Master.pdf

Merkblatt der Swissmedic zum Thema „Eigenständige Medizinprodukte-Software" (Jan 2016)
https://www.swissmedic.ch/dam/swissmedic/de/dokumente/medizinprodukte/mu500_00_005d_mbeigenstaendigemedizinprodukte-software.pdf.download.pdf/mu500_00_005d_mbeigenstaendigemedizinprodukte-software.pdf

eHealth Suisse: Guideline for app developers,manufacturers and distributors: https://www.e-health-suisse.ch/fileadmin/user_upload/Dokumente/2018/E/180731_Leitfaden_fuer_App_Entwickler_def_EN.pdf

Guidance on the use of AGILE practices in the development of medical device software
https://my.aami.org/aamiresources/previewfiles/TIR45_1208_PREVIEW.PDF

Hints regarding tool validation
http://my.aami.org/aamiresources/previewfiles/TIR360803_preview.pdf

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swiss made software

ISS at a glance

- Fully dedicated to **MedTech**
- **> 40 high profile employees** (Engineers, Scientists, Medical Doctors)
- Projects, services and products for MedTech companies in the fields of Clinical Services, Regulatory Affairs, Software Development, Quality & Engineering Support
- **Certified** per ISO 13485* (including IEC 62304 SW lifecycle process), audited CRO services (BVMA)
- **International** customers in various subfields of the MedTech industry
- Dedicated to "**Doing**" rather than "Consulting only"
- Founded in **2003** as spin-off of Ziemer Group, an established manufacturer of ophthalmic High Tech devices
- Located in **Biel**, a core area of Switzerland's watchmaking and high-tech industry, Office in **Geneva.**

*** Scope of ISO 13485**: Development and development services for **hardware and embedded software** for medical products as well as **stand-alone software** as medical products, **Design and development verification and validation, Clinical evaluations**, **clinical studies and PMCF studies, Technical documentation** of medical devices

ISS
INTEGRATED SCIENTIFIC SERVICES
A MEDTECH COMPANY

ISS Services from a Project Perspective

	Idea	Implementation	Market Introduction	Maintenance
BD, Consult. Down-to-earth	Business Model Dev.	Project Management	Paralegal Services	Project Coaching
Q & Eng. Avoid problems	ISO 13485/FDA 21CFR 820	Risk Mmt., Tech File, Audit Support, V&V, CAPA, Complaint handling		
RA Services Global Markets	RA Strategy	RA-Intelligence	Global Registrations	PMS / Re-Registrations
Clinical Srv. CRO for MedTech	Cl. Strategy	Study Planning, Approvals, Operations, CEP/CER, Medical Writing, PMCF		
Software Eng. Applied IEC 62304	Req. Engineering	SW-Development	SW Validation	Product Support

Q&A