SAFE TO SAY

WELCOME TO DEVICE PLAYGROUND RULES IN MEDICAL DEVICES

Tami Harel

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align | invisalign | iTero | exocad

PIP (POLY IMPLANT PROTHESES) SCANDAL

1997 — PIP approved for marketing in Europe

2001 — Start using unapproved silicone in implants

2002 — First reports of potential problem: *ruptures, inflammation, scarring*

2010 — PIP company closed after enforced recall

2011 — French government recommended removing PIP implants in *30000* women

2012 — The penalties were given to the founder and CEO

2017 — French court ordered the NB to pay 60 million euros in damages

(MDR) + unannounced audit

DID YOU KNOW?

NO.01

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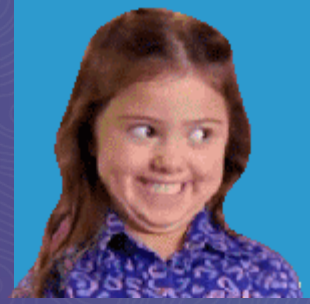
WHAT IS THE CONNECTION BETWEEN APPLE AND ALIGN?



ECG WATCH APP

NSR

AF

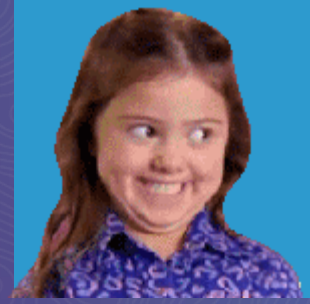
HEALTH APP

Not approved for diagnosis, just information –
De Novo process, clinical study of 600 subjects + usability

DID YOU KNOW?

NO.02

APPLE HAS DELAYED THE RELEASE OF THE WATCH FOR MONTHS DUE TO NEED OF **FDA** APPROVALS



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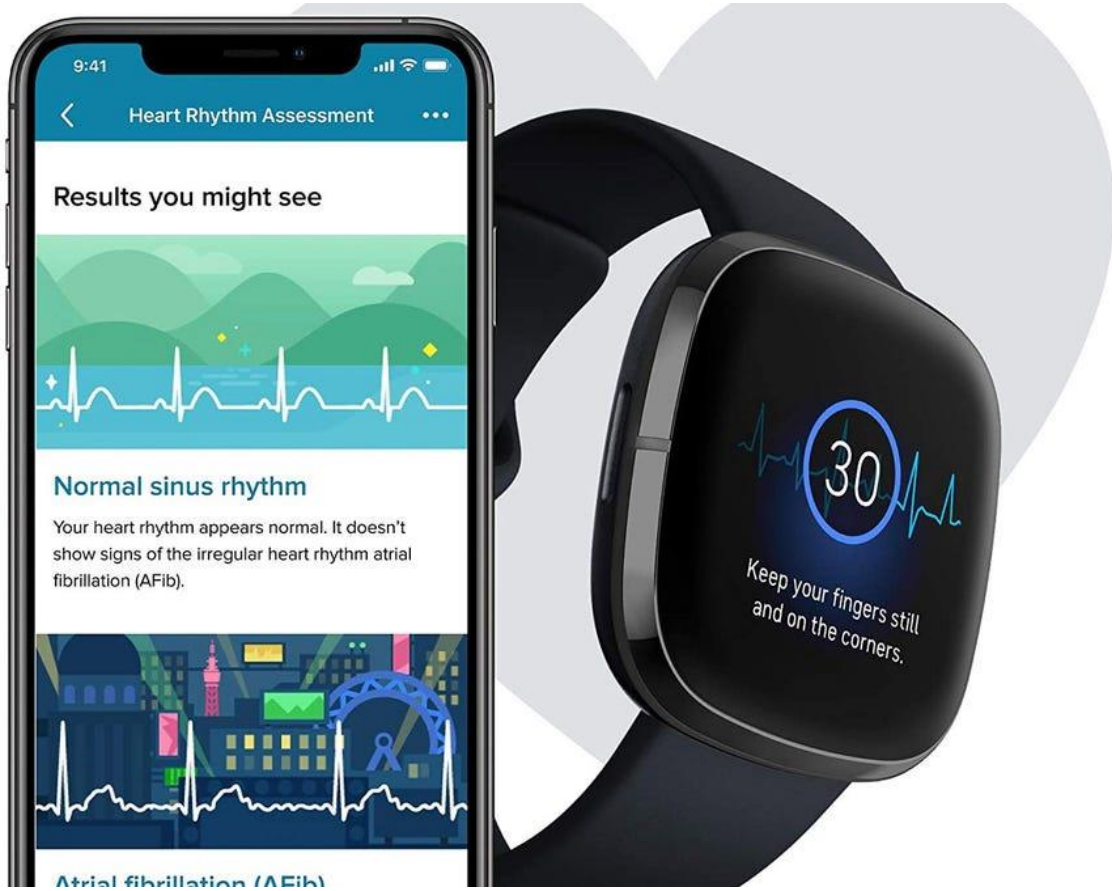
FITBIT ECG APP

Cleared through 510k process :
Usability & clinical study on 475 subjects



MEDICAL DEVICE DEFINITION
(FROM MDR ARTICLE 2)

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:

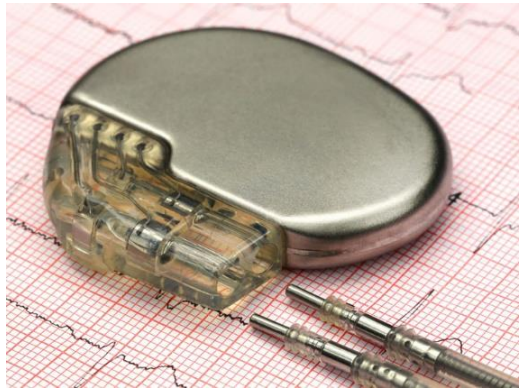
- diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,
- investigation, replacement or modification of the anatomy or of a physiological or pathological process 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.

EXAMPLES OF MEDICAL DEVICES



Design & Development

Certification

Post market surveillance

Obsolete

MEDICAL DEVICE REGULATORY REQUIREMENTS

Medical devices must comply with regulatory requirements through all lifecycle stages

Regulatory requirements are defined by local law, for example :

- USA (21 CFR - Code of Federal Regulations)
- Europe (MDR – Medical Device Regulation, IVDR – In-Vitro Device Regulation)
- Australia (TGA – Therapeutic Goods Act)

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DESIGN AND DEVELOPMENT

Manufacture shall establish and maintain procedures to control the design of the device in order to ensure that specified design requirements are met


Disney+

PROBLEMS DUE TO INSUFFICIENT V&V

1

Cause: the upgrade did not handle properly scanners that have previous scans from older version;

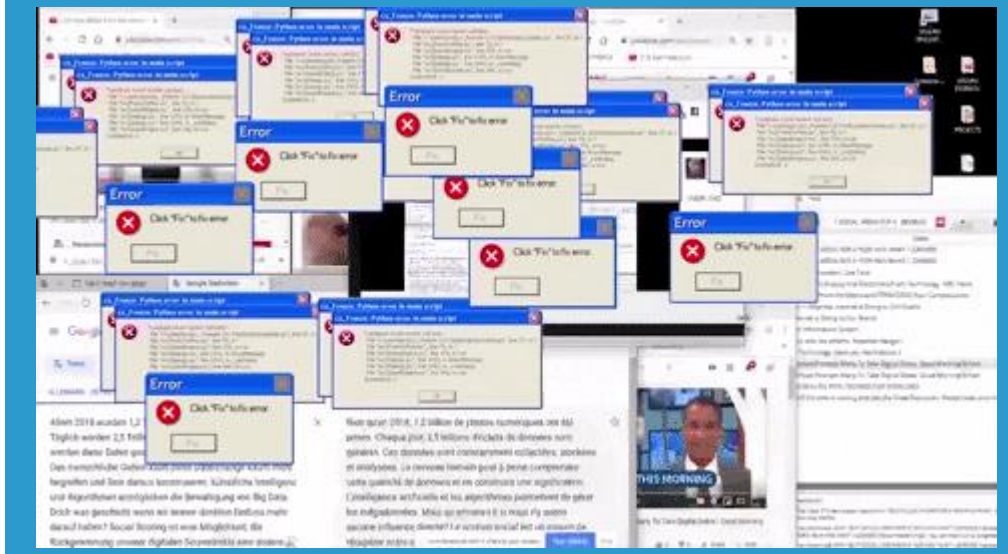
Testing was supposed to simulate this case i.e., create a scan in the older version and then upgrade from previous versions

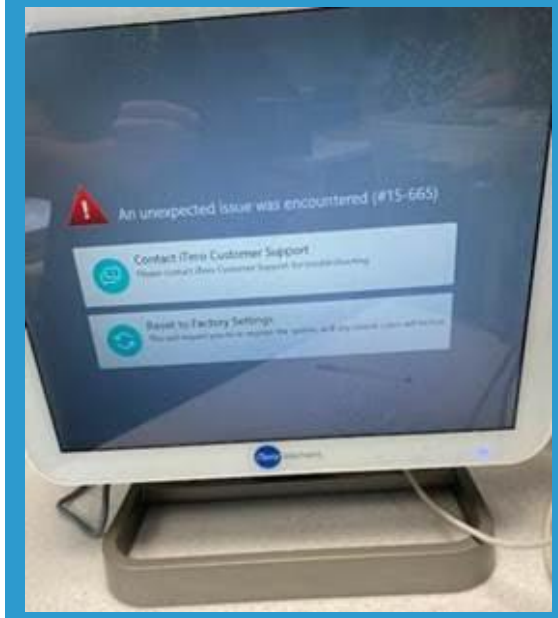
Outcome: LMR stopped;

required 3 weeks to release a new version +

hours spent on:

- SW fix
- impact assessment
- risk analysis
- re-testing
- documentation





2 **Issue occurred :** Problems detected in the field with screen resolution and touch screen problems while working with plastic sheath

Cause: ADV made changes to the FPGA in the mPPC and this change was not tested thoroughly:

- Although the defect of the change in screen resolution was detected during testing, not all scenarios were analyzed and tested
- A change in screen calibration parameters – resulted that in screens with the plastic sheath the touch didn't work as needed. This scenario was not tested

Outcome : The 21A LMR on the mPPC is currently stopped, customer frustration and revert to the previous FPGA version

3

Navigation system for spine surgery, uploads patient's CT scan for registration.

Issue occurred: surgery could not be performed with the navigation system

Cause: SW was modified; re-analysis regarding all possible scenarios in the scan due to this change was not properly performed

Outcome: Not a safety issue, however - immediate bug fix was required and SW upgrade to all systems in the field

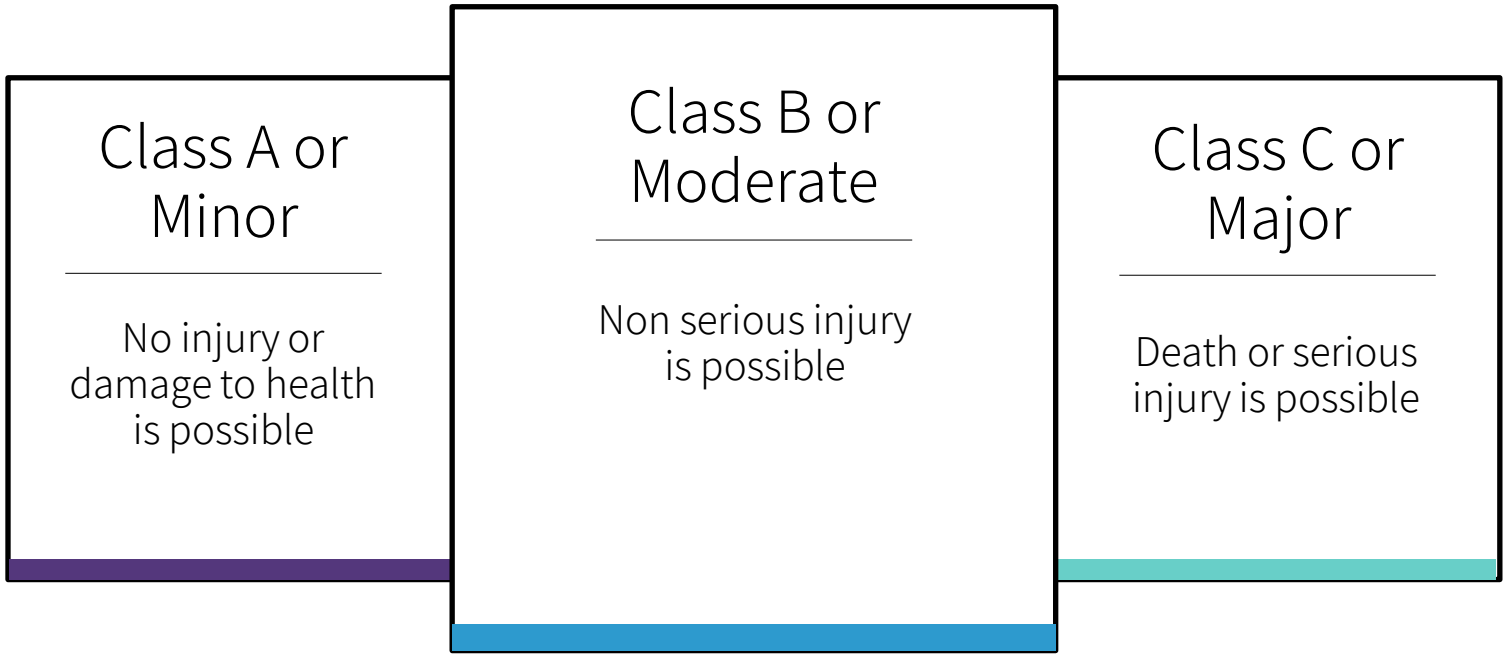
Implications: money, bad impression, delay in other development activities

STANDARDS AND GUIDANCE DOCUMENTS

- Risk Management
- Electrical safety , EMC , RF, Laser
- SW
- Usability
- Cybersecurity
- Biocompatibility
- Cleaning and disinfection
- Labeling (labels & IFU)
- Specific to devices : CAD/CAM impression device, X-ray systems, navigation systems, etc.

DESIGN AND DEVELOPMENT FOR SW (IEC/EN 62304)

SW safety classification according to risk



Level of development requirements and documentation is determined based on risk level

SW DEVELOPMENT PROCEDURES

- SW maintenance process – **Defect fixes**
- Implementing modifications in SW – **Change Control**
- SW risk management – **Part of risk management**
- SW configuration management – **Part of SW development process**
- SW Problem Resolution - **SPR**

RISKS IN ALIGN SW (EXAMPLES)

SW Defect

Light continuously ON,
no pulses
Light intensity increases

Inaccurate 3D model
Crown doesn't fit – reduced support & stabilization through adhesion to tooth substance

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RISKS IN SW - CYBERSECURITY (RANSOM ATTACK)

University of Vermont (UVM) Medical Center , USA

Digital tools locked for 1 month:

- electronic health records (EHRs)
- payroll programs
- surgeries had to be rescheduled
- cancer patients had to go elsewhere for radiation therapy

The center never paid the ransom

Attack cost: ~ $50 million (mostly from lost revenue)

Hilel Yafeh has just experienced the same thing

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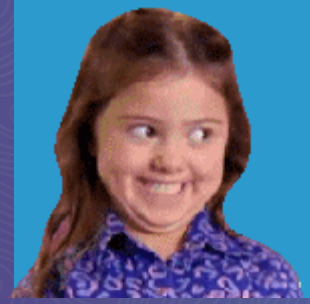
הידעת?
בכל יום נפרצות בממוצע
כ-900 רשומות רפואיות
(ארה"ב בלבד)



QUALITY MANAGEMENT SYSTEM (QMS)

- Organizational structure, responsibilities, procedures, processes, and resources for implementing quality management

- Manufacturers must establish and follow quality systems procedures and instructions to help ensure that their products **consistently meet applicable requirements and specifications**

MEDICAL DEVICE REGULATORY REQUIREMENTS

Medical devices must comply with regulatory requirements through all its lifecycle stages:

CLASSES OF MEDICAL DEVICES

Medical Devices are classified based on their potential risk to user / patient

Higher risk devices ⟶ additional requirements & evidence

USA			
Classification	**Example**	**Sub- type**	**Avg. time for marketing approval**
Class I	elastic bandages, mercury thermometers	Exempt (~45% of medical devices*)	Immediate (after registration and listing)
Class II	Da Vinci system, SW devices, navigation systems	Mostly 510k, there are some exempt (~43% of medical devices*)	~4-6 months
Class III	Implantable pacemakers, breast implants	PMA (~10% of medical devices*)	~8-12 months Preparation is much longer (rigorous clinical studies)

* https://www.fda.gov/medical-devices/consumers-medical-devices/learn-if-medical-device-has-been-cleared-fda-marketing

MEDICAL DEVICE REGULATORY REQUIREMENTS

Medical devices must comply with regulatory requirements through all its lifecycle stages:

POST MARKET SURVEILLANCE (PMS) REQUIREMENTS

Monitor the device after certification and in-market use

Proactive

- Safety notifications by regulatory bodies
- Reports of adverse events with similar devices
- Questionnaires / feedback from users
- Clinical studies with the device itself
- Clinical studies with similar devices

||

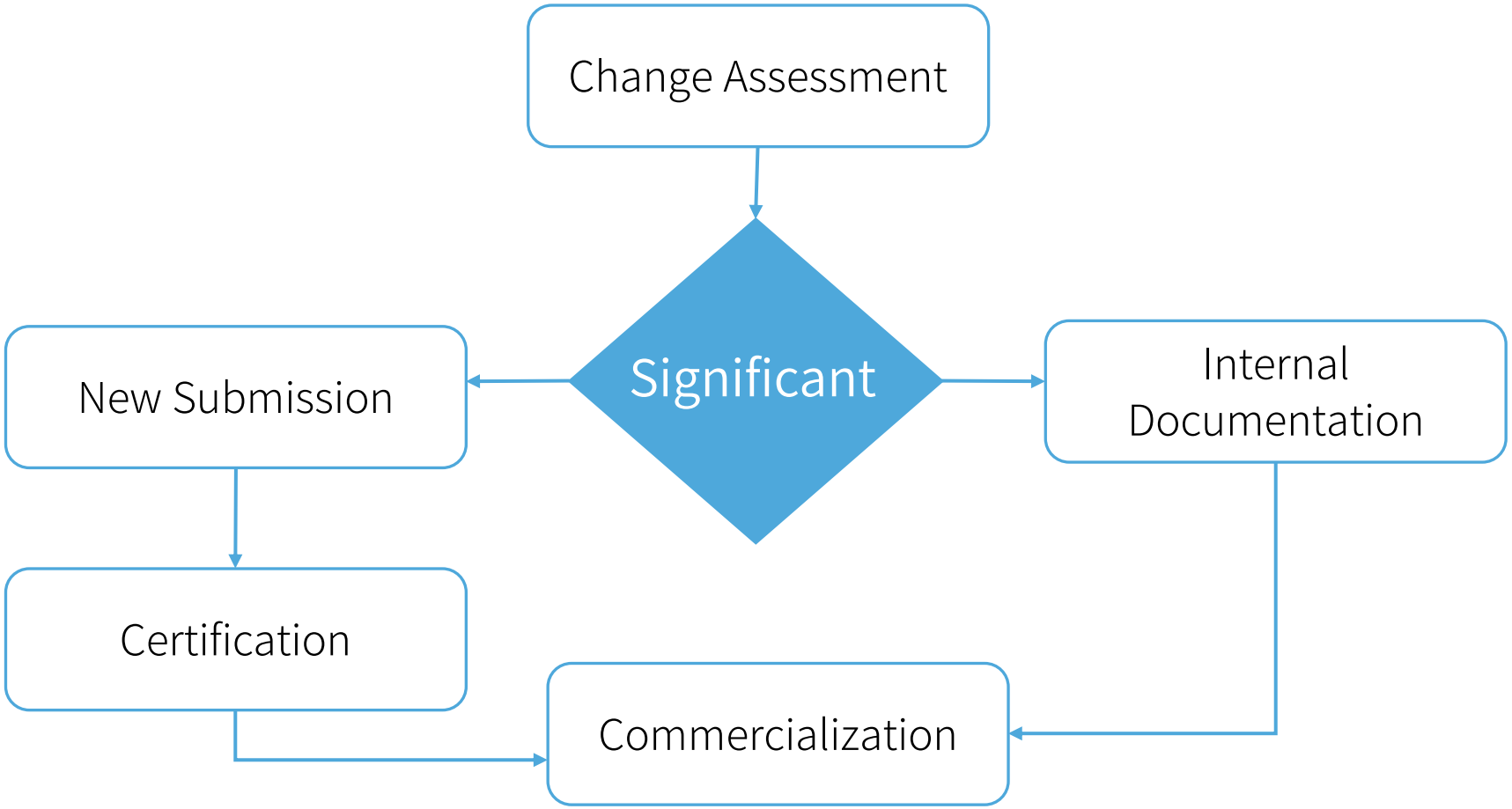
Reactive

- Reports of adverse events with the device itself
- Customer complaints (trend analysis)
- Non-compliance issues (recall, correction)
- Maintenance and service reports

WHY DO WE NEED TO MONITOR THE DEVICE IN THE FIELD?

- New Risks?
- Need to update warnings in User Manual?
- New Adverse Events?
- Need to update Contraindications?

CHANGES TO A MEDICAL DEVICE



CHANGES TO A MEDICAL DEVICE

Significant Change*

- New / broader indication for use
- New or major change in operating system
- Change in algorithm
- New diagnostic or therapeutic feature
- Replacement of user input by closed loop algorithm

* Significant change shall be analyzed and determined based on local regulations

Non-Significant Change

- Cosmetic changes
- Added features that do not affect safety and essential performance
- Change in labeling just for better clarification

Replacing one of the scanner electronic board components with an identical one , from another supplier. Verification is required, but no submission

ADD NIRI – WHAT TYPE OF CHANGE?

- Significant change
- Why?
  - Change in Intended Use / Indication for use
  - Added feature that affects essential performance

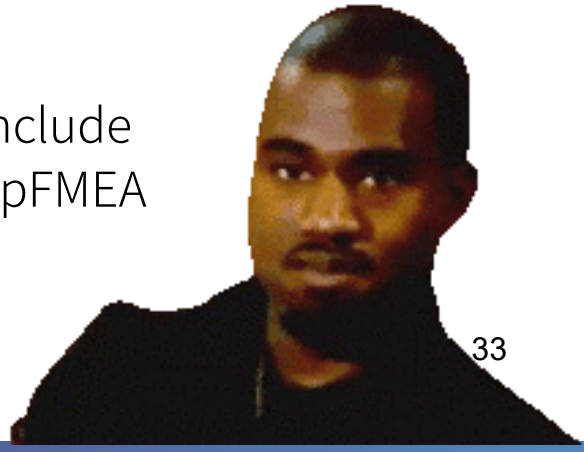
QUALITY AUDITS BY REGULATORY AUTHORITIES

- An audit is performed by the regulatory body at defined intervals to determine that :
  - the organization complies with its quality system procedures
  - the procedures are implemented effectively
  - the procedures are suitable to achieve quality system objectives
- Audits can be performed without prior notification to the manufacturer
- Noncompliance findings are rated according to severity.
- Major noncompliance can lead to site closure or shipment hold

PHILIPS SITE CLOSURE IN CLEVELAND, USA

Site that designed and manufactured CT scanners was closed following FDA quality audit inspection.

- FDA findings were regarding numerous **mishandled quality control issues**:
  - **Complaint handling** - not all investigated as required, not all followed Company's procedure, missing justifications for reason of "no necessary further investigation"
  - **CAPA procedure** had not been adequately established
  - **Risk analysis** was inadequate and incomplete
  - **Product conformity issues** : purchasing, incoming inspection, design change, MDR, process control
  - **Example :** Most recent annual review for the Ingenuity CT system did not include complaints/post market data as a data source for potential updates to the pFMEA



SMART SOCK (OWLET INC.)

- **Smart Sock** tracks a baby's HR, oxygen levels and sleep trends.
- The **Smart Sock** was released to the US market without FDA approval.
- FDA issued a *warning letter* to the company that this device requires obtaining FDA approval prior to commercialization and ceased its commercialization.
- Owlet Inc. stock sank more than 23% following the warning letter.
- Owlet claimed for the safety of its product, saying the company's technology has been used with more than 1 million babies and that the **Smart Sock** has been evaluated by third parties.
- From their current Website in USA:

The Owlet Sock family of products is currently unavailable. Check back in the coming weeks to see the newest addition to the nest.

SUMMARY

- Medical device must be designed, developed, marketed and serviced according to local regulatory requirements
- Noncompliance with these requirements may lead to company's shut down, legal actions against executive managers or cease of its products' commercial distribution