Khon Kaen University
50 Years of Social Devotion

Ethical Review of Medical Devices Research

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Medical devices

- An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:
  - intended for use in man or other animals for
    - diagnosis of disease or other conditions, or
    - cure, mitigation, treatment, or
    - prevention of disease.

21 CFR Part 807

Medical devices

- intended to affect the structure or any function of the body of man or other animals, and
  - which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and
  - which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."

21 CFR Part 807

Medical devices control in Thailand

http://www.fda.moph.go.th/fda_eng/frontend/theme_1/info_data_main.php?ID_Info_Main=41

Medical devices to be licensed

- Condom
- Examination glove
- Surgical glove
- Disposable hypodermic hygienic syringe
- Disposable insulin syringe
- HIV test for diagnosis

http://www.fda.moph.go.th/fda_eng/frontend/theme_1/info_data_main.php?ID_Info_Main=41

Medical devices to be notified

- HIV test for other purposes
- Medical equipment for physical therapy
- Alcohol-Detector test equipment
- Implant silicone breast

http://www.fda.moph.go.th/fda_eng/frontend/theme_1/info_data_main.php?ID_Info_Main=41

Post-marketing Control

- Most of medical devices sale in Thailand
- Requirement
  - Certificate of Company Registration*
  - Certificate of free sale –CE*
  - Catalogue or Device specification*
  - Certificate of Factory Registration (GMP: producing, storing, distribution, etc)*

http://www.fda.moph.go.th/fda_eng/frontend/theme_1/info_data_main.php?ID_Info_Main=41

Asean Medical Device Directive 2015

- Definition:
  - Medical device
  - In vitro diagnostic (IVD) medical device
- Registration of Medical Devices
  - The regulatory Authority may exempt certain medical device
  - Custom-made medical device –no registration need
  - Others are similar to US, EU

AMDD Classification of Medical Devices

Non-IVD medical devices

- Class A – Low risk
- Class B – Low-moderate risk
- Class C- Moderate-high risk
- Class D- High risk

IVD medical devices

- Class A –Low Individual Risk and Low Public Health Risk
- Class B Moderate Individual Risk and/or Low Public Health Risk
- Class C- High Individual Risk and/or Moderate Public Health Risk
- Class D- High Individual Risk and High Public Health Risk

Asean Medical Device Directive 2015

- Common requirement:
  - Relevant essential principles and methods used to demonstrate conformity
  - Medical device description
  - Summary of design verification and validation
  - Medical device labelling
  - Risk analysis
  - Physical manufacturer information
- Clinical Investigation:-is mentioned, taking into account the Helsinki Declaration

U.S. Food and Drug Administration

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Unintentional Injection of Soft Tissue Filler into Blood Vessels in the Face: FDA Safety Communication

English (en)

Internal Market, Industry, Entrepreneurship and SMEs

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Guidance

The European Commission provides a range of

Classification of Medical devices

- Device Class and Regulatory Controls
- 1. Class I General Control
- 2. Class II General Controls and Special Controls
- 3. Class III General Controls and Premarket Approval

21 CFR Part 807 subpart E

MDD classification (EU)

- Class I: low risk
  - sticking plaster, corrective glasses)
- Class Iia: medium-low risk
  - Endotracheal tube, dental filling material
- Class Iib: medium-high risk
  - X-ray Machine, bone plate &s crew
- Class III: high risk
  - Heart valve, total hip prosthesis, pacemaker, implantable defibrillator

Premarket Notification 510(K)

- A 510(k) must demonstrate that the device is substantially equivalent to one legally in commercial distribution in the United States:
  - (1) before May 28, 1976; or
  - (2) to a device that has been determined by FDA to be substantially equivalent.

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/RegistrationandListing/ucm053185.htm[9]

IMPORTANT NOTE: Only the class I devices with an asterisk (*) are also exempted from the GMP regulation, except for general requirements concerning records (820.180) and complaint files (820.198), **as long as the device is *not* labeled o otherwise represented as *sterile*.**

Class II Devices

The Food and Drug Administration (FDA) has also published a list of class II (special controls) devices (those devices are annotated as "(II)"), subject to certain limitations, that are now exempt from the premarket notification requirements under the Food and Drug Administration Modernization Act of 1997 (the Modernization Act). FDA believes that these exemptions will relieve manufacturers from the need to submit premarket notification submissions for these devices and will enable FDA to redirect the resources that would be spent on reviewing such submissions to more significant public health issues. FDA is taking this action in order to meet a requirement of the Modernization Act. Class II devices are annotated "(II)". Please note that class II devices are NOT exempt from GMP requirements.

Class I and Class II Exempt Devices

PART 862	CLINICAL CHEMISTRY AND CLINICAL TOXICOLOGY DEVICES
PART 864	HEMATOLOGY AND PATHOLOGY DEVICES
PART 866	IMMUNOLOGY AND MICROBIOLOGY DEVICES
PART 868	ANESTHESIOLOGY DEVICES
PART 870	CARDIOVASCULAR DEVICES
PART 872	DENTAL DEVICES
PART 874	EAR, NOSE, AND THROAT DEVICES
PART 876	GASTROENTEROLOGY-UROLOGY DEVICES
PART 878	GENERAL AND PLASTIC SURGERY DEVICES
PART 880	GENERAL HOSPITAL AND PERSONAL USE DEVICES
PART 882	NEUROLOGICAL DEVICES
PART 884	OBSTETRICAL AND GYNECOLOGICAL DEVICES
PART 886	OPHTHALMIC DEVICES
PART 888	ORTHOPEDIC DEVICES
PART 890	PHYSICAL MEDICINE DEVICES
PART 892	RADIOLOGY DEVICES

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Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

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Premarket Approval (PMA)

- Product requiring PMAs are
  - Class III devices are high risk devices that pose a significant risk of illness or injury, or
  - devices found not substantially equivalent to Class I and II predicate through the 510(k) process.
- The PMA process is more involved and includes the submission of clinical data to support claims made for the device.

Investigational Device Exemption (IDE)

- An investigational device exemption (IDE) allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support
  - a Premarket Approval (PMA) application or
  - a Premarket Notification 510(k) submission to FDA.

21 CFR part 812

Investigational Device Exemption (IDE)

- Clinical studies with devices of significant risk must be approved by FDA and by an Institutional Review Board (IRB) before the study can begin.
- Studies with devices of non-significant risk must be approved by the IRB only before the study can begin.

21 CFR part 812

Significant risk devices

1) Is intended as an implant (and…)
2) Is purported or represented to be for a use in supporting or sustaining human life (and)
3) Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or preventing impairment of human health (and…)
4) Otherwise (and presents a potential for serious risk to the health, safety, or welfare of the subject.

21 CFR Part 812.3 (m)

Humanitarian Device Exemption (HDE)

- An Humanitarian Use Device (HUD) is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year.

21 CFR part 814 subpart H

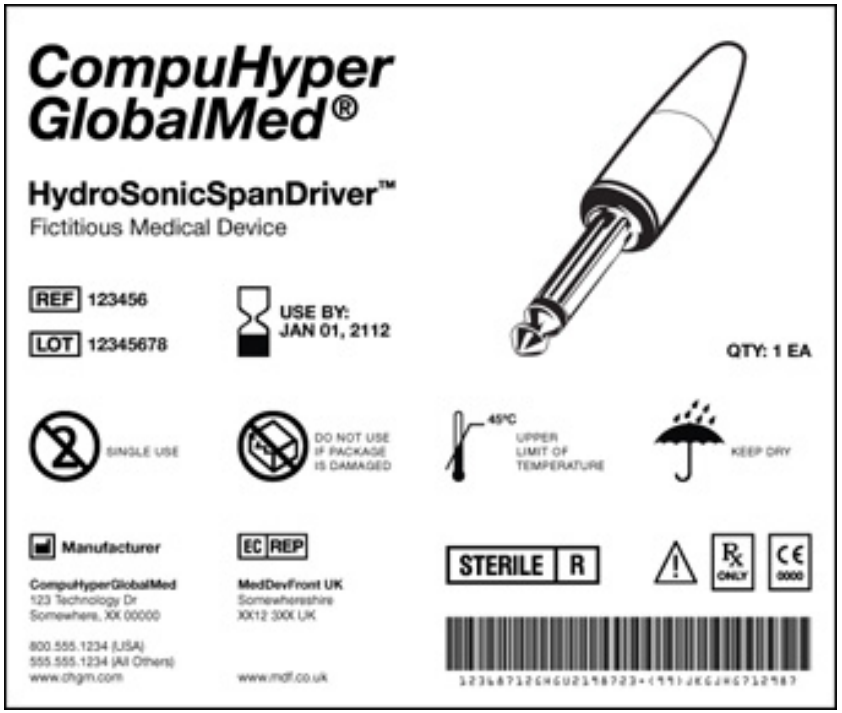
Humanitarian Device Exemption (HDE)

- A device manufacturer`s research and development costs could exceed its market returns for diseases or conditions affecting small patient populations.
- The HUD provision of the regulation provides an incentive for the development of devices for use in the treatment or diagnosis of diseases affecting these populations.

21 CFR part 814 subpart H

Quality System Regulation (QS)/Good Manufacturing Practices (GMP)

- The quality system regulation includes requirements related to the methods used in and the facilities and controls used for:
  - designing,
  - purchasing,
  - manufacturing,
  - packaging,
  - labeling,
  - storing,
  - installing and
  - servicing of medical devices.



21 CFR Part 820

Quality System Regulation (QS)/Good Manufacturing Practices (GMP)

- Manufacturing facilities undergo FDA inspections to assure compliance with the QS requirements.

21 CFR Part 820

Example of Medical devices

- Tongue depressor*
- Elastic bandage
- Medical Chair and table*
- Patient examination glove
- Examination Gown*
- Tuning fork
- Urine strips
- Stethoscope
- Otoscope
- Pregnancy test
- Ultrasound
- Surgical tools
- Implant
- Mobile Medical Application

* Exemption for GMP

Mobile Application

- "a software application that can be executed (run) on a mobile platform (i.e., a handheld commercial off-the-shelf computing platform, with or without wireless connectivity, or a web-based software application that is tailored to a mobile platform but is executed on a server."

http://www.raps.org/regulatoryDetail.aspx?id=18500#sthash.ePp5d3wQ.dpuf

Mobile Medical Application

- a mobile app that meets the definition of device in section 201(h) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)4; and either is intended:
  - to be used as an accessory to a regulated medical device; or
  - to transform a mobile platform into a regulated medical device.

http://www.raps.org/regulatoryDetail.aspx?id=18500#sthash.ePp5d3wQ.dpuf

Example of Mobile Medical App

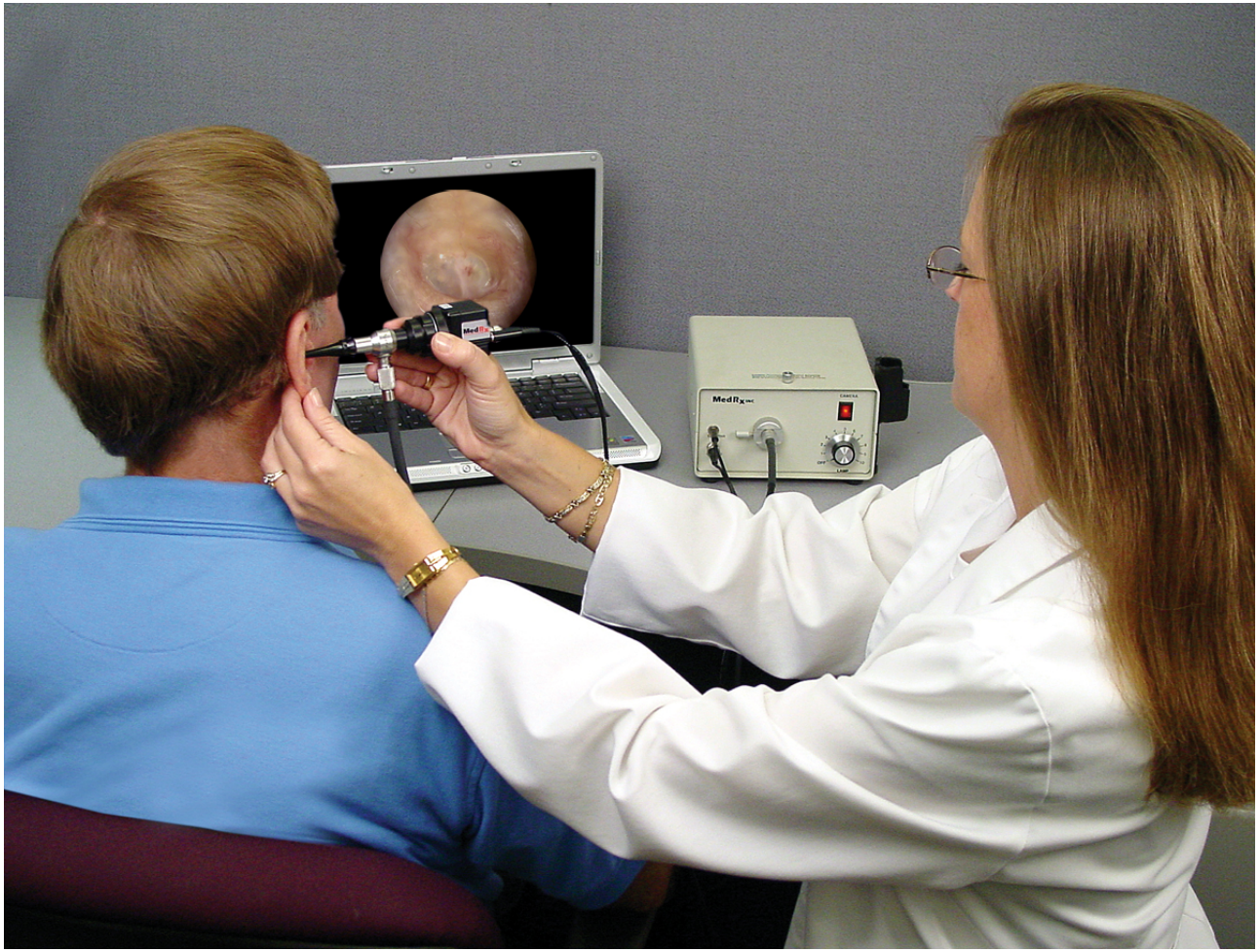
Mobile Medical App under FDA control

- PACS
- I-stroke system
- Glucose meter
- Nystagmograph
- Uhear™
- Oximeter
- Apnea monitor
- Skin Scan

Mobile App that is not medical device

- Medical dictionaries
- Surgical training video
- CPR game
- Magnifying glass app.
- BMI calculator
- Runkeeper
- Diet control
- Elder tracking

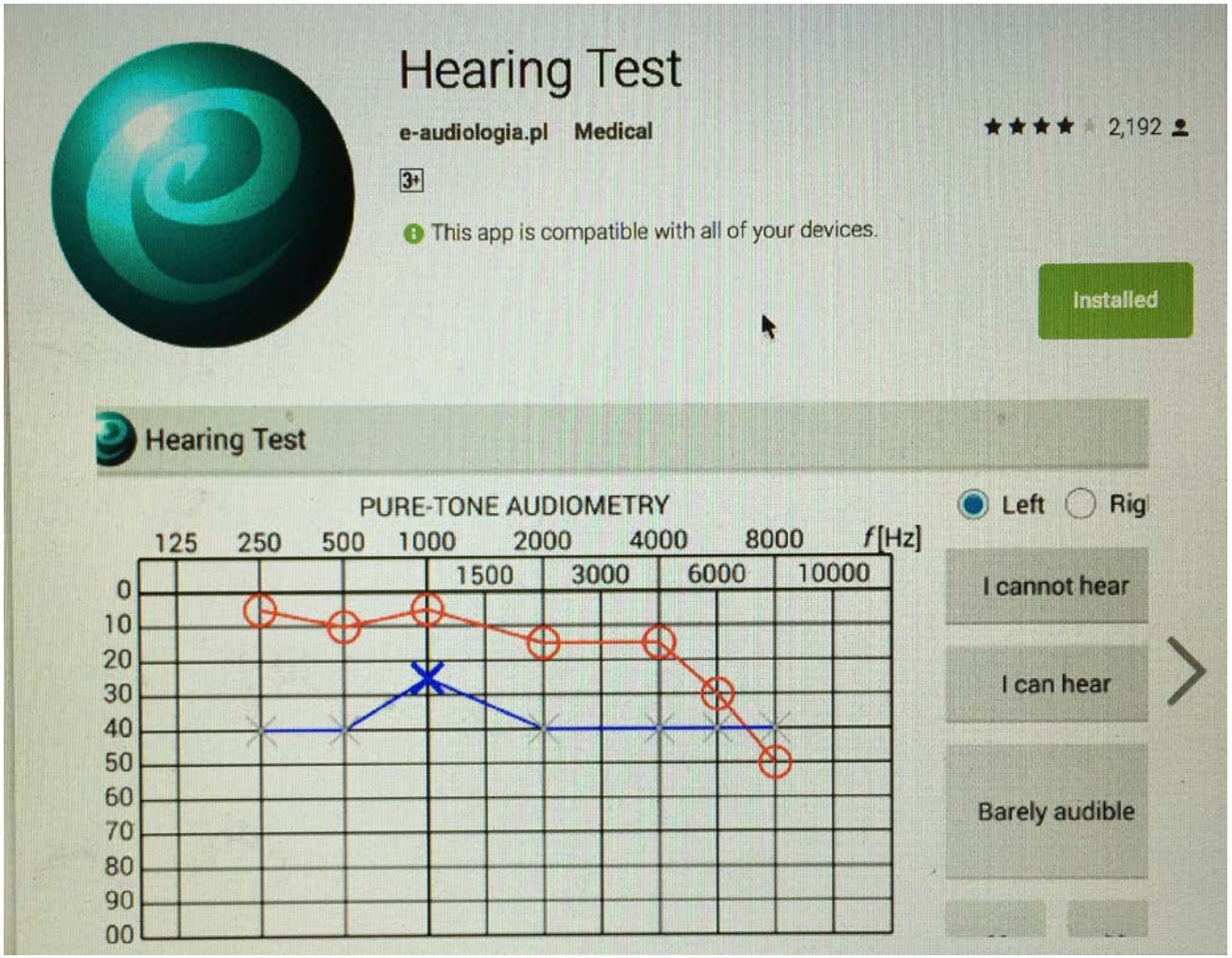
Example of Medical devices



Example of Medical devices

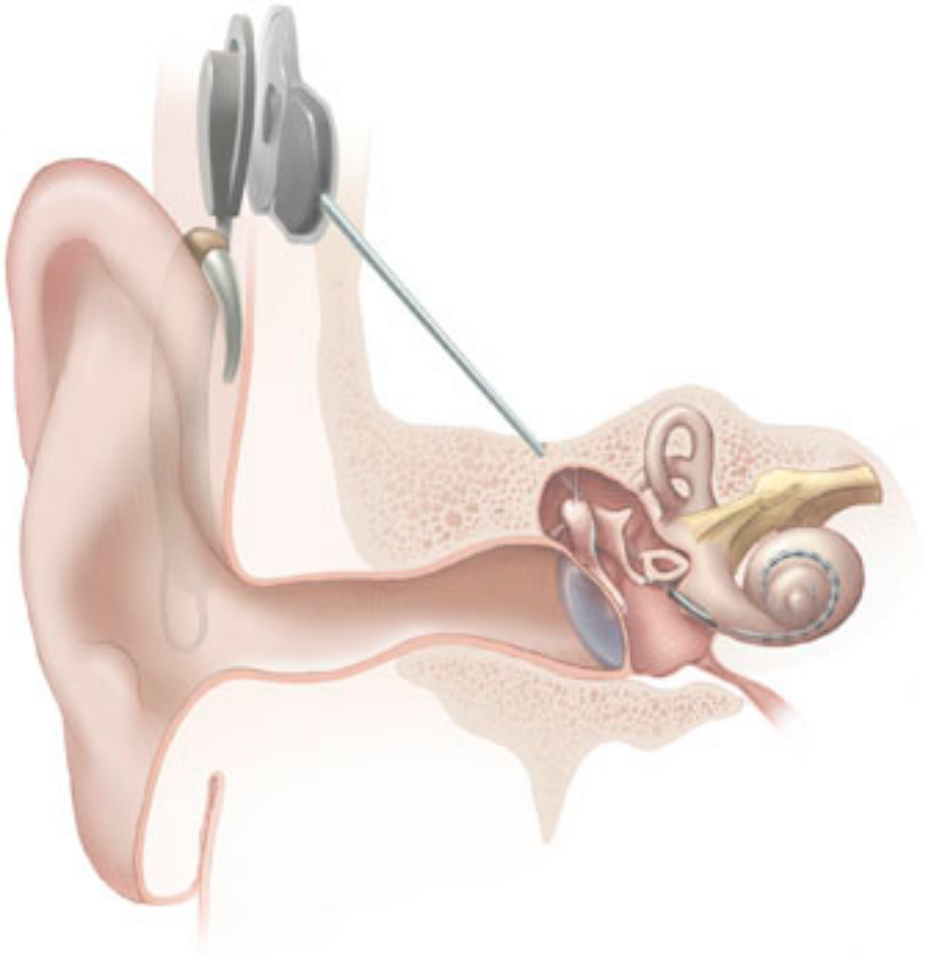
Example of Medical devices

Example of Medical Application



Low VS High Risk Device

Low or High Risk Device?



ETHICAL ISSUES WHEN REVIEWING MEDICAL DEVICES RESEARCH

Ethical issues of Medical devices

- Risk from using a device (e.g. Robotic surgery)
- Risk from procedure associated with using a device(e.g. Stent)
- Clinical investigational Plan of Medical devices≠ pharmaceutical study
- RCT is rarely used (endpoint is safety & performance)
- Device study measure the performance against claim

Ethical issues of Medical devices

- Use of medical device –learning curve
- Inventor of the device -might be one of the investigators
- Effective blinding and the use of placebo are difficult
- Route of administration is often a single surgical procedure
- A medical device has a local effect

Ethical issues of Medical devices

- A actual clinical use of the specific device may be in the post-market clinical study.
- Period for follow up can be much longer.
- DSMBs are not used.
- Interim analysis of study data may be feasible
- Definitions of adverse events are different
- Qualification of the investigator team

Case study-I

- บริษัทเอกชนจากประเทศในกลุ่มยุโรป ต้องการศึกษาประสิทธิภาพของท่อระบายน้ำดีแบบใหม่ที่ผลิตจากพลาสติกเปรียบเทียบกับท่อโลหะที่ใช้อยู่เดิม
- การรักษาท่อน้ำดีอุดตันทำโดยการส่องกล้องผ่านคอ เข้าหลอดอาหาร กระเพาะ ลำไส้ส่วน duodenum (Endoscopic Retrograde Cholangiopancreatogram, ERCP) เพื่อใส่ท่อเข้าไปขยายบริเวณท่อน้ำดีที่อุดตัน
- ในเวชปฏิบัติทั่วไปใช้ท่อโลหะ หรือท่อที่ทำจากวัสดุอื่น เช่น silicone เป็นต้น
- ผลข้างเคียงที่สำคัญคือ ท่ออุดตันใหม่ และท่อทะลุออกนอกทางเดินน้ำดี

คำถาม-I

- เกี่ยวข้องกับการวิจัยเครื่องมือแพทย์หรือไม่
- เป็น Significant or non-significant risk device
- ประเด็นสำคัญที่ต้องพิจารณามีอะไรบ้าง
  - ข้อมูลความปลอดภัย (rejection rate, allergy, perforation rate, occlusion rate etc)
  - Treatment plan for study-related injury or device failure including insurance.
  - Qualification of PI and Conflict of Interests
  - ถ้าระเบียบวิธีวิจัยถูกต้อง ให้ข้อมูลแก่อาสาสมัครครบถ้วน จะอนุมัติรับรองในทำทีสถาบันท่านหรือไม่

Case study-II

- นักวิจัยคิดค้นอุปกรณ์กระตุ้นไฟฟ้าผ่านทางกระโหลกศีรษะเพื่อรักษาอาการเสียงรบกวนในหู ต้องการทำวิจัยทดสอบประสิทธิภาพของเครื่องมือนี้
- คำถาม
  - เป็นเครื่องมือแพทย์หรือไม่
  - ความเสี่ยงสูงหรือความเสี่ยงต่ำ
  - ต้องการข้อมูลใดบ้าง
  - ถ้าระเบียบวิธีวิจัยถูกต้อง ให้ข้อมูลแก่อาสาสมัครครบถ้วน จะอนุมัติรับรองในทำทีสถาบันท่านหรือไม่