image biopsy lab

Experiences with FDA

Christoph Götz, PhD

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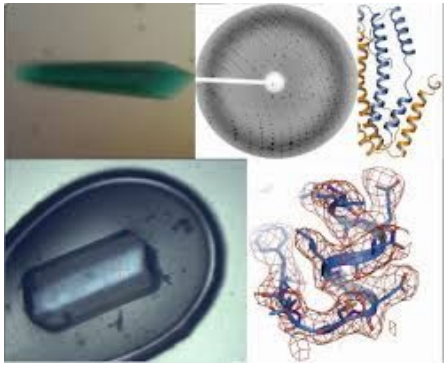
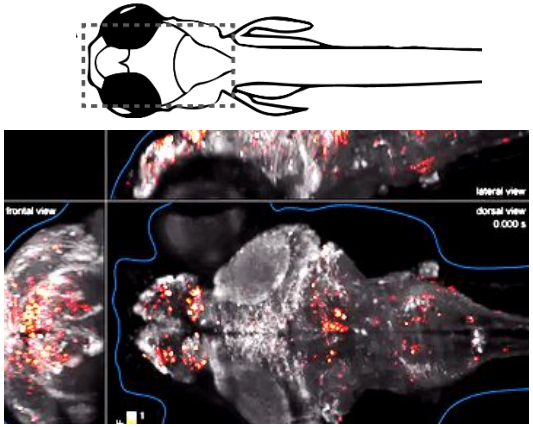
My Background

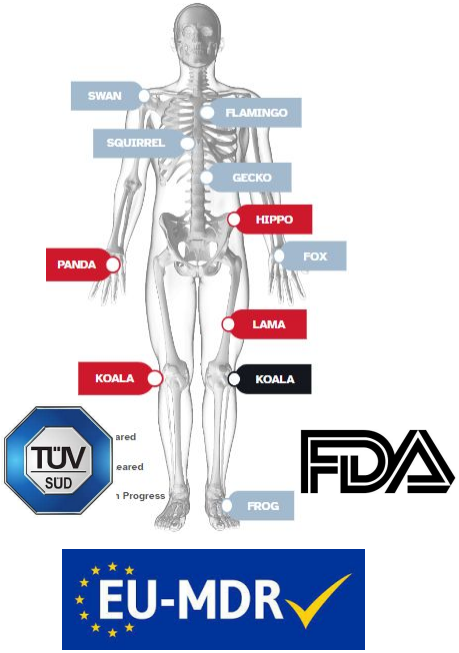
Molecular Biology
Biotechnology



Quantum Biology / Neuroscience



AI Business and Regulatory
PRRC/QM
AI tech & Processes



Friedrich-Alexander-Universität Erlangen-Nürnberg

IMP Research Institute of Molecular Pathology

mfpl MAX F. PERUTZ LABORATORIES

universität wien

Did you know that MDR and FDA are fundamentally different?

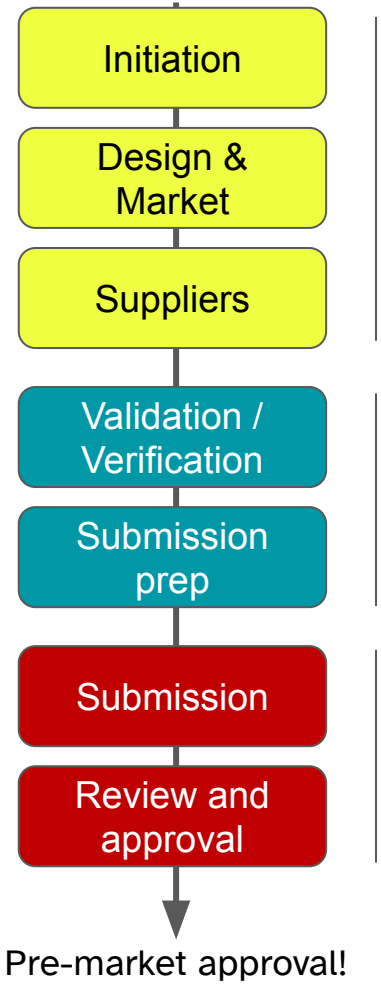
MDR = **Audit system first & PMS**

FDA = **Pre-market approval & Audit later**

Outline of the talk

Process and pitfalls

from start to end

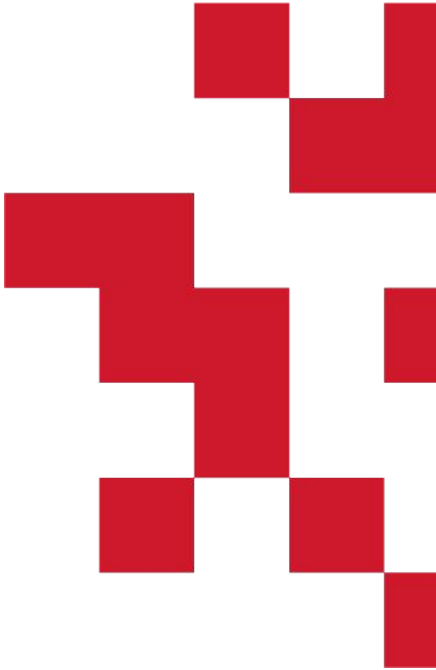


My Experience:

9
FDA & CE (MDD/MDR) clearances

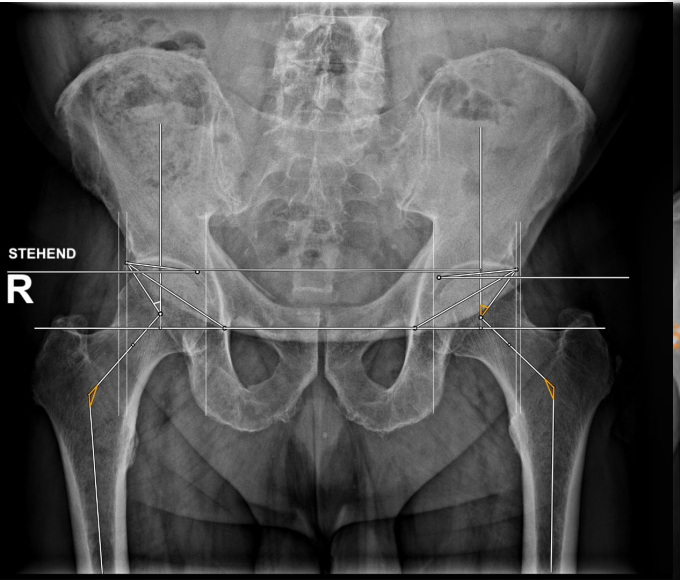
2 CE Class IIa, 5 CE Class I and 2 FDA cleared product modules… **MDR certified!**

What we do



We **automate, standardize and prioritize** musculoskeletal imaging diagnostics

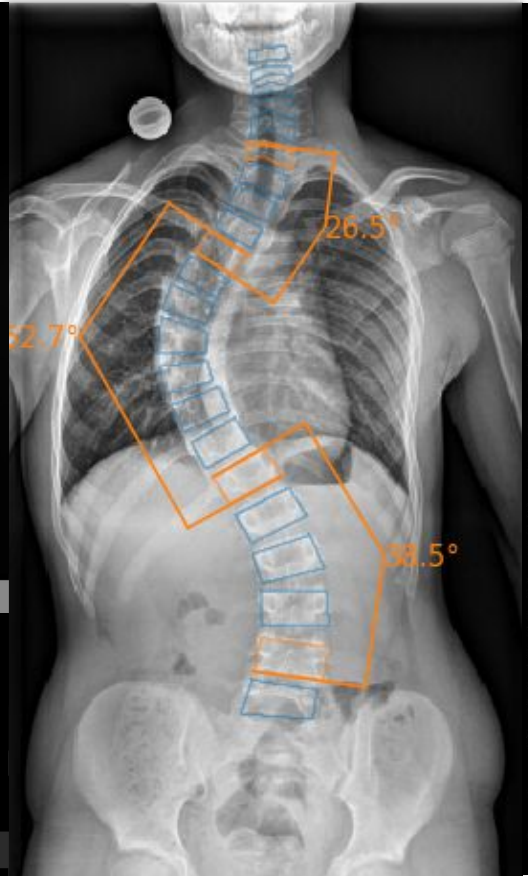
AI solutions support companion diagnostics for optimal MSK management



Hip Measurements	R	L
CCD-Angle[1]	134°	132°
LCE-Angle[1]	33°	36°
Tönnis Angle[2]	7°	6°
Sharp Angle[2]	34°	30°
Femoral Head Coverage[2]	91%	95%
Extrusion Index[2]	9%	5%
Pelvic Obliquity	0° | 1mm	

CCD: Caput Collum Diaphyseal Angle
LCE: Angle between body axis and "Center to End of the Roof" line

Waldt S, Eibler M und Wörtler K, Messverfahren und Klassifikationen in der muskuloskelettalen Radiologie 2. ed., Thieme, Stuttgart, 2017.
Tannast M, Hanke MS, Zheng G, et al. What are the radiographic reference values for acetabular under- and overcoverage? Clin Orthop Relat Res 2015; 473: 1234–1246.

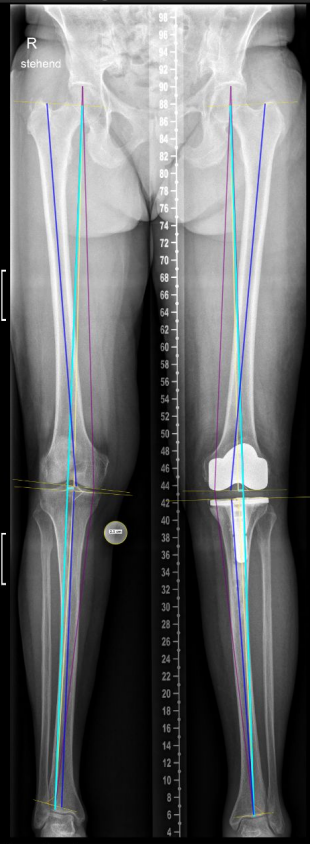


Measurements calibrated with sphere of configured diameter: 2.5 cm

Length measurements	R	L
MAD[3]	-7 mm	-6 mm
Femur length	44.3 cm	44.6 cm
Tibia length	35.6 cm	36.1 cm
Full leg length	79.7 cm	80.4 cm
Leg Length Discrepancy		
The left leg is longer		+ 7 mm
Angle measurements		
HKA[2,3]	valgus 2.1°	valgus 1.6°
AMA[2]	5.6°	6.2°
JLCA[2]	-2.1°	0.9°
mLPFA[1,2]	92.0°	91.5°
mLDFA[1,2], LCFA[4]	84.4°	90.0°
mMPTA[1,2], MCTA[4]	88.6°	90.7°
mLDTA[1,2]	77.2°	84.9°

Legend	
MAD	Mechanical axis deviation
HKA	Hip-knee-ankle angle (mechanical tibia-femur axis angle)
AMA	Anatomical-mechanical axis angle (angle between anatomical and mechanical femur axes)
JLCA	Joint line convergence angle
mLPFA	Mechanical lateral proximal femur angle
mLDFA	Mechanical lateral distal femur angle
mMPTA	Mechanical medial proximal tibial angle
LCFA	Lateral coronal femoral component angle
MCTA	Medial coronal tibial component angle
mLDTA	mechanical lateral distal tibia angle

1) Waldt, S., Eiber, M., & Wörtler, K. (Eds.). (2011). Messverfahren und Klassifikationen in der muskuloskelettalen Radiologie. Georg Thieme Verlag.
2) Paley, D. (2002). Principles of Deformity Correction. Springer Berlin Heidelberg.
3) Lin, Y.-H., Chang, F.-S., Chen, K.-H., Huang, K.-C., & Su, K.-C. (2018). Mismatch between femur and tibia coronal alignment in the knee joint: classification of five lower limb types according to femoral and tibial mechanical alignment. BMC Musculoskeletal Disorders, 19(1).
4) Mizu-uchi, H., Matsuda, S., Miura, H., Okazaki, K., Akasaki, Y., & Iwamoto, Y. (2008). The evaluation of post-operative alignment in total knee replacement using a CT-based navigation system. The Journal of Bone and Joint Surgery. British Volume, 90-B(8), 1025–1031.



- Initiation
- Design & Market
- Suppliers
- Validation / Verification
- Submission prep
- Submission
- Review and approval

Setting up Processes and System

CFR21 Part 11 compliance:

- Most important for submission:
  - 820.30 Design Control
  - 820.181 Tech Files
- System only in case of Audit

FDA specifics:

- Pathways:
  - PMA
  - 510k & predicates
  - De Novo
- Cybersecurity
- Human factors engineering

Learning:

Clear objectives & understanding of what your device does and doesn't!

Select the right guidances and regulations early enough and implement them.

Identify gaps of your system and close them!

Initiation

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Design the right product for the right market

Understand the market:

- Incentives & Reimbursement
- Who pays, who uses?
- What features differ to EU?
- What could be a predicate device?

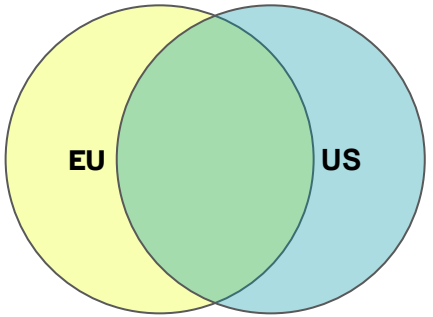
What we did:

- Survey 600 physicians
- Test pricing and features
- De-feature our EU product for US market entry

Learning:

Necessity of market research and regulatory understanding in design.

Be prepared to build and maintain two slightly different versions of the product (one per market)



Know your customer and factor in potential differences

Initiation

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Ask FDA early and find strong local partners

Pre-submission of design draft with FDA:

- know that what you *think you need* is what you *actually need*.
- “Free” consultation to Benefit-Risk, study statistics

Supplier criteria:

- Access to right datasets (US Patients) and HR (US doctors)
- Explicit contracts and thoroughly planned study
  - eCRF records
  - Quality assurance
  - Project management

Learning:

Selecting experienced suppliers and ensure adequate documentation.

Contract research organization (CRO) will avoid many headaches.

Might be expensive, but much less risk of failed study and delays.

Pros before Bros

Initiation

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It’s all about the Data.

Classic questions:

- “How does your device work on US population?”
- “What was the qualification of your readers?”
- “What was the performance on this and that sub-group?”

Rest of tech file (Risk, traceability etc) needs to be there but is almost never the discussion in the submission meetings.

Learning:

- Know your clinic & disease
- Design your study accordingly:
  - Local data
  - Local readers
  - Enough data on Limitations
  - Ensure data integrity

Solid Local Data, Strong Validation

Initiation

Design & Market

Suppliers

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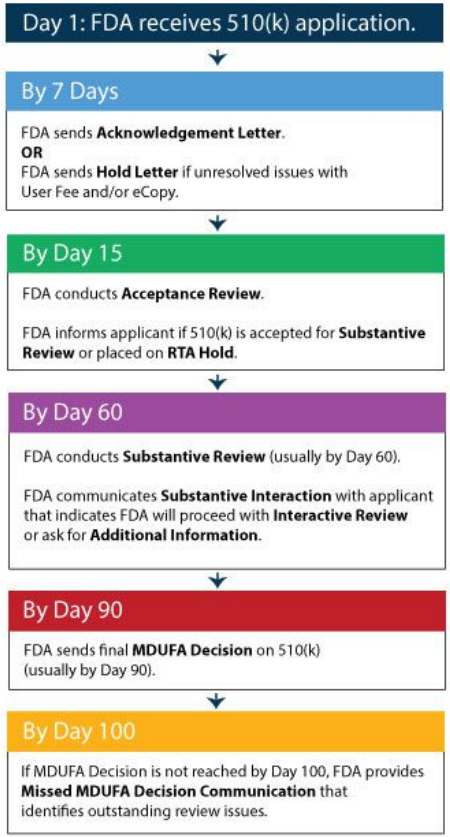
Navigating Document Preparation

Formalities

- Timely small business application saves lots of money
- Plan resources for review
- Understand the process



FDA is very transparent and reliable on timelines

https://www.emergobyul.com/news/how-long-fda-review-process-510k-medical-device-submissions

Initiation

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Submitting to the FDA

- Make sure you fulfill the formal requirements for submission
  - Tech File FDA =! MDR
- Until 2023: FedEx of USB-stick of tech-file to Washington
- Now FDA accepts e-submissions for 510ks only
- Communicate openly and learn the lingo: “Does the agency agree with answer A?”
- Make sure you have a US physician that knows the study and argues in favor of safety and effectiveness of the device

Get your team ready for review

Initiation

Design & Market

Suppliers

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Review and approval

The Clock is ticking

Limited contingent of days to answer remaining questions:

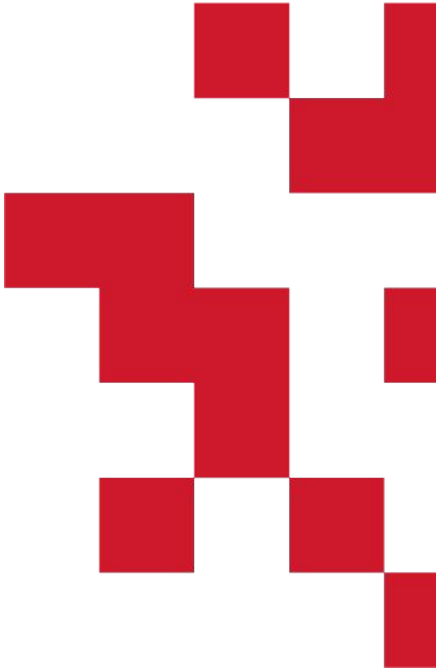
- FDA interdisciplinary team of experts asks excellent questions (usually)
- US physician and you argue in multiple conference calls with FDA
- Convince with data! Use calls to confirm if data is sufficient to “address the agencies’ concerns”
- If FDA accepts all questions within time frame: prep for on-site audit within the next years or do MDSAP

Learning:

- Make sure you have resources, data and contingency plans in place
- Else: get better data and submit from scratch

Solid Data and Benefit-Risk Arguments Win!

Summary



Initiation	Understand Guidelines and Process
Design & Market	Know your market & US population
Suppliers	Good contracts with expert suppliers
Validation / Verification	Vet your study design and gather enough data
Submission prep	Briefing of local physician advocate and correct formatting
Submission	Keep deadlines and communicate the right way
Review and approval	Present the right arguments in time

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www.imagebiopsy.com

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