Proven Ways to Overcome Today's Top Regulatory Challenges

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Proven Ways to Overcome Top Regulatory Challenges

OSMA: Addressing Challenges as an Industry

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Orthopaedic Surgical Manufacturers Association

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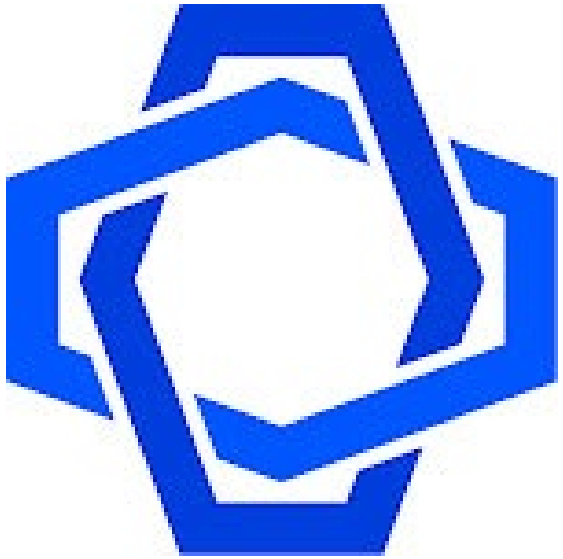

The Orthopaedic Surgical Manufacturers Association (OSMA) is a nonprofit organization composed exclusively of manufacturers specializing in orthopaedic surgical appliances, implants, instruments, equipment, and orthobiologics.

OSMA is one of the longest-standing trade associations devoted to the manufacture of medical devices used in orthopaedic surgical procedures.

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OSMA Member Companies

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OSMA's Vision

Our vision is to enhance the implementation of global regulations and foster productive interactions for the benefit of patients, industry and regulators. We are committed to creating an environment where cutting-edge technologies, innovative solutions, and transformative ideas converge to enhance patient care.

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OSMA Mission: Striving to meet our vision through the following strategic objectives

Advocate

Advocating clear, consistent, and efficient implementation of government regulations and industry standards.

Educate

Educating our stakeholders through hosting interactive educational programs with subject matter experts.

Facilitate

Fostering collaboration between industry, regulatory authorities, and other members of the orthopaedic ecosystem.

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Advocate

These committees advocate for clear, consistent, and efficient implementation of government regulations and industry standards.

- **Communication and Engagement Committee:** The Communication and Engagement Committee focuses on fostering effective communication and engagement both within OSMA and with external stakeholders. It plays a crucial role in maintaining transparency, disseminating information, and ensuring members are informed about important developments.

- **Relationships and Intelligence Sharing Committee:** The Relationships and Intelligence Sharing Committee is dedicated to building and nurturing relationships with various industry stakeholders, including regulatory agencies, healthcare professionals, and other organizations. It also facilitates the sharing of valuable intelligence within the orthopaedic surgical field.

Educate

These committees are responsible for educating members, healthcare professionals, the FDA, and relevant international agencies on regulatory standards.

- **Work Prioritization Committee:** The Work Prioritization Committee is responsible for identifying and prioritizing key educational initiatives and projects within OSMA. It plays a pivotal role in ensuring that educational efforts align with the organization's goals and objectives.

- **Meeting Planning Committee:** The Meeting Planning Committee takes charge of organizing and coordinating OSMA's meetings, conferences, and educational events. It ensures that these gatherings run smoothly and provide valuable opportunities for members to learn and collaborate.

- **Working Groups:** Working groups are temporary teams formed to address specific issues or projects within OSMA. They bring together subject matter experts to tackle targeted challenges and achieve specific objectives.

Facilitate

These committees are responsible for educating members, healthcare professionals, the FDA, and relevant international agencies on regulatory standards.

- **Structure and Governance Committee:** The Structure and Governance Committee oversees the overall structure and governance of OSMA. It plays a vital role in ensuring that the organization's policies, bylaws, and governance procedures are sound and effectively support its mission.
- **Nominating Committee:** The Nominating Committee ensures that the organization is led by capable and dedicated individuals. It is responsible for the nomination and selection of individuals to serve in leadership roles within OSMA, including the Board of Directors.
- **Finance Committee:** The Finance Committee is in charge of overseeing OSMA's financial matters, including budgeting, financial planning, and fiscal responsibility. It ensures the organization's financial stability and prudent management of resources.

Session Agenda

- The Use of Real-World Evidence for Regulatory Submissions
- Orthopedic Alliance Roundtable
- MR Testing and Labeling

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Proven Ways to Overcome Top Regulatory Challenges

Real-World Evidence

Introduction: Real-World Data (RWD)/Real-World Evidence (RWE)

Challenge: Leverage RWE to increase regulatory approval efficiency and reduce clinical trial costs

Objective:

- Explain the concept of real-world evidence (RWE) in the context of medical devices.
- Discuss current regulatory guidance and compare EU and FDA perspectives
- Outline steps to use RWE to enhance product approval efficiency.

Definition of Real-World Evidence (RWE)

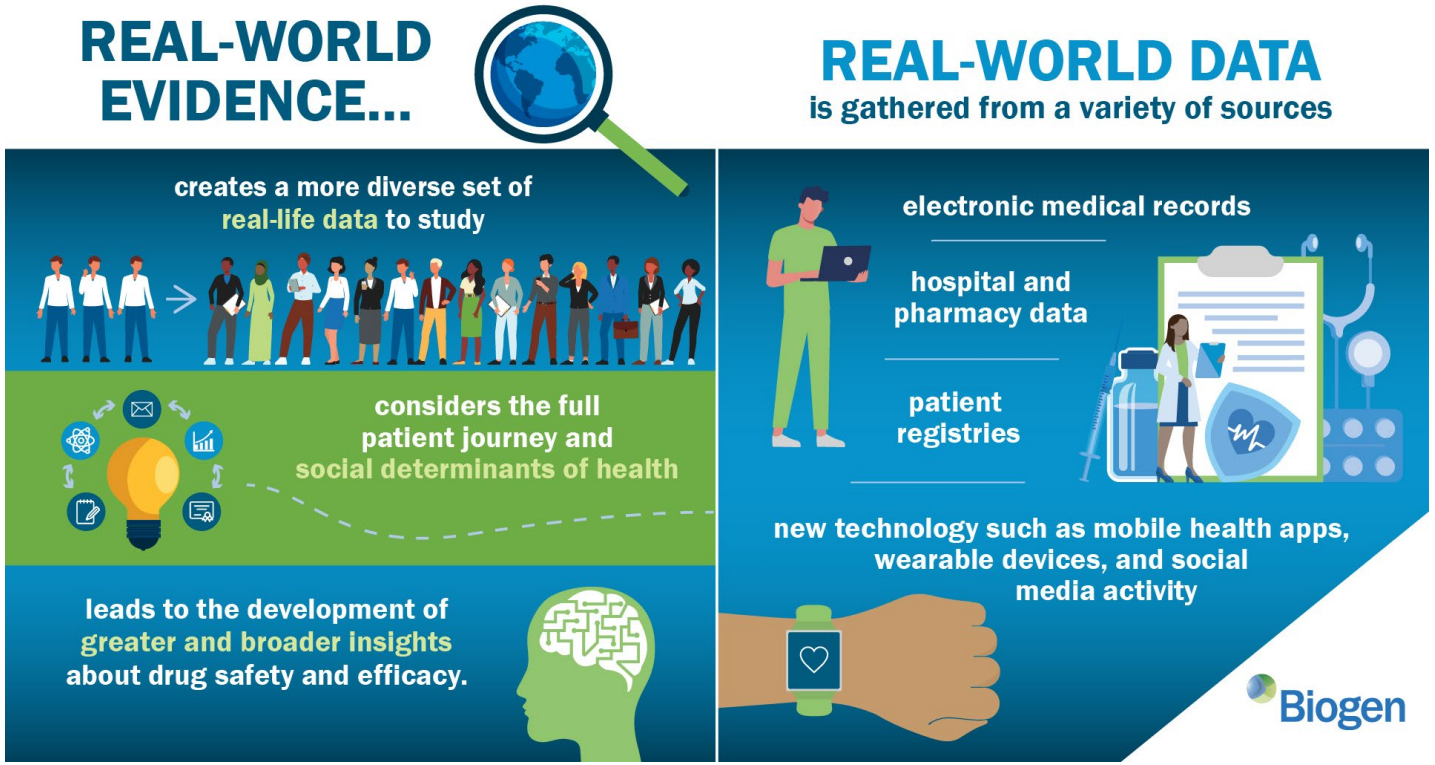
What is RWD/RWE?

- RWD: Healthcare data collected from sources other than clinical trials
- RWE: Derived from RWD

Importance of RWE:

- **Used today:**
  - To complement clinical trial data.
  - Provides insights into long-term effects and broader patient populations.
- **Uses tomorrow:** Gain confidence to utilize RWE over:
  - Post-market clinical trials
  - Specific pre-market clinical trials

Types of Real-World Data (RWD)



RWD Sources:

- **Electronic Health Records (EHRs)**: Clinical data from patient visits.
- **Claims and Billing Activities**: Financial records reflecting healthcare utilization.
- **Product and Disease Registries**: Data on patient outcomes and disease progression.
- **Patient-Generated Data**: Information from patient surveys and wearable devices.

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Current Regulatory Guidance on RWE

U.S. Food and Drug Administration (FDA):

- **FDA's RWE Program**: Framework to evaluate the use of RWE in regulatory decisions.
- **Guidance Documents**:
  - "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices"
  - "Considerations for the Use of Real-World Data and Evidence"

European Medicines Agency (EMA):

- **Guidance on RWD**: Integration of RWD for post-market surveillance and regulatory submissions.
- **Recommendations**: Use of RWE for safety and efficacy evaluations.

Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices

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Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-use-real-world-data-and-real-world-evidence-support-regulatory-decision-making-drug

FDA Guidance Recommendations

Ensuring Data Relevance and Reliability:

- **Data Quality**: Accurate, complete, and up-to-date data
- **Representativeness**: Ensures data adequately reflects the target patient population and clinical settings to generalize findings.
- **Standardization**: Standardized data collection and reporting practices to facilitate comparison and integration of RWE from different sources.

FDA Guidance Recommendations

Rigorous Study Design and Methodological Best Practices:

- **Clear Objectives**: Define specific research questions and study goals to ensure relevance to regulatory decision-making.
- **Pre-Specified Protocols**: Develop before data collection to minimize bias and ensure transparency.
- **Statistical Analysis**: Employ robust statistical methods to account for confounding variables and ensure the validity of the results. Including propensity score matching, instrumental variables, and other techniques.
- **Hybrid Studies**: Combine RWE with randomized controlled trials (RCTs) to provide a more comprehensive assessment of device performance.

FDA Guidance Recommendations

Comprehensive Regulatory Submissions and Evidence Quality:

- **Documentation**: Data sources, study design, methodology, and analysis to ensure reproducibility.
- **Transparency**: Of all aspects of the study, including any limitations or potential biases in the data.
- **Adherence to Standards**: Follow established regulatory standards and guidelines to ensure that the evidence meets the required quality and reliability criteria for regulatory approval.

EU Regulatory Guidance

Key guidance documents and initiatives relevant to the use of RWE in the EU:

- **Real-World Evidence Framework by EMA**:
  - The European Medicines Agency (EMA) outlines the use of real-world data (RWD) in generating RWE for both pre-authorization and post-authorization assessments. It emphasizes the importance of RWE in complementing traditional clinical trials and enhancing the understanding of medicinal products' safety and efficacy (European Medicines Agency) (European Medicines Agency).
- **European Health Data Space (EHDS)**: (Frontiers).
- **DARWIN EU®**: (Frontiers) (European Medicines Agency).
- **Guidelines on Registry-Based Studies**: (European Medicines Agency).
- **Reflection Papers and Ongoing Pilots**: (European Medicines Agency) (European Medicines Agency).

RWE in the EU vs FDA

Framework and Approach:

- **EU**: centralized framework with initiatives to harmonize data use across member states.
- **FDA**: decentralized approach, diverse sources of RWE and flexibility for regulatory needs.

Data Sources and Accessibility:

- **EU**: standardized framework: integrating electronic health records (EHRs), registries, and national databases.
- **FDA**: Utilizes a wide array of data, including EHRs, claims data, and patient-generated data.

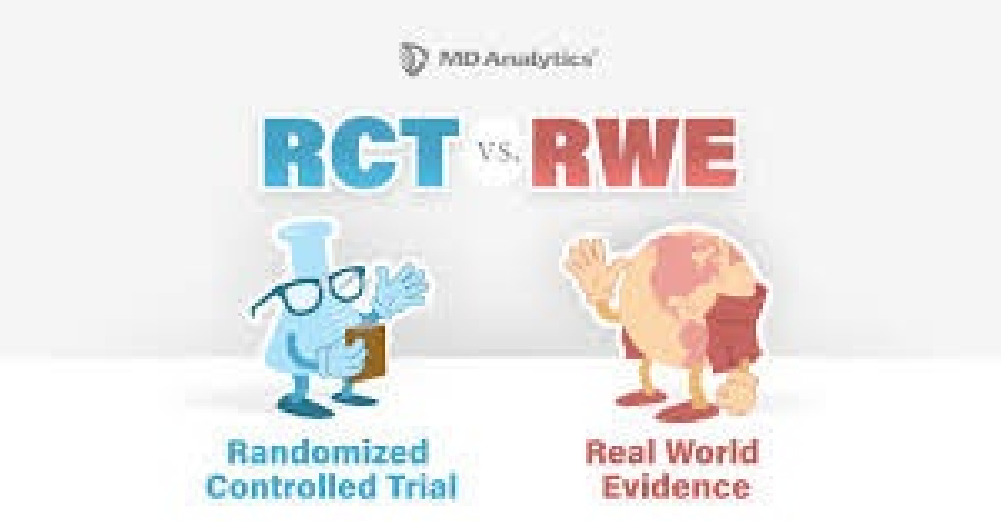
Regulatory Application:

- **EU**: Both pre-authorization and post-authorization phases, to complement clinical trials.
- **FDA**: primarily for post-market surveillance, safety monitoring, labeling changes/new indications.

Guidance and Standards:

- **EU**: guidelines and reflection papers emphasizing methodological rigor and standardization.
- **FDA**: flexible guidance documents focusing on best practices, study design considerations, and data reliability without stringent standardization.

Benefits of Using RWE



Enhanced Understanding of Product Performance:

- Real-world use and outcomes in diverse populations.

Faster Regulatory Approvals:

- Reduced need for extensive clinical trials.

Cost Efficiency:

- Lower research and development costs.

Post-Market Surveillance:

- Continuous monitoring of device safety and effectiveness.

Steps Forward: Increasing Efficiency with RWE

Integration with Regulatory Processes:

- Incorporate RWE early in the product lifecycle.

Standardization of Data Collection:

- Develop standardized protocols for data collection and reporting.

Advanced Analytical Techniques:

- Employ artificial intelligence and machine learning to analyze large datasets.

Dr. Erturan: RWE Article January 2024

- **Understanding Performance:** RWE helps gauge medical device performance in clinical practice.
- **Advantages:** RWE provides broader patient data, long-term insights, and faster decisions.
- **Quality Issues:** RWE can suffer from variable data quality and lack of randomization.
- **Orthopedic Challenges:** RWE in orthopedics faces complex outcomes and regulatory issues.
- **Pharma Success:** RWE's success in pharma suggests potential for orthopedics.

https://bonezonepub.com/2024/01/15/building-the-pathway-to-successful-use-of-rwe/

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OSMA RWE Working Group

January 2024 OSMA RWE Working Group

Summary: Challenges and Considerations

- **Data Privacy and Security**:
  - Protecting patient information while utilizing RWD.
- **Regulatory Acceptance**:
  - Gaining regulatory bodies' trust in RWE methodologies.
- **Quality Control**:
  - Ensuring high standards of data integrity and reliability.

Conclusion

Summary:

- RWE offers a promising complement to traditional clinical trials.
- Regulatory bodies are increasingly recognizing the value of RWE.
- Strategic steps can help maximize the potential of RWE in medical device approvals.

Call to Action:

- Embrace and invest in RWE initiatives.
- Foster collaboration across the healthcare ecosystem.
- Continue to innovate in data collection and analysis techniques.

Proven Ways to Overcome Top Regulatory Challenges

Orthopedic Alliance
Roundtable

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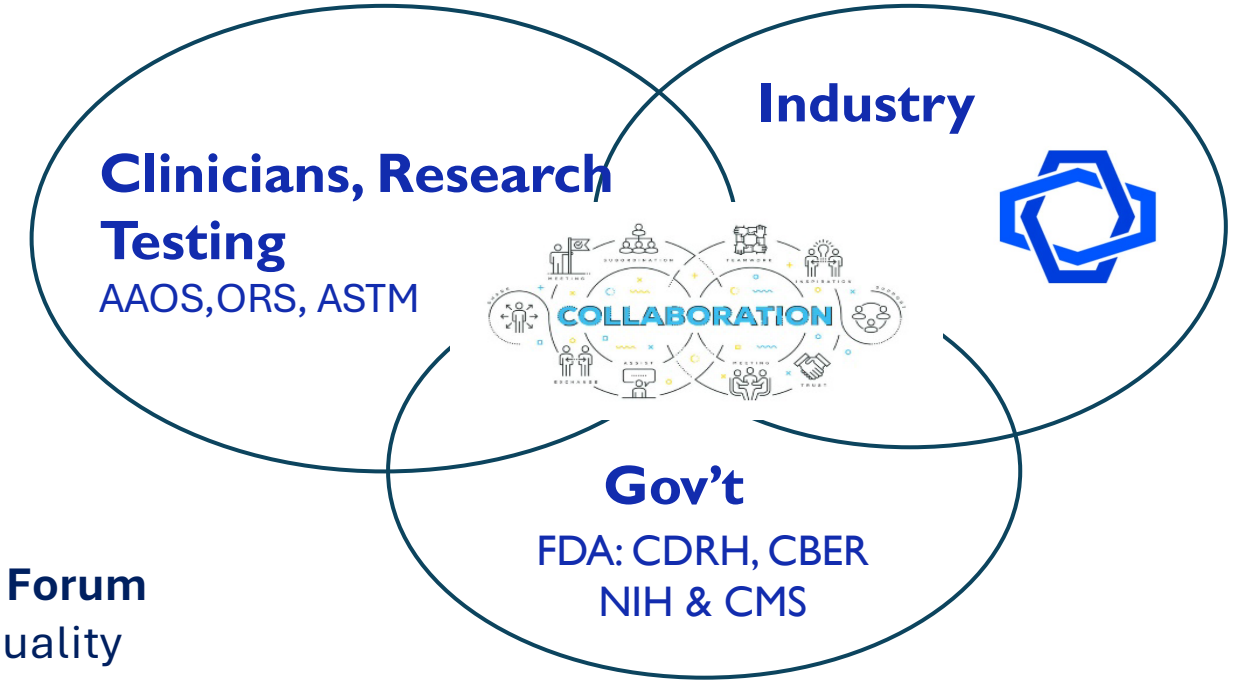
Orthopaedic Alliance Roundtable (OAR)

Orthopaedic Alliance Roundtable (OAR)

formerly AAOS Orthopaedic Device Forum



1995-Formation of AAOS Orthopaedic Device Forum
Prioritization of patient safety and product quality

2019-Present- OSMA Establishment of OAR
(Building on the Forum Legacy of Foundational Principles)

Why OAR?

ORTHOPAEDIC

The topics, discussions and outputs may be far reaching but the foundational tie is the impact to the orthopaedic community.

ALLIANCE

The utilization of key stakeholders' collaboration to impact the delivery of safe and effective solutions to patients.

ROUNDTABLE

An ongoing discussion designed to articulate critical issues, discuss innovative opportunities and advocate for solutions that benefit the orthopaedic ecosystem.

Orthopaedic Alliance Roundtable (OAR)

Shared Goals and Accountability

Communication

Optimize efforts towards efficient orthopaedic solutions through leveraged communication

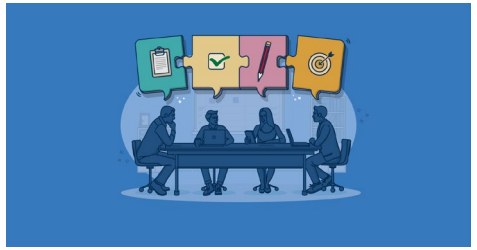
Education

Education among stakeholders and beyond on issues relevant and impactful to the orthopaedic community

Shared Experience and Expertise

Relying upon shared experience and expertise, provide innovative contributions to challenges which impact all of us

Role of OAR



- Educate on areas of subject matter expertise
- Communicate priorities and needs of member organizations
- Identify areas of collective priorities that would benefit from OAR engagement
- Appoint SMEs to drive OAR work items
- Serve as advisory board to provide guidance/ input to OAR working groups

Re-Launch Kick-Off Meeting October 18, 2019

- Unified desire to re-constitute group with refreshed purpose and shared accountability

- Advancing the science and scope of orthopaedic solutions
  - Collaborate among stakeholder groups to foster more predictable and efficient approaches to bring products to the market and address complex issues (process and technology)
  - Apply regulatory science principles to support innovation

- Identify critical (multi-stakeholder, multi-disciplinary) items that the surgical community, scientific community, orthopaedic community, patients, and industry can address in a common space (collaboratively)

2024 Workplan:
Defining OAR Priorities and Near-Term Deliverables

High-Level OAR Strategic Priorities

- Establish OAR as a CDRH Collaborative Community
- Expand Use of RWD/ RWE in the Orthopaedic Space
- Optimize Availability of Anti-Infective Solutions for Orthopaedic Patients
- Promote Innovation in International Consensus and Standards
- Address New Regulatory/Policy Needs for Novel Orthopaedic Technologies
- Foster a Spirit of Simplicity

Orthopaedic Alliance Roundtable (OAR)

2022 Goals:

- *Establish OAR as a CDRH Collaborative Community*

FDA's Collaborative Communities

What Is a Collaborative Community?

A collaborative community is a continuing forum in which private- and public-sector members, which can include the FDA, work together on medical device challenges to achieve common objectives and outcomes. They are convened by interested stakeholders and may exist indefinitely, produce deliverables as needed, and tackle challenges with broad impacts. Collaborative communities may develop for a number of reasons, including when:

- Challenges and outcomes are complex
- Partners are interrelated
- Incremental or unilateral efforts to address the challenge have been ineffective
- Partners seek to optimize efforts, including preventing duplication of efforts
- Better outcomes could be achieved with integrating different perspectives, experiences, resources, and expertise.

For more information: Fostering Collaborative Communities to Improve Patient Healthcare (FDA Voices, December 4, 2018)

Benefits of OAR Establishment as a Collaborative Community

- First Orthopaedics-Related CC
- Continued FDA Commitment
- Increased Scope of OSMA Impact
- Greater Footprint (network & publication potential)
- Improved Brand Recognition
- Shared Vision/ Accountability

Orthopaedic Alliance Roundtable (OAR)

Collaborative Community Milestones:

- APPLICATION (Draft Charter) Sent to FDA on March 23, 2022
- Provisional FDA Approval Received on July 7, 2022
- Final FDA approval pending receipt of signed OAR charter and OAR website address
- FDA will publish a Federal Liaison Letter
  - Outlines how FDA will participate in the CC

Governance and Sustained Engagement Mechanism

OSMA (Convener)

Steering Committee with Chair/ Co-Chair

- Preside over OAR meetings (bi-annual)
- Set meeting agendas with input from the membership pool
- Review and approve meeting minutes (which will be disseminated for a full group review and archived at OSMA)
- Appoint **Subcommittees** or **Working Groups**
  - Develop and execute specific deliverables in support of OAR's strategic plan. These groups will be comprised of subject matter experts appointed by the **Steering Committee** to drive specific OAR work items.

Members at Large who will represent interested parties across the orthopaedic ecosystem

Orthopaedic Alliance Roundtable (OAR) Structure and Governance

OAR Steering Committee (with OSMA Representative(s))

Subject Matter Experts

OSMA Working Group Chairs

CC Working Groups

CC Working Groups

OSMA Working Groups

OAR Stakeholder Interviews

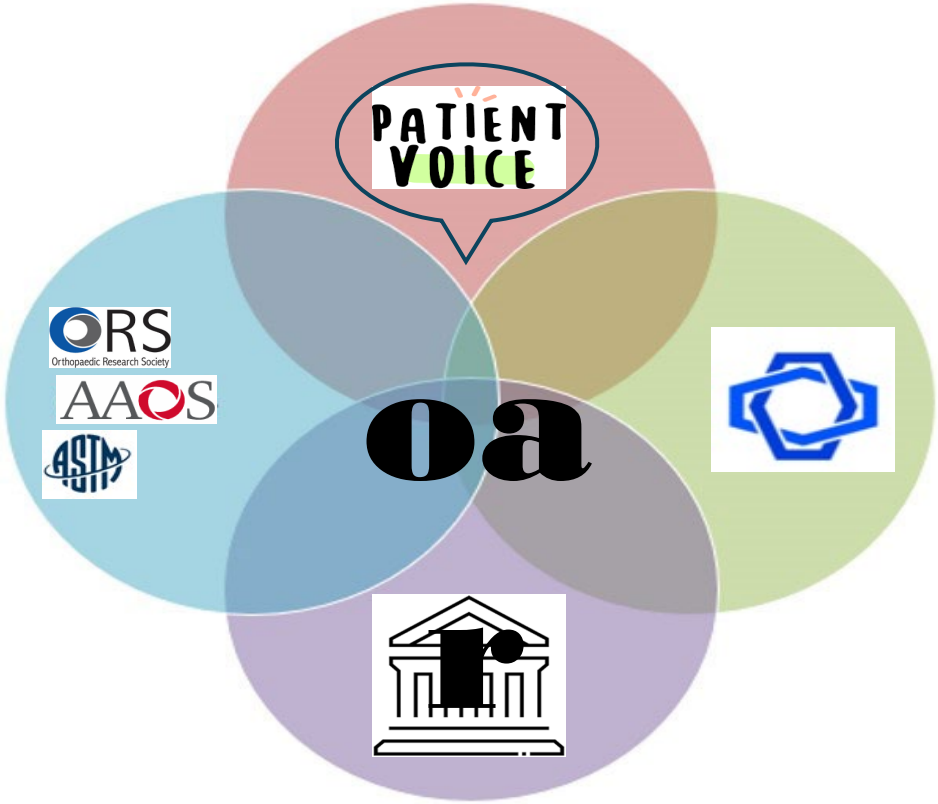
Purpose:

- Establish/re-establish prior relationships
- Affirm OSMA's continued interest in OAR
- Seek individual stakeholder feedback on the:
  - Value of OAR
  - Top-level areas of OAR strategic priority
  - OAR structure and governance

Next Steps

- Complete stakeholder interviews
- Finalize charter with OAR member signatures and send to FDA
- Draft 2024 work plan
- Identify patient representative(s)
- Continue to build out OAR collaborative community structure and operational/ governance model

Questions??


PATIENT VOICE
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Orthopaedic Research Society
AAOS
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Proven Ways to Overcome Top Regulatory Challenges

MRI Compatibility

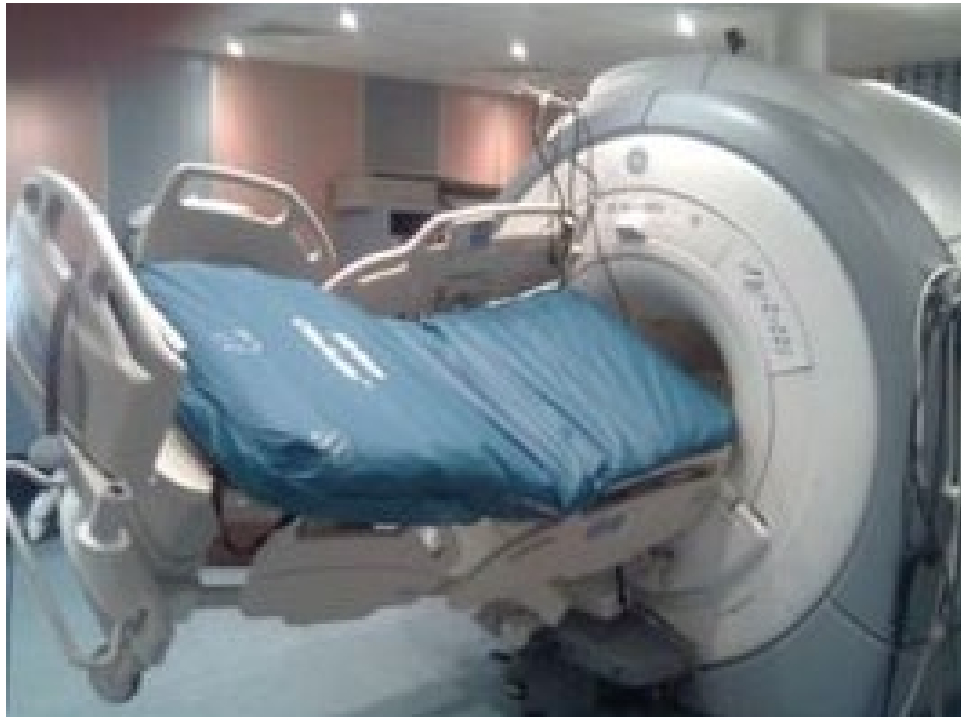
Introduction: MRI Compatibility

Challenge: A standardized phantom for MR heating of bone contacting devices doesn't exist. Companies are receiving and handling deficiencies in different ways.

Objective:

- Explain the need for MR labeling and testing
- Discuss current FDA guidance and submission feedback
- Describe future work within OSMA and ASTM to standardize MR testing for bone related devices

The Need for MR Labeling and Testing



Importance of MR Compatibility:

- Ensures safe use of medical devices during MRI scans.

Potential Risks:

- **Thermal Injuries**: Heating of devices leading to burns.
- **Magnetic Interference**: Device malfunction or displacement.
- **Image Artifacts**: Distorted images affecting diagnosis.

Why Seek MRI Compatibility Clearance?

- CE Marking Requirement
- International requirements – Japan, Australia
- Provide information to patients, surgeons and imaging centers

Historical MRI Submission Requirements

Testing performed per standards:

- Magnetically Induced Heating – ASTM F2052
- Magnetically Induced Torque – ASTM F2213
- Magnetic Resonance Image Artifact – ASTM F2119
- RF Induced Heating during Imaging – ASTM F2182
- Once the worst case for heating has been defined through the use of the ASTM standard, human body simulations are performed in the Virtual Population to determine the clinically relevant temperature rise

Labeling

- MRI Statement in Package Insert (IFU)

Historical MRI Submission Approach

- Developed systems approach for MRI compatibility
- Developed a worst-case model for both hips and knees at 1.5T and 3.0T
  - First Hip clearance: 2015
  - First knee clearance: 2017
- Additional components released after those initial clearances were compared to the original systems tested

FDA Guidance Document – May 2021: Testing and Labeling Medical Devices for Safety in the MRI Environment

- At the time of release, Industry believed the major impact was the requirement for a Patient Implant Card that would provide the patient information about the MR status of the device
- Guidance specified for devices with heating values over 4˚ C for 15 minutes of scanning that a temperature rise for 60 minutes needed to be reported
- Limited discussion of adjacent tissue
- FDA webinar held in June 2021 did not discuss any additional testing requirements

Evolving Impact of FDA Guidance Document Additional Information Request – Q4 2021 to Q2 2023

- Filed multiple submissions for MRI Compatibility after the FDA guidance was released
  - Q3 2021 through Q2 2022
- No significant questions on testing were received
- MRI parameters remained unchanged
- Information on Patient Implant Card was requested

Evolving Impact of FDA Guidance Document Additional Information Requests – May 2022

- 510(k) for hip system received additional information request in May 2022.
  - No change to labeling parameters
  - Question received requested heating over 60 minutes of scan time.
- Teleconference held with FDA to clarify additional information request
  - Pointed out the disparity as 510(k)s without this information that had just cleared
- FDA indicated that they were enforcing this portion of the guidance document from this point forward
- During this call there was no mention of a need for testing in “adjacent tissue” or “tissue of interest”

Evolving Impact of FDA Guidance Document Additional Information Requests – September 2022

- Knee submission - received request for testing in tissue of interest
- To better understand FDA's request, teleconferences with FDA were held to discuss requirements:
  - FDA indicated that this testing requirement had not been clearly communicated when guidance document was issued
  - FDA believes that heating values are under reported for devices since the ASTM standard does not require testing in bone
  - FDA believes this is a patient safety issue despite the lack of complaints/literature about issues with passive implants
- FDA communicated new testing requirements to orthopaedic companies at the OSMA meeting on 3 November 2022

Evolving Impact of FDA Guidance Document Differences in Testing Requirements

- Testing performed in tissue of interest is in addition to the testing required by the ASTM standards.
- Testing involves modeling bone in the ASTM gel phantom.
- No standard exists for testing in tissue of interest.
- After worst case is determined, devices are placed into the Human Body model. New simulations needs to be run to account for bone. Testing may result in higher heating values.
- Heating values over a 60-minute scan time are now required. A maximum heating value of 6˚C is acceptable. To achieve this requirement, scan parameters may need to be adjusted.

Evolving Impact of FDA Guidance Document
Strategy to Respond to Additional Information Request

- Developed a protocol for testing in tissue of interest. By collaborating with internal SMEs, consultant and feedback from FDA.
- Prior to responding, protocol was reviewed with FDA, and found to be acceptable
- Testing was completed and submitted as response to Additional Information Request.
- Labeling was revised based upon results of new test requirements.

Evolving Impact of FDA Guidance Document Outcome

- Gained clearance on submission that received additional information request
- Received similar additional information requests for other recent submission for MRI compatibility
- Developed test methods and strategy to meet FDA's expectations for MRI compatibility testing

Downstream Effect on Other Submissions US and Global

- Impact to labeling for compatible components may drive additional 510(k) submissions
- Notified Body has indicated that the testing based on FDA requirements will be considered a significant change submission
    - This is a significant change because of the new test method, and the revised labeling – different heating values and scan parameters
- International registrations may be required based on changes to labeling and testing performed

Key Considerations for MRI Submissions

Testing Strategy

- Systems approach include compatible components which drive worst-case assessment

Knowledge of Standards and Guidance Document

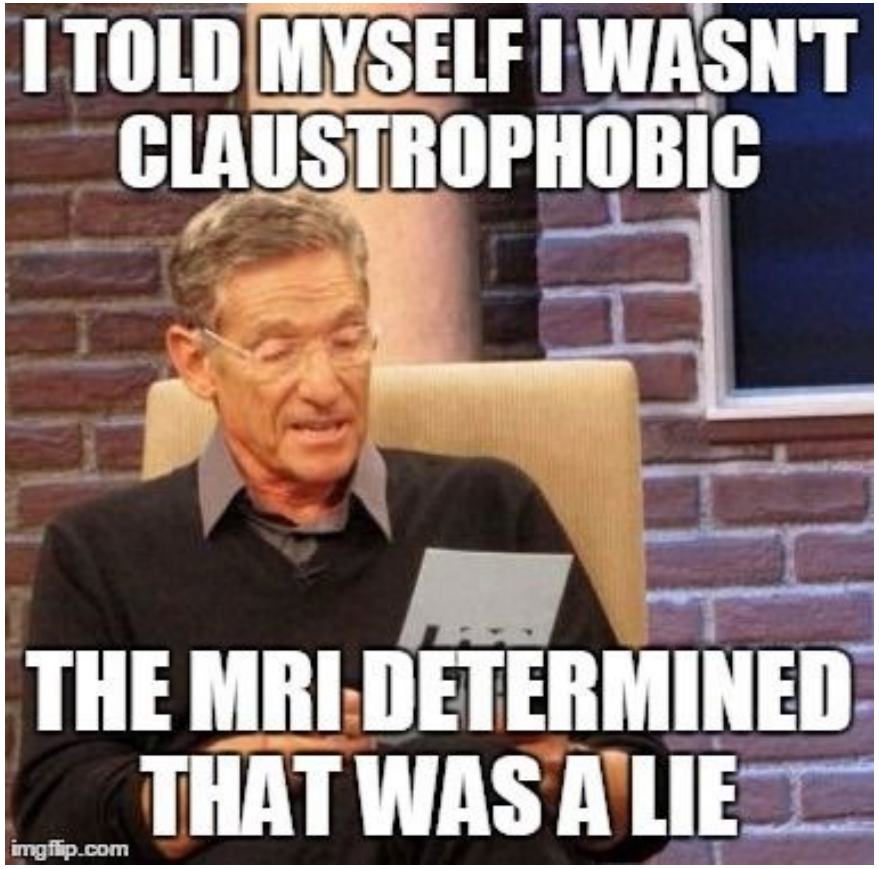
- Internal Subject Matter Expert
- Consultant with Expertise in MRI testing/analysis

Labeling Requirements

- IFU and PIC

Partner with FDA

- Q Submission or interactively during review



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ASTM Update – June 2024

ASTM F2182-19e2 (Revision Overview)

Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging

- **Plans for phantom material to also incorporate other materials where appropriate/helpful (mention of phantom material to be more representative of other tissues of interest)**
- **Notes that measured RF heating in phantom is not fully predictive of device heating in patient, but still useful for determining worst-case device configuration**
- **Added appendix sections on computational modeling as a complement to physical testing**
  - Worst-case configuration determination and in-vivo temperature rise good examples for use of computational modeling
  - Developing decision tree for determining how best to estimate in-vivo temperature rise

Breaking News: OSMA Strategic Partners

Summer 2024: OSMA will vote on including Strategic Partners in meetings and working groups
Strategic Partners are:

- Testing labs
- Contract Manufacturers
- Suppliers
- Consultants
- Individuals in the Orthopedic Space

Interested? Go to http://OSMA.net and follow the new members links to let us know!

Thank You & Questions?

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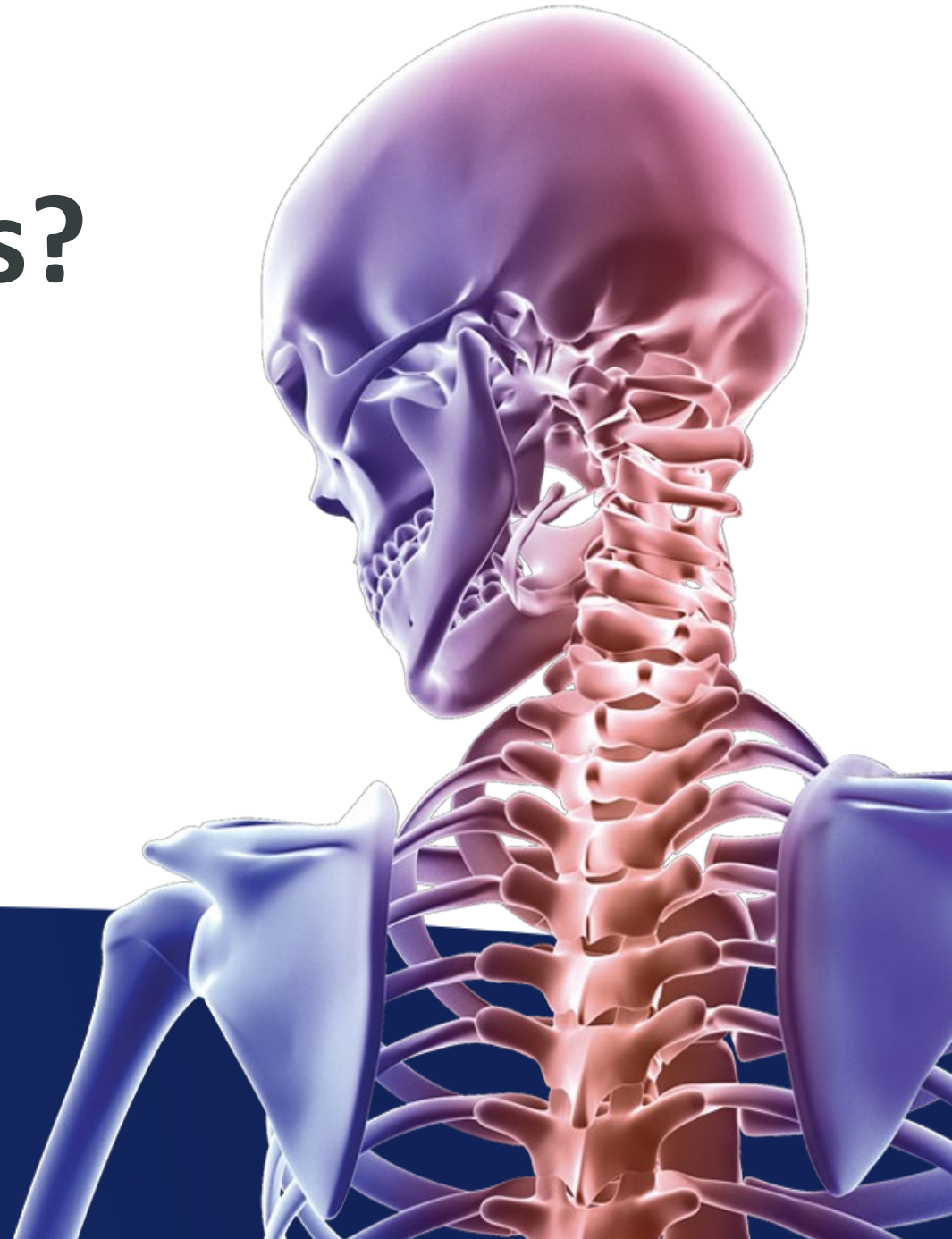

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