Supplementary file: Overview of research areas (incl. authors & voting results)

1

1st EFORT

European Consensus

on Medical & Scientific Research Requirements for the Clinical Introduction of Orthopaedic Joint Replacement Devices

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EFORT Implant & Patient Safety Initiative

RESULT | 1st European Consensus on "Medical & Scientific Research Requirements for the Clinical Introduction of Orthopaedic Joint Replacement Devices"

1 | BIOLOGICAL SAFETY / BIOCOMPATIBILITY & STERILITY

	How can the biological safety of a final finished medical device with limited, prolonged, and long-term implantation be established (including potential degradation products and novel materials/indications)?	**Voting result:** **97%** **35/1/0** (Agree/ Disagree/ Abstain)
	R. Mayer, D. Bergadano, I. Wüstefeld, M. Bohner	

2 | PRE-CLINICAL METHODS

	What are potentials and what are limitations of pre-clinical testing in the field of arthroplasty? Which demands must the test methodology of pre-clinical testing in the field of arthroplasty meet?	**Voting result:** **100%** **39/0/0**
	L. Cristofolini, T.M. Grupp, C. Kaddick, M. Morlock, M.L. Ruspi, D. Janssen	

3 | INTERFACE COMPATIBILITY / INTERFACE GEOMETRY

	How can be confirmed that all interfaces (implant – instrument only) are geometrically / dimensionally compatible and fulfil the intended purpose, i.e., the interface is functional in clinical practice?	**Voting result:** **98%** **40/0/1**
	C. Rieker, M. Bernardoni, C. Schilling, M. Woiczinski, J. Bridgens	

4 | MECHANICAL COMPONENT TESTING THA (static/dynamic)

	Are there standard methods to establish that the implant will withstand the endurance habitual and peak loads that must reasonably be expected (i.e., single implant parts as well as complete arthroplasty combination)? Are there additional test methods to establish that an implant will withstand the endurance habitual and peak loads that must reasonably be expected (i.e., single implant parts as well as complete arthroplasty combination)?	**Voting result:** **93%** **37/1/2**
	M. Bernardoni, L. Cristofolini, J.P. Kretzer	

5 | MECHANICAL COMPONENT TESTING TKA (static/dynamic)

Part 1	Are there standard methods to establish that the implant will withstand the endurance habitual and peak loads that must reasonably be expected (i.e., single implant parts as well as complete arthroplasty combination)?	**Voting result:** **98%** **41/1/0**
	C. Kaddick, C. Schilling, D. Janssen, J.P. Kretzer	
Part 2	Are there additional test methods to establish that an implant will withstand the endurance habitual and peak loads that must reasonably be expected (i.e., single implant parts as well as complete arthroplasty combination)?	**Voting result:** **91%** **32/1/2**
	C. Kaddick, C. Schilling, D. Janssen, J.P. Kretzer	
Part 3	Are there additional numerical test methods to establish that an implant will withstand the endurance habitual and peak loads that must reasonably be expected (i.e., single implant parts as well as complete arthroplasty combination)?	**Voting result:** **95%** **40/1/1**
	C. Kaddick, C. Schilling, D. Janssen, J.P. Kretzer	

6 | MECHANICAL COMPONENT TESTING (clinical perspective)

	How can be established from a clinical perspective that the implant will withstand the endurance habitual and peak loads that must reasonably be expected (i.e., single implant parts as well as complete arthroplasty combination)?	**Voting result:** **90%**
	M. Morlock, J.P. Kretzer, R.A. Schierjott, F. Traina, R. Larrainzar-Garijo, G.N. Duda, C. Kaddick	**38/1/3**

7 | BIOTRIBOLOGY (wear simulation, wear debris and biological response)

	Can standard test methods in total hip and knee arthroplasty (THA, TKA) show that the planned articulations enable the function of the joint replacement throughout the expected implant lifetime without producing a critical amount of wear?	**Voting result:** **98%**
	T.M. Grupp, C. Kaddick, J.P. Kretzer, C. Rieker, J. Fisher	**40/0/1**

8 | BIOTRIBOLOGY (beyond standard testing)

	What kind of proof apart from traditional standard test methods (each for TKA and THA) can be applied to show that the planned articulations (i.e., also including patella-trochlea) enable the function of the implant / the joint throughout the expected implant lifetime without producing a critical amount of wear?	**Voting result:** **95%**
	T.M. Grupp, C. Kaddick, J.P. Kretzer, C. Rieker, J. Fisher	**38/0/2**

9 | BIOTRIBOLOGY (clinical perspective)

	From a clinical point of view, what kind of proof can show that the planned articulations (i.e., also including patella-trochlea) enable the function of the implant / the joint throughout the expected implant lifetime without producing a critical amount of wear?	**Voting result:** **93%**
	M. Jäger, M. Dreischarf, T.M. Grupp, C. Rieker	**37/1/2**

10 | BIOTRIBOLOGY (clinical follow-up)

	How can we detect wear/debris complications at an early follow-up?	**Voting result:** **88%**
	E. Garcia-Rey, J. Cordero-Ampuero, G. Babis, F. Benazzo, M. Morlock	**35/4/1**

11 | SIZE RANGE AND ANATOMICAL DESIGN OF THE IMPLANTS

	How can the appropriateness of the implant geometry, sizing range and increments be assessed with respect to the reconstruction of anatomical structures?	**Voting result:** **98%**
	D. Janssen, M. Bernardoni, I. Dupraz, R.A. Schierjott	**40/1/0**

12 | SIZE RANGE AND ANATOMICAL DESIGN OF THE IMPLANTS (clinical erspective

	How can it be clinically assessed that provided implant sizes can cover the majority of the patients' characteristics in terms of size increments and range and that the implant's geometry allows appropriate reconstruction of the anatomical structures?	**Voting result:** **97%** **37/0/1**
	F. Benazzo, B. Grimm, C. Mazzà, F. Mancino, R.A. Schierjott	

13 | MODULARITIES / INTERFACES

	How can the in vivo behaviour of interfaces between implant components (e.g., head-conus-connection, not articulation partners) be assessed pre-clinically, for example concerning the consequences of micro motion or corrosion processes?	**Voting result:** **92%** **35/1/2**
	J. P. Kretzer, T.M. Grupp, C. Kaddick, R. Mayer, M. Morlock	

14 | MODULARITIES / INTERFACES (clinical perspective)

	How can the in vivo behaviour of interfaces between implant components (e.g., head-conus-connection, not articulation partners) be assessed clinically, for example concerning the consequences of micro motion or corrosion processes?	**Voting result:** **84%** **32/2/4**
	F. Traina, M. Morlock, R. Mayer, A. Hart	

15 | IMPLANT FIXATION (cemented implants)

	How can be assessed pre-clinically if a reasonable primary and secondary stability, as well as a physiological application of force / force transmission into the underlying bone can be achieved when using a cemented implant?	**Voting result:** **93%** **39/3/0**
	L. Cristofolini, T.M. Grupp, V. Jansson, R. Mayer	

16 | IMPLANT FIXATION (cementless implants)

	How can the primary and secondary stability and physiological load transfer to the peri-prosthetic bone of cementless implants be assessed in a pre-clinical stage?	**Voting result:** **97%** **37/0/1**
	D. Janssen, C. Schilling, J.P. Kretzer, R. Mayer	

17 | IMPLANT FIXATION (clinical perspective)

	How to assess primary and secondary stability of orthopaedic joint replacement devices in a clinical setting. How to apply/obtain/ensure optimal force / force transmission into the underlying bone (probably some comments on the place for telemetrised examinations of implants is expected?)	**Voting result:** **90%** **36/1/3**
	J. Kärrholm, M. Dreischarf, R. Mayer, R.G.H.H. Nelissen	

18 | IMPLANT FIXATION (clinical methods)

	What are the radiologic methods and parameters to estimate primary stability of implant fixation to the bone? What are recommended time points for evaluating subsidence/ loosening of implant components? How can be decided which method for clinical examination is best for evaluating implant fixation depending on the implant and	**Voting result:** **97%** **38/0/1**
	J. Kärrholm, M. Dreischarf, J. Cordero-Ampuero, P. Heesterbeek, R. Mayer, R.G.H.H. Nelissen	

19 | JOINT STABILITY AND KINEMATICS

	How can one prove in a pre-clinical setting that an implant enables the reconstruction of a functionally satisfying and stable joint, including an appropriate range of motion and best possible preservation / restoration of kinematics?	**Voting result:** **98%** **39/1/0**
	W. Taylor, B. Innocenti, G. Duda, T.M. Grupp, M. Woiczinski	

20 | TRANSFERABILITY OF RESULTS (in between devices)

	To what extent can pre-clinical/clinical results of a specific product be transferred to another device?	**Voting result:** **92%** **34/3/0**
	D. Bergadano, J. Bridgens, T.M. Grupp, A.-P. Schulz	

21 | TRANSFERABILITY OF RESULTS (pre-clinical/clinical)

	To what extent can pre-clinical test results of a product be transferred into the clinical setting?	**Voting result:** **90%** **36/1/3**
	M. Jäger, F. Traina, A. Giurea, T.M. Grupp, S. Rusch	

22 | EVALUATION OF INSTRUMENTS AND USABILITY

Part 1	How can be assessed from a pre-clinical point of view if the handling of an implant including the implant-specific instruments is uncomplicated and if the workflow runs smoothly, achieves the desired results and does not lead to undue stress for patient and surgeon?	**Voting result:** **95%** **36/0/2**
	A. Giurea, F. Benazzo, A. Blom, M. Bernardoni, C. Schilling, F. Traina, R. Mayer, S. Overgaard	

Part 2	How can be assessed from a clinical point of view if the handling of an implant including the implant-specific instruments is uncomplicated and if the workflow runs smoothly, achieves the desired result and does not lead to undue stress for patient and surgeon? *A. Giurea, F. Benazzo, A. Blom, M. Bernardoni, C. Schilling, S. Overgaard, F. Traina, R. Mayer*	**Voting result:** **97%** **37/0/1**

23 | MODIFICATIONS / ADJUSTMENTS

	What are additional requirements to implement function-relevant modifications/ adjustments during the PMCF phase of a device? What are additional requirements to implement non-function-relevant modifications/ adjustments during the PMCF phase of a device? *J. Bridgens, M. Bernadoni, C. Schilling, S. Rusch, P. Massin, R. Larrainzar-Garijo, F. Traina, V. Jansson*	**Voting result:** **95%** **38/1/1**

24 | PRE-CE STUDIES / SAFETY STUDIES (potentials/limitations)

	What are potentials and what are limitations of a pre-CE study (or safety study) in the field of arthroplasty? *A. Blom, D. Bergadano, I. Wüstefeld, J. Cobb, F. Haddad, M. Jäger, H. Achakri, M. Fink, A.-P. Schulz*	**Voting result:** **95%** **35/0/2**

25 | PRE-CE STUDIES / SAFETY STUDIES (study design)

	Which requirements to the study design of pre-CE studies/safety studies exist? *A. Blom, D. Bergadano, I. Wüstefeld, J. Cobb, F. Haddad, M. Jäger, H. Achakri, M. Fink, A.-P. Schulz*	**Voting result:** **92%** **35/1/2**

26 | PERIOPERATIVE AND SHORT-TERM POSTOPERATIVE (SERIOUS) ADVERSE EVENTS

	Is it possible to prove pre-clinically that the implantation procedure and the implants do not induce unreasonably high rates of adverse events or complications (directly implant-related, e.g., inter-periprosthetic fractures, substantial bleeding, substantial migration, and generally related to the surgery / procedure, e.g., fast track, modified surgical approaches)? *F. Siccardi, S. Rusch, S. Overgaard, A. Giurea, T.M. Grupp, A.-P. Schulz*	**Voting result:** **95%** **35/0/2**

27 | PERIOPERATIVE AND SHORT-TERM POSTOPERATIVE (SERIOUS) ADVERSE EVENTS (clinical perspective

	How can be proven clinically, that the implantation procedure and the implants do not induce unreasonably high rates of adverse events or complications (directly implant-related, i.e., inter-operative periprosthetic fractures, substantial bleeding, substantial migration, and generally related to the surgery / procedure, i.e., fast track, modified surgical approaches)? *F. Siccardi, S. Rusch, S. Overgaard, A. Giurea, T.M. Grupp, A.-P. Schulz*	**Voting result:** **92%** **35/1/2**

28 | REVISION RATE / SURVIVAL TIME

	A.Revision rate / survival time How can different factors regarding patients, at short or long-term, be considered in survival analysis?	**Voting result:** **97%** **37/0/1**
	V. Jansson, A. Blom, B. Bordini, A. Lübbeke	

29 | PMCF (post-market clinical follow-up) STUDIES

	What are potentials and limitations of PMCF studies in the field of arthroplasty?	**Voting result:** **95%** **35/0/2**
	A. Lübbeke-Wolf, H. Achakri, D. Bergadano, I. Wüstefeld, J. Bridgens,	
	M. Jäger, H. Windhagen, P. Massin, E. Garcia-Rey, R. Larrainzar-Garijo	

30 | REGISTRY STUDIES

	What are potentials of registry studies in the field of arthroplasty?	**Voting result:** **95%** **36/1/1**
	V. Jansson, A. Blom, S. Overgaard, R. Nelissen, B. Bordini	

31 | FUNCTIONALIZED IMPLANTS/ BIOMATERIALS/ SURFACES/ INNOVATIONS

	How is it possible to evaluate functionalized surfaces or novel aspects of implants for which no standardized / established test methods yet exist and where no proof of function is yet defined?	**Voting result:** **89%** **34/0/4**
	G.N. Duda, M. Jäger, B. Masson, E. Garcia-Rey, M.A. Pérez Ansón,	
	G. Reilly, R.A. Schierjott	

32 | IN SILICO TRIALS (Big Data Analytics, Machine Learning, System Biology models, system physiology models

Part 1	In what ways can In Silico Trials methodologies (whether mechanistic like Finite Element Analysis or data-based like machine learning) contribute to the assessment and evaluation of implants?	**Voting result:** **97%** **36/0/1**
	M. Viceconti, B. Grimm, W. Van der Weegen, F. Traina, I. Wüstefeld,	
	C. Mazzà, M. Dreischarf, C. Lohmann	
Part 2	How is it possible to use elements of in silico pre-clinical and clinical trials (i.e., FEA, multi-body simulations), AI/ML & Big Data as basis for implants, instruments, procedure (e.g., pre-op planning, pre-op positioning)?	**Voting result:** **95%** **35/0/2**
	M. Viceconti, B. Grimm, W. Van der Weegen, F. Traina, I. Wüstefeld,	
	C. Mazzà, M. Dreischarf, C. Lohmann	

NOTE: Please note that the following research questions have not been addressed:

Biological safety/biocompatibility & sterility (clinical perspective)

Joint stability & kinematics (clinical perspective)

Functional result/clinical outcome

One of the research topics was withdrawn during the Conference due to quality reasons.