Evolution of European Union Medical Device Regulation: perspective with the clinical evaluation of dual mobility acetabular cups (DMACs) by the French National Health Technology Assessment agency

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Introduction

The **CE marking** allows the placing on the market and free movement of medical devices (MDs) within the European Union. **European Union Medical Device Regulation (EU MDR) 2017/745**[1], entered into force in 2017 and shall apply from 26 May 2020, reinforces significantly the clinical evaluation and investigations of implantable medical devices (IMDs).

In France, the **National Committee for Evaluation of Medical Devices and Health Technologies (CNEDiMTS) of the French National Authority for Health,** has conducted a clinical assessment of each dual mobility acetabular cup (DMAC) which is a component of hip prostheses largely implanted in France. In deed, after a first assessment in 2007, the lack of evidence remains for that type of MDs. Therefore, the scope of this assessment was to verify the clinical effectiveness and safety of each DMAC under a brand (commercial) name[2] compared to the single mobility acetabular cup. The purpose of this assessment was to help the Ministry of Solidarity and Health to maintain their reimbursement under brand name and no longer under generic description. In conclusion, the committee issues an opinion and states on:

- ✓ A sufficient expected service (sufficient "**service attendu**" in French **: sufficient SA)** in favour of a refund;
- ✓ Or an insufficient expected service (insufficient **"service attendu"** in French **: insufficient SA)** against a refund.

Once the CNEDiMTS gives its opinion, the Ministry of Solidarity and Health takes the final decision on the reimbursement.

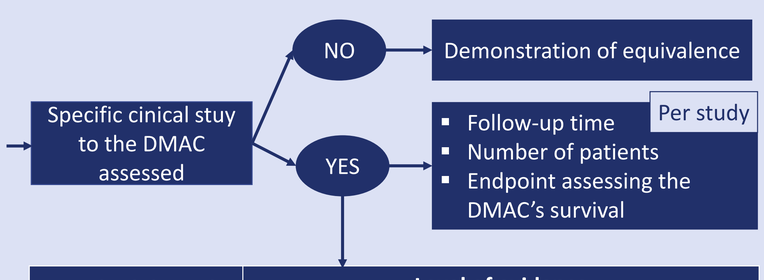
→ The aim of this study was to compare the **regulatory changes for clinical evaluation of IMDs made by the EU MDR** with the **clinical assessment of DMACs by the CNEDiMTS**.

Methods

1 Analysis of CNEDiMTS opinions

- ✓ A **retrospective analysis**
- ✓ Of **the clinical data** described in the DMAC opinions issued by the CNEDiMTS
- ✓ From the beginning of the individual evaluation of DMACs in **november 2014 until the first quarter of 2019.**
- ✓ To collect CNEDiMTS' opinions **in favour or against a reimbursement** of each DMAC
  - ➢ Sufficient "SA"
  - ➢ Insufficient "SA"

Based on the clinical data of each DMAC.



Methodological quality	Level of evidence		
	High	Intermediary	Low
Type of study	Interventional	x	Non interventional
Randomization	Randomized	x	Non randomized
Publication in a scientific review	Published	x	Non published
Type of observational study	Cohort Register	Case-control	Case serie
Data collection	Prospective	x	Retrospective
Comparator group	Comparator	x	No comparator
Number of center	Multi-center	x	Single-center

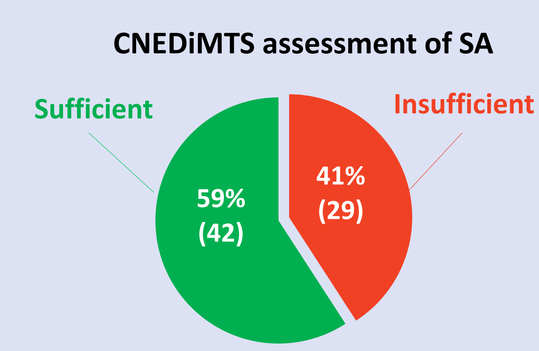
2 Comparison with the clinical requirements of the EU MDR

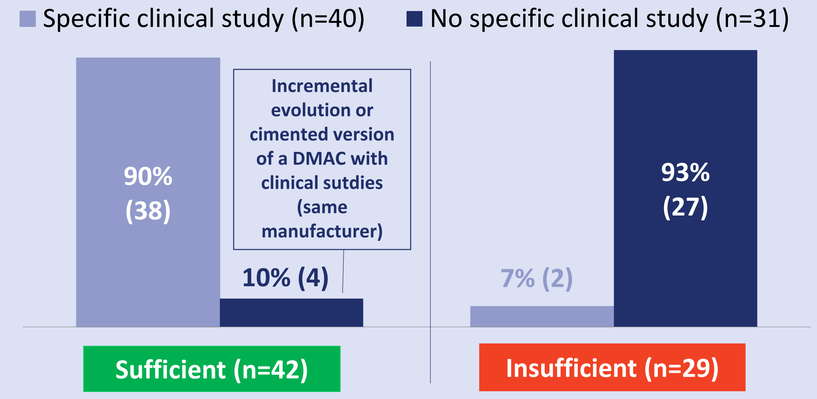
It is **only a projection** : data and opinions from the CNEDiMTS assessment were compared **with the enhanced clinical requirements of the European regulation**.

Field of the EU MDR compared	EU MDR: Expected changes for commercialisation of IMDs	CNEDiMTS: Expected changes for the reimbursemnt of DMACs
Clinical Investigation	Mandatory **clinical investigation** of IMDs	Presence of a **specific clinical study** of the DMAC
Clinical Evaluation	Evaluation of the **clinical benefit** of IMDs	At least one **endpoint assessing the survival** in favour of the DMAC
Demonstration of equivalence	Equivalence possible with another IMD: • from **the same manufacturer** or • from **another manufacturer** if the two manufacturers have a **contract** in place that explicitly allows the manufacturers of the second IMD full access to the technical documentation on an ongoing basis	Assuming that no contract is concluded between two different manufacturers: a demonstration of equivalence comparing the DMAC **to another DMAC from the same manufacturer**
Post-market follow-up	Requires **post-market clinical follow-up**	Request for a **real life study** (post-registration study)

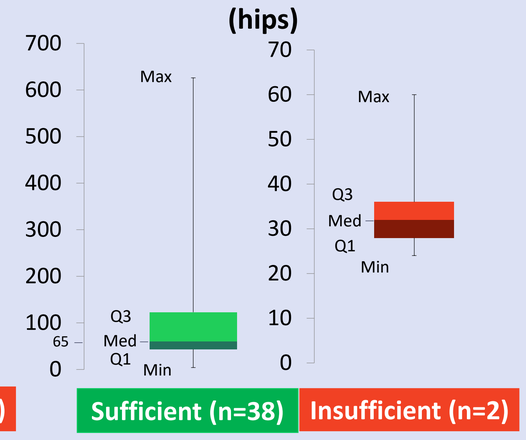
Results

1 Analysis of CNEDiMTS opinions





N=40 DMACs with specific clinical study to the DMAC



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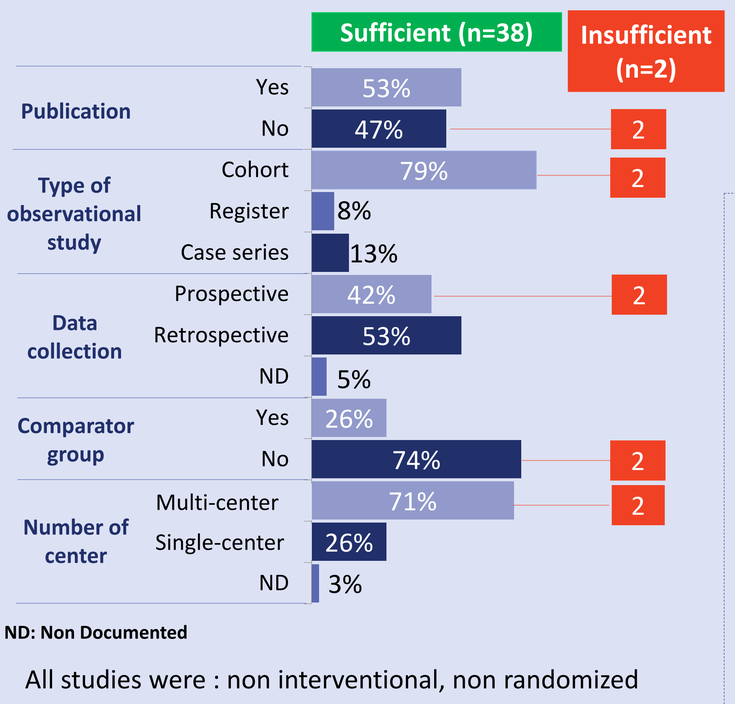
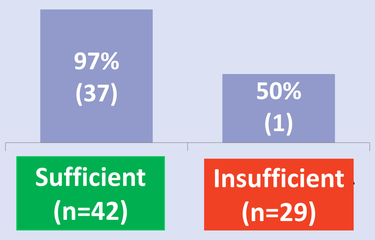
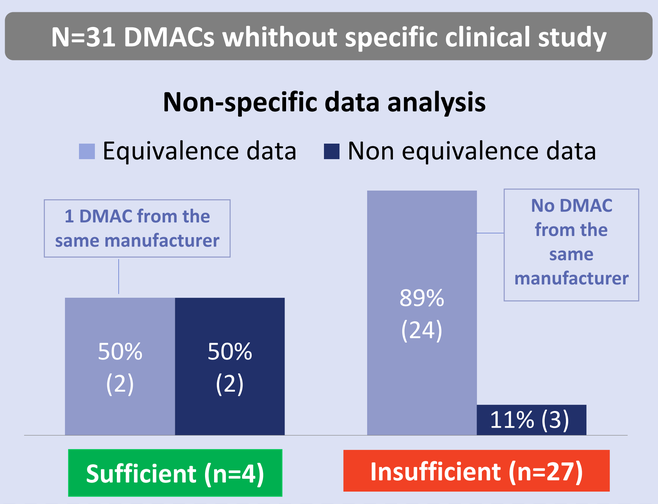


ND: Non Documented

All studies were : non interventional, non randomized



N=31 DMACs whithout specific clinical study



2 Comparison with the clinical requirements of the EU MDR

Field of the EU MDR compared	Data expected for commercialisation of DMACs	EU MDR: Projection: opinions (DMACs) that would obtain CE marking under the new regulation	CNEDiMTS: Opinions (DMACs) that have obtained sufficient SA and therefore in favour of a reimbursement
Clinical Investigation	Presence of a **specific clinical study** of the DMAC among all DMACs (n=71)	56% (40/71)	53% (38/71)
Clinical Evaluation	At least one **endpoint assessing the survival in favour** of the DMAC among DMACs with specific clinical study (n=40)	95% (38/40)	92,5% (37/40)
Demonstration of equivalence	Demonstration of **equivalence to another DMAC from the same manufacturer** among DMACs without specific clinical studies (n=31) (assumption : no contract between 2 different manufacturers)	3% (1/31)	13% (4/31)
Post-market follow-up	**Post-market clinical follow-up** among the DMACs that have obtained sufficient SA (n=42)	100% (42/42)	100% (42/42) : post-registration studies
Total	Among all DMACs (n=71)	**55% (39/71)**	**59% (42/71)**

Conclusion

The CNEDiMTS has finally granted an opinion in favour of reimbursement for a large majority of DMACs with:

- ✓ **a specific clinical investigation/study** to the DMAC assessed,
- ✓ **at least one endpoint of DMAC's survival,**
- ✓ and **a median clinical follow-up time** of at least six months for patients.

According to the clinical data available, **no added value** has been demonstrated compared to the single mobility acetabular cup. The committee had to take into account the **low level of evidence** in the data to state on the clinical interest of DMACs. As a result, there is no clear decision threshold formulated *a priori* (no minimum number of patients, no minimum expected methodological quality criteria). This is why the CNEDiMTS has requested a **post-registration study** to monitor the DMACs with sufficient SA over the long term.

The CNEDiMTS assessment may anticipate the clinical requirements expected by the **EU MDR requiring:**

- ✓ **clinical studies with a clinical benefits** for IMDs,
- ✓ and a **significant restriction for equivalency**.

Real life monitoring studies could be designed to meet both the requirements of CE marking under the EU MDR and those of post-registration monitoring studies required for reimbursement.

Sources: [1] Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices (https://eur-lex.europa.eu)
[2]JORF n°0089 du 14 avril 2017 texte n° 162 -Code de la sécurité sociale avr 14, 2017 (https://www.legifrance.gouv.fr)

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