Identifying and Defining the Strategic Pathway for the Clinical Data through Design Development and Clinical Evaluation

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Bioevents
Sharing Biomed Knowledge

CSMD 2024

I am speaking at

The 3rd Conference on

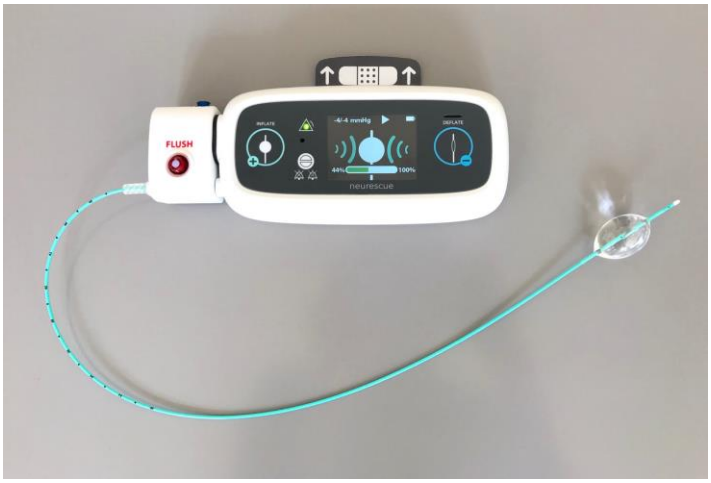
Clinical Studies with Medical Devices and IVD

29-30 May 2024 | London, UK

Register and Join me at the Event

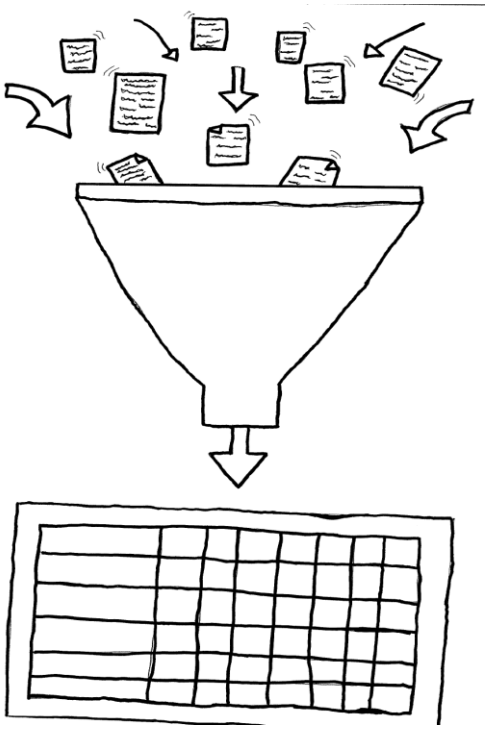
www.csmd2024.com

NEURESCUE device journey (2017-2024)



- 2 CT scan studies (1 published)
- 1 pilot animal study
- 1 blinded RCT animal study (published)
- Cadaver feasibility study (published)
- Usability study US
- 1 GLP-compliant animal study
- 510(k) authorization
- Investigational Device Exemption (IDE)
- Community consultation study
- 3 initiated acute clinical studies
- 2 finalized acute feasibility studies
- 3 publications and 4 on its way
- Initial process of an RCT
- Initial process of CE mark

Agenda

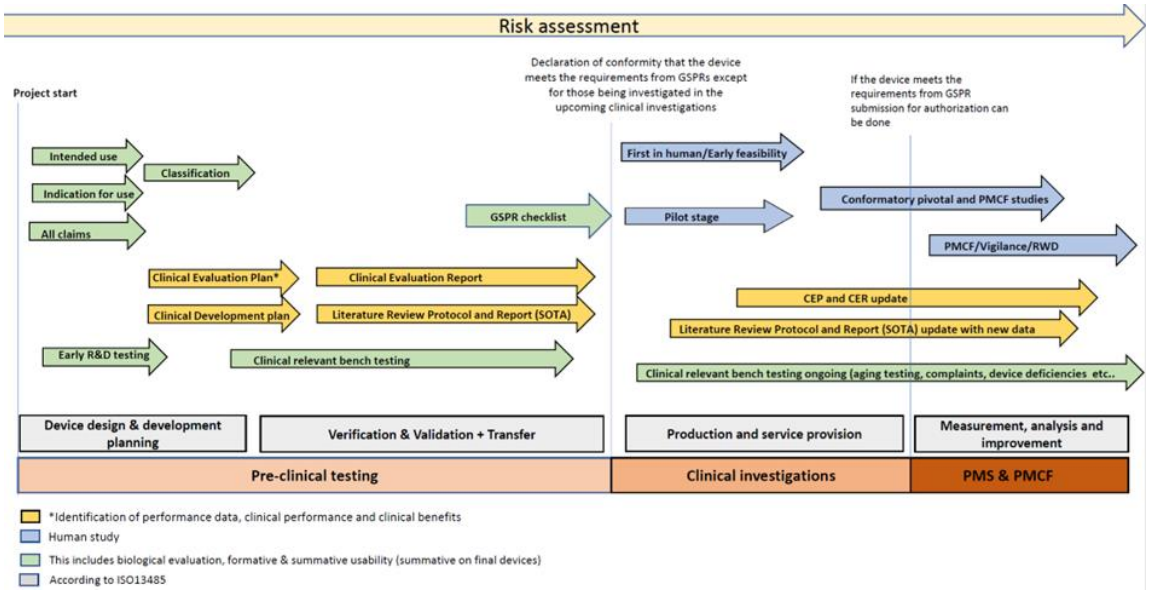


MDR Chapter VI, Annex XV: Clinical Evaluation & Clinical Investigation

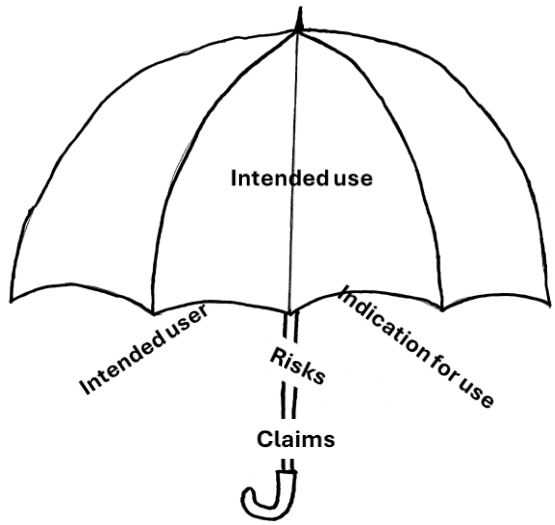
21 Articles (§§ 61 – 82), and 2 Annexes (XIV, XV)

- Art. 61 Clinical Evaluation, Annex XIV Part A
- Art. 62 General requirements regarding clinical investigation
- Art. 63 Informed Consent
- Art. 64 Clinical investigations on incapacitated subjects
- Art. 65 Clinical investigations on minors
- Art. 66 Clinical investigations on pregnant or breastfeeding women
- Art. 67 Additional national measures
- Art. 68 Clinical investigations in emergency situations
- Art. 69 Damage compensation
- Art. 70 Application for clinical investigations
- Art. 71 Assessment by Member States
- Art. 72 Conduct of a clinical investigation
- Art. 73 Electronic system on clinical investigation
- Art. 74 Clinical investigations with devices authorizes to bear the CE marking
- Art. 75 Substantial modification to a clinical investigation
- Art. 76 Corrective measures to be taken by Member States and information exchange between Member States
- Art. 77 Information by the Sponsor at the end of a clinical investigations or in the event of temporary hold or early termination
- Art. 78 Coordinated Assessment procedure for clinical investigations
- Art. 79 Review of coordinated procedure
- Art. 80 Recording and reporting of adverse events occurring during clinical investigations events
- Art. 81 Implementation act (e.g. forms, categories of devices, timelines)
- Art. 82 Requirements regarding other clinical investigations

Annex VIX Clinical Evaluation and Post market clinical follow up
Annex XV Clinical Investigation



Intended use umbrella



Definition MDR 2017/745

(22) the ability of a device to achieve its intended purpose as stated by the manufacturer;

(52) The ability of a device, resulting from any direct or indirect medical effects which stem from its technical or functional characteristics, including diagnostic characteristics, to achieve its intended purpose as claimed by the manufacturer, thereby leading to a clinical benefit for patients, when used as intended by the manufacturer;

(53) 'clinical benefit' means the positive impact of a device on the health of an individual, expressed in terms of a meaningful, measurable, patient-relevant clinical outcome(s), including outcome(s) related to diagnosis, or a positive impact on patient management or public health;

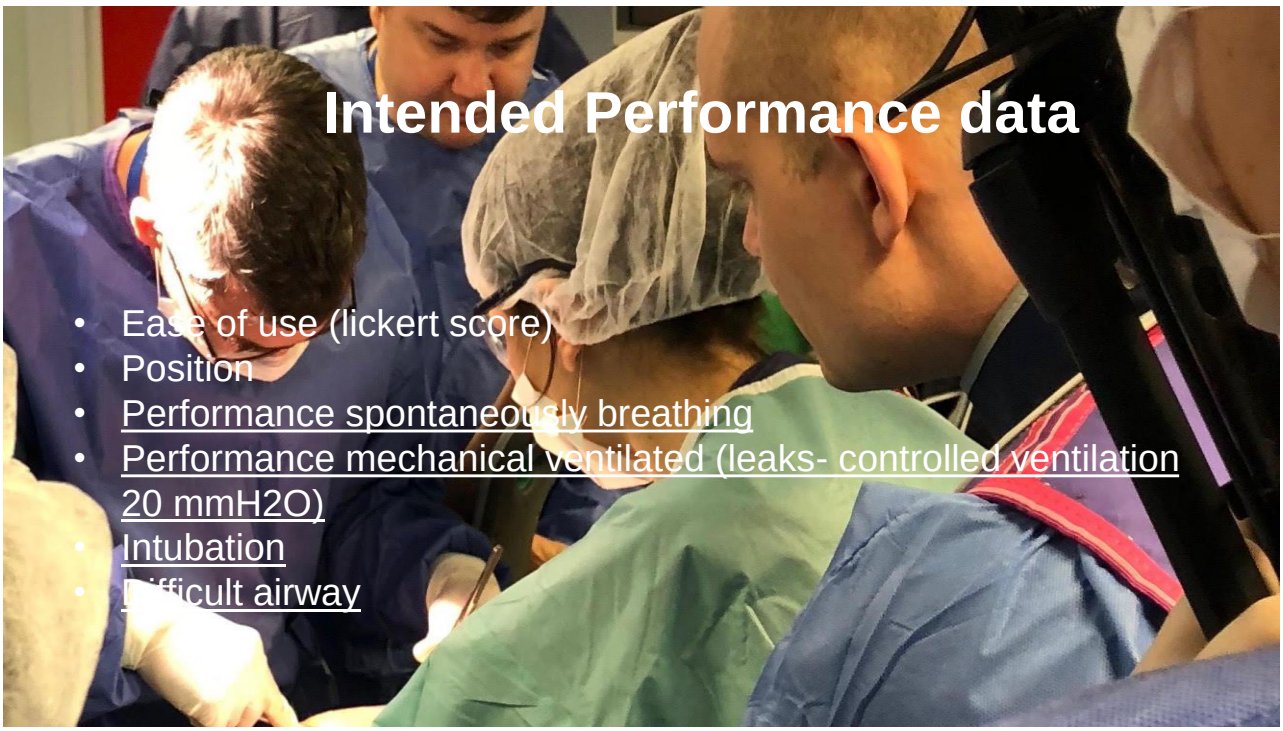
Clinical Evaluation Plan & Clinical Documentation Plan

- Intended performance data
- Intended clinical performance
- Intended clinical benefits
- Intended claims
- Risk assessment

Intended Use & Indication for use

- Define your performance data.
  - **Intended use:** *an advanced supraglottic airway device used to ventilate spontaneously breathing patients as well as assist-controlled ventilation. It is also designed to facilitate tracheal intubation.*
  - **Indication for use:** *patients evaluated as eligible for a supraglottic airway.*
  - *It is also **indicated** in a known or unexpected difficult airway*

The first SGA to be approved was the LMA by Dr. Brain in 1992.



Intended Performance, clinical performance, clinical benefit & claims

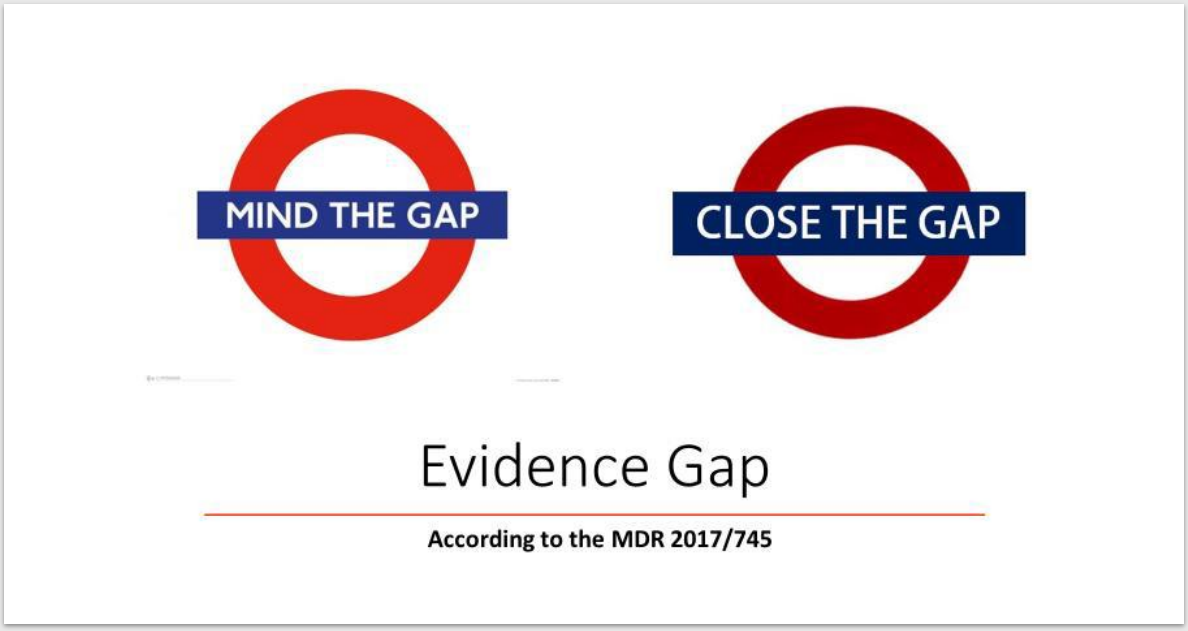
Performance data no.	Performance	Clinical performance	Clinical benefit	Claim
1	Spontaneous ventilation	No air leaks Good positioning	Used during anesthesia with spontaneous breathing patients	Airway device for spontaneous breathing patients during anesthesia
2	Mechanical ventilation 20mmHg	No air leaks	Ventilation during anesthesia No regurgitation	Airway device for ventilation of patient during anesthesia
3	Intubation	Bridging device to intubation	The SGA can be used as a rescue device	Intubation airway
4	Intubation difficult airway	Bridging a difficult airway to safe intubation	Safe intubation of the patient	1st rescue strategy in a cannot ventilate - cannot intubate situation.

Performance data and clinical development plan

Performance data number	Performance to be generated	Clinical development
1	Spontaneous ventilation in anesthetized patients	Human studies
2	Mechanical ventilation in anesthetized patients (20 mmHg)	Human studies
3	Intubation possibilities	Mannequin and cadaver studies
4	Intubation difficult airway	Difficult airway case reports

Clinical Development Plan (ISO14155 Annex 1)

Regulatory status	Pre-market	Post-market
Clinical development	Feasibility pilot RCT Mannequin studies/Cadaver studies Case reports	Post-market follow up studies
Type of design	Conformity and exploratory	Conformity to support safety and performance and post-market clinical follow-up. Registry studies, case reports.
Description of clinical investigations	First in human feasibility Mannequin and cadaver investigations	Post market clinical follow up studies
Burden to subjects	Interventional and non-interventional follow-up	Interventional and none-interventional follow up.



Clinical evidence according to MDR 2017/745

(52) clinical evidence' means clinical data and clinical evaluation results pertaining to a device of a **sufficient amount and quality** to allow a qualified assessment of whether the device is safe and achieves the intended clinical benefit(s), when used as intended by the manufacturer;

MDCG 2020-6: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC

Appendix III – Suggested hierarchy of clinical evidence for conformation of conformity with relevant GSPR under the MDR.

Hierarchy of clinical evidence

Rank	Types of clinical data and evidence	Considerations / comments
1	Results of high quality[62] clinical investigations covering all device variants, indications, patient populations, duration of treatment effect, etc	This may not feasible or necessary for certain well-established devices with broad indications (eg Class IIb legacy sutures, which could be used in every conceivable patient population)
2	Results of high quality clinical investigations with some gaps	Gaps must be justified / addressed with other evidence in line with an appropriate risk assessment, and clinical safety, performance, benefit and device claims. Assuming the gaps can be justified, there should be an appropriate PMCF plan to address residual risks. Otherwise, manufacturers shall narrow the intended purpose of the device until sufficient clinical data has also been generated.
3	Outcomes from high quality clinical data collection systems such as registries[63]	Is there sufficient evidence of the quality of the data collected by the registry[64, 65]? Are the devices adequately represented? Are the data appropriately stratified? Are the endpoints appropriate to the safety, performances and endpoints identified in the clinical evaluation plan?
4	Outcomes from studies with potential methodological flaws but where data can still be quantified and acceptability justified[66]	Many literature sources fall into this category, due to limitations such as missing information, publication bias, time lag bias, etc. This applies equally to publications in the peer-reviewed scientific literature. However, for legacy devices where no safety or performance concerns have been identified, these sources can be sufficient for confirmation of conformity to the relevant GSPRs if appropriately appraised and the gaps are identified and handled. High quality surveys may also fall into this category.
Class III legacy devices and implantable legacy devices which are not well-established technologies should have sufficient clinical data as a minimum at level 4. Those devices which are well-established technologies may be able to confirm conformity with the relevant GSPRs via an evaluation of cumulative evidence from additional sources as listed below. Reliance solely on complaints and vigilance is not sufficient.		

MDCG 2020-6/Appendix III/12 Ranks

Sufficient amount and quality of evidence

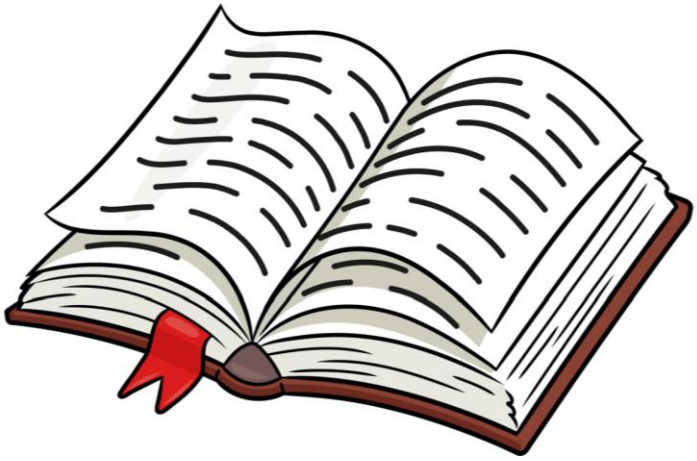
	A	B	C	D	E
1		**SGA01/Spontaneous**	**SGA02/Ventilation**	**SGA03/Intubation**	**SGA04/Difficult airway**
2	**CIP Do Nr**	**REC-0000329**	**DOC-0000476/DOC-0000481**	**DOC-0000484**	**DOC-0000291**
3	**CIR Doc Nr**	**DOC-0000335**	**DOC-0000527/DOC-0000542**	**DOC-0000647/DOC-0000709**	**DOC-0000281**
4	**Publication**	**N/A**	**DOC-0001197**	**N/A**	**DOC-0000843**
5	**Intended Use: an advanced supraglottic airway device used to ventilate spontaneously breathing patients as well as assist controlled ventilation. It is also designed to facilitate tracheal intubation.**				
	Supporting data	**Primary performance endpoint**: Feasibility: ease of insertion and Spontaneously breathing anesthetized subjects **Primary safety endpoints:** Leaks, regugitation, nauseau	**Primary performance endpoint:** Feasibility: ease of insertion. Ventilated subjects **Secondary endpoint:** Safety endpoints, sore throuat, nausea, regugitation	**Primary performance endpoint:** Ease of intubation by specialist in airway management	**Primary performance endpoints:** Success full bridging to intubation in a difficult aitrway. **Primary safety endpoints:** Leaks durin Manual ventilation (highpressure), regugitation, nauseau **Secondary endpoints:** Time to successful intubation, ease of successful intubation

Clinical-relevant bench testing!

Sufficient evidence & quality

	SGA01/Spontaneous	SGA02/ventilation	SGA03/Intubation	SGA04/Intubation difficulat airway
CIP Do Nr	DOC-0000476/DOC-0000481	DOC-0000484	DOC-0000291	DOC-0001113
CIR Doc Nr	DOC-0000527/DOC-0000542	DOC-0000647/DOC-0000709	DOC-0000281	DOC-0000287
Publication	DOC-0001197	DOC-0009009	DOC-0000843	DOC-0000840
Intended Use: an advanced supraglottic airway device used to ventilate spontaneously breathing				
Evidence /quality	Feasibility cae series 20 patients (Rank 3)	Prospective RCT (Rank 1)	Cadaver study (rank 11)	Caseseries 10 patients (Rank 3 or 9)
Indication for use: patients evaluated as eligible for a supraglottic airway. It is also indicated in a known or unexpected difficult airway				

Sufficient quality



- Evidence level
- Good Laboratory Practice
- ICH/GCP compliant
- ISO14155 compliant
- Regulatory requirements (MDR/21 CFR)
- GDPR/HIPAA
- Good documentary practice (eTMF, CTMS)

Clinical Evaluation Report

- Intended performance, Intended clinical performance, and intended clinical benefit are now valuable data for confirmed
  - Performance data
  - Clinical performance data
  - Clinical benefits that can be weighed against the risks and support the:
    - Intended use
    - Indication for use
    - Intended user and all Claims

Thank you

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