



# Expert decision and opinion in the context of the Clinical Evaluation Consultation Procedure (CECP)

## Expert panels on medical devices and in vitro diagnostic devices (Expanded)

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### Scope of this expert decision

This decision reflects the views of independent experts (MDR Article 106) on the relevance to produce an opinion on the clinical evaluation assessment report (CEAR) of the notified body for this device. The expert decision is provided in the context of the clinical evaluation consultation procedure (CECP), which is an additional element of conformity assessment by notified bodies for specific high-risk devices (MDR Article 54 and Annex IX, Section 5.1).

### Scope of this expert opinion

This scientific opinion reflects the views of independent experts (MDR Article 106) on the clinical evaluation assessment report (CEAR) of the notified body. The advice is provided in the context of the clinical evaluation consultation procedure (CECP), which is an additional element of conformity assessment by notified bodies for specific high-risk devices (MDR Article 54 and Annex IX, Section 5.1).

The notified body is obliged to give due consideration to views expressed in the scientific opinion of the expert panel and in particular in case experts find the level of clinical evidence not sufficient or have serious concerns about the benefit-risk determination, the consistency of the clinical evidence with the intended purpose including the medical indication(s) or with the post-market clinical follow-up (PMCF) plan.

Having considered the expert views, the notified body must, if necessary, advise the manufacturer on possible actions, such as specific restrictions of the intended purpose, limitations on the duration of the certificate validity, specific post-market follow-up (PMCF) studies, adaption of instructions for use or the summary of safety and clinical performance (SSCP) or may impose other restrictions in its conformity assessment report.

In accordance with MDR Annex IX, 5.1.g., the notify body shall provide a full justification where it has not followed the advice of the expert panel in its conformity assessment report.

## 1 ADMINISTRATIVE INFORMATION

<b>Date of start of procedure</b>	16/05/2025
<b>Notified Body number</b>	NB2797
<b>Internal CECP dossier #</b>	EMA/EX/0000272454
<b>Medical device type</b>	Endocardial atrial and ventricular lead
<b>Intended purpose</b>	Chronic pacing and sensing in the right atrium and/or right ventricle when used with a compatible pulse generator. In addition, pacing and sensing in the left bundle branch area is indicated with a single or dual chamber pacemaker as an alternative to the right ventricle. Both intended purposes are for the treatment of bradycardia.
<b>Risk class / type</b>	<input checked="" type="checkbox"/> class III implantable <input type="checkbox"/> class IIb active device intended to administer or remove medicinal products(s)
<b>Screening step: medical field / competence area</b>	Circulatory system

## PART 1 - DECISION OF SCREENING EXPERTS: NOTIFICATION OF NB AND COMMISSION REGARDING THE INTENTION TO PROVIDE AN OPINION

### 1.1 Decision of the screening experts

Table covers all three criteria, intended to support their consistent and conscientious application

Date of decision	27/05/2025
Screening panel decision	
Is there intention to provide a scientific opinion?	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Insufficient information to reach a conclusion
In case the information was found insufficient to reach a conclusion: summary of reasons (see MDR Annex IX Section 5.1 point c)	
N/A	
Summary as to why there is intention to provide an opinion	
Given the moderate-to-high degree of novelty and potential moderate clinical impact, an opinion is warranted, particularly to assess adequacy of the benefit-risk ratio, PMCF planning, and consistency of the data with the expanded intended purpose.	
Summary as to why there is <u>no</u> intention to provide an opinion	
N/A	
Any other comments	
While the CEAR is structured and comprehensive, some methodological uncertainties in the long-term safety outcome suggest that expert feedback might be beneficial, especially considering the device's role in conduction system pacing, a rapidly evolving clinical field.	

### 1.2 Assessment of the three screening criteria

<b>Criterion 1: Novelty of device under assessment and possible clinical / health impact</b>
<b>1.1 Overall degree of novelty</b>
<input type="checkbox"/> No novelty: Neither device nor clinical procedure is novel <input type="checkbox"/> Low level of novelty <input checked="" type="checkbox"/> Medium level of novelty <input type="checkbox"/> High level of novelty
<b>Short description of the novelty, including main dimension(s) of novelty</b>
The INGEVITY+ lead, while CE-marked for conventional right atrial/ventricular pacing, is now proposed to be used for an expanded indication that includes left bundle branch area pacing (LBBAP). This

represents a medium level of novelty due to the adaptation of an existing lead design (stylet-driven active fixation) for a new anatomical pacing target (left bundle branch area) which involves new procedural techniques and may impact clinical outcomes.

**1.2 Possible negative clinical / health impact resulting from novelty**

**Estimated\* possible clinical and/or health impact related to the novel aspects of the device**

\* This can entail uncertainty. Not only *known* clinical / health impacts but also *possible* ones (conceivable uncertainties, hazards, risks) should be taken into account but need to be supported by a scientific, clinical or technical reasoning.

- No clinical or health impact
- Minor clinical or health impact
- Moderate clinical or health impact
- Major clinical or health impact

**Possible major clinical or health impact related to the novel aspects of the device**

Potential impacts relate to mechanical trauma during deep septal placement, capture threshold variability over time, and operator variability. These risks could affect long-term lead performance and patient safety, especially in less experienced centres.

**Criterion 2: Scientifically valid health concerns leading to significantly adverse changes in the benefit-risk profile of a specific group / category of devices and relating to**

- a) Component(s)
- b) Source material(s)
- c) Impact on health in case of failure of the device

**2.1 Information received from the Secretariat:**  Yes  No

**2.2 Other information available to the Experts:**  Yes  No

**Criterion 3: Significant increase of serious incidents of a specific group / category of devices relevant for the device under assessment (if information is available, it will always be provided by the expert panel secretariat)**

**3.1 Information received from the Secretariat?**  Yes  No

### 1.3 Indication of appropriate thematic panel in case opinion is required

Indication of appropriate thematic panel and competence area		
	Expert panels	Medical and scientific/technical competence areas (these may correspond to sub-groups)
<input type="checkbox"/>	<b>Orthopaedics, traumatology, rehabilitation, rheumatology</b>	<input type="checkbox"/> 1. Joint replacements (hip, knee, shoulder) <input type="checkbox"/> 2. Spinal devices <input type="checkbox"/> 3. Non-articulating devices, rehabilitation
<input checked="" type="checkbox"/>	<b>Circulatory system</b>	<input type="checkbox"/> 1. Prosthetic heart valves and devices for heart valve repair <input type="checkbox"/> 2. Cardiovascular stents (metallic and bio-resorbable) and vascular prostheses <input checked="" type="checkbox"/> 3. Active implantable cardiac devices and electrophysiological devices <input type="checkbox"/> 4. Structural interventions and new devices (e.g. LAA/PFO occluders, heart failure devices) <input type="checkbox"/> 5. Cardiac surgery including extracorporeal membrane oxygenation, cardiopulmonary bypass devices, artificial hearts and left ventricular assist devices
<input type="checkbox"/>	<b>Neurology</b>	<input type="checkbox"/> 1. Central and peripheral nervous system devices <input type="checkbox"/> 2. Implants for hearing and vision (sensory recovery) <input type="checkbox"/> 3. Neurosurgical devices
<input type="checkbox"/>	<b>Respiratory, anaesthesiology, intensive care</b>	<input type="checkbox"/> Respiratory and anaesthetic devices
<input type="checkbox"/>	<b>Endocrinology and diabetes</b>	<input type="checkbox"/> Endocrinology and diabetes devices
<input type="checkbox"/>	<b>General and plastic surgery Dentistry</b>	<input type="checkbox"/> 1. Surgical implants and general surgery <input type="checkbox"/> 2. Plastic surgery and wound care <input type="checkbox"/> 3. Maxillofacial surgery & Devices for dentistry e.g. oral surgery, implantology, dental materials etc.
<input type="checkbox"/>	<b>Obstetrics and gynaecology including reproductive medicine</b>	<input type="checkbox"/> Devices for obstetrics and gynaecology
<input type="checkbox"/>	<b>Gastroenterology and hepatology</b>	<input type="checkbox"/> Devices for gastroenterology and hepatology
<input type="checkbox"/>	<b>Nephrology and urology</b>	<input type="checkbox"/> Devices for nephrology and urology
<input type="checkbox"/>	<b>Ophthalmology</b>	<input type="checkbox"/> Devices for ophthalmology

## PART 2 - SCIENTIFIC OPINION OF THE THEMATIC EXPERT PANEL/SUB-GROUP

### 2.1 Information on panel and sub-group

Date of opinion	14/07/2025
Expert panel name	Circulatory system
Sub-group of expert panel (where relevant)	Active implantable cardiac devices and electrophysiological devices

### 2.2 Detailed aspects of the opinion as required by MDR Annex IX Section 5.1

<b>Opinion of the expert panel on the specific aspects of the clinical evaluation assessment report of the notified body (CEAR)<sup>1</sup></b>
<b>1. Overall opinion on the NB's assessment of the manufacturer's clinical evaluation report</b>
The NB presented a thorough and detailed assessment of the manufacturer's clinical evaluation, including a discussion of some of its limitations. The panel has provided suggestions for additional collection of clinical data in the post-marketing phase, which are listed in section 4.
<b>2. Opinion on the NB's assessment of the adequacy of the manufacturer's benefit-risk determination</b>
<p>In the opinion of the experts, the NB has performed a balanced assessment of the benefit / risk ratio associated with the implantation of the device. No new device-related hazards were identified in the clinical literature review on LBBAP implants.</p> <p>The clinical data used for the pre-market assessment of the proposed new indication came from the following sources:</p> <ul style="list-style-type: none"><li>• INSIGHT-LBBA: a retrospective analysis, non-randomised, multi-centre, and US only observational study of ING+ leads that had been previously implanted in the LBBA;</li><li>• LATITUDE: Boston Scientific remote monitoring database, where patients transmit data to an in-home monitoring device which then sends the data to the LATITUDE server;</li><li>• National Cardiovascular Device Registry (NCDR): contains data from centres in the US that implant pacemakers and defibrillators. NCDR was used to obtain ING+ data, but also to compare this data to other leads.</li></ul> <p>No difference between data sources was observed for either of the primary performance endpoints (no safety data was available in LATITUDE). For both primary performance endpoints, the results for both data sources were sufficient for the analysis and do not meaningfully differ from one another.</p>

<sup>1</sup> According to Annex IX Section 5.1 of Regulation (EU) 2017/745 - Assessment procedure for certain class III and class IIb devices.

A summary of the main results is presented in table 8-13:

**Table 8-13: Subgroup Analyses - Data Source (p 141-142 CER)**

Endpoint	Data Source(s)	Statistics	Data Source		P-value
			INSIGHT	LATITUDE	
Primary Safety 1	INSIGHT	Leads free from LRC / N at risk Kaplan-Meier LRC-Free Rate (Lower CL)  Performance goal: >90%	448 / 456 97.9% (95.8%)	No safety data	N/A
Primary Performance 1	INSIGHT & LATITUDE	Measurements $\leq 2V$ / N Measurements $\% \leq 2V$ (Lower CL) Performance goal: >80%	240 / 241 99.6% (97.7%)	684 / 690 99.1% (98.1%)	0.68
Primary Performance 2	INSIGHT & LATITUDE	Measurements $\geq 5 mV$ / N Measurements $\% \geq 5 mV$ (Lower CL) Performance goal: >80%	193 / 200 96.5% (92.9%)	717 / 748 95.9% (94.2%)	0.84

Regarding these data sets, there are some limitations, adequately identified by the NB, in particular:

- Clinical evidence consists mostly of comparison of success rates and safety of device implantation with 3 to 12 months follow-up with performance goals set by a state-of-the-art literature review.
- No randomised study against a standard of care has been performed to demonstrate the clinical benefits of the device: potential for data quality issues arising from retrospective data collection.
- The safety objective does not include procedure-related adverse events AE, or patient-related adverse events not identified as possibly lead-related.
- The implant success is evaluated using only descriptive statistics.
- The device was implanted under off-label conditions in the clinical practice, i.e., without the support of a specific implant guidance from approved instructions for use.
- Some patients were implanted in the LBBA without using a confirmation method as provided in the guidelines.

The panel agrees with these conclusions of the NB.

**3. Opinion on the NB's assessment of the consistency of the manufacturer's clinical evidence with the intended purpose, including medical indication(s)**

The panel agrees with the NB's conclusion that the clinical data used for the assessment is consistent with the new medical indication claimed for the device.

**4. Opinion on the NB's assessment of the consistency of the manufacturer's clinical evidence with the PMCF plan**

The panel suggests the collect of the following additional data as part of the PMCF-plan:

- MRI compatibility and available safety data, including the risk of ventricular arrhythmia and myocardial lesions due to gradient magnetic field induced currents in the lead and at the extremity

- of the lead during MRI sequences as well as an increase in stimulation threshold shortly and lately after MRI acquisitions (close stimulus energy threshold monitoring);
- Monitor diagnostic performance and safety of device implantation in relation to the experience and annual average number of pacemaker implantation of physicians to confirm that the proctoring plan is adequate for both experienced and less experienced physicians/centres;
  - Collect cardiac conditions associated to the implantation of the device that may be associated with an increased risk of complications (e.g., history of anterior or inferior ST-segment elevation myocardial infarction (STEMI), hypertrophic cardiomyopathy, other cardiac diseases);
  - Closely monitor possible complications following the extraction of the lead more than 2-3 years after its implantation in the septum (e.g., thrombosis, cardiac lesions, abscess);
  - In addition to the implant success rate, collect all possible complications following the implantation (incidence of septal perforation and possible induced thrombo-embolic events, pericardial effusion, tamponade, device infection, ventricular arrhythmia on pacemaker memory, death);
  - Monitor the evolution of stimulation threshold over time and confirm the absence of divergent safety margins (compared to conventional pacing).

### 2.3 Summary of expert panel opinion

The device INGEVITY+ lead is CE marked for conventional right atrial/ventricular pacing. This request for a clinical consultation procedure concerns an extension of indication for left bundle branch pacing. This represents a medium level of novelty due to the use of the existing lead design (stylet-driven active fixation) in a new anatomical pacing target (left bundle branch area) which involves new procedural techniques and may impact clinical outcomes.

The notified body has performed a thorough assessment by reviewing the existing literature and clinical studies and assessing the clinical evidence provided by the manufacturer. The expert panel agrees that the benefit-risk determination is adequate.

Clinical evidence consists mostly of comparison of success rates and safety of device implantation with 3 to 12 months follow-up obtained from retrospective studies compared to the results obtained with standard of care in a retrospective analysis. No prospective randomised study demonstrating the clinical benefits of the new device has been performed against a standard of care. The limitations of the analysis were identified adequately by the notified body.

The implantation and use of this device shows a similar performance and safety profile to other LBBAP devices, with no new safety concerns identified. The device and implantation procedure do carry risks, which need to be further categorised since LBBAP is a developing area of pacing and no long-term data is available.

Therefore, regarding the PMCF plan, additional data collection is suggested, as described in section 4.

### 2.4 Recommendations

The panel suggest expanding the PMCF-plan to confirm that the safety of device implantation is consistent across centres and physicians, collecting more precisely the type of clinical events that occur after lead implantation and during follow-up, and evaluating the possible impact of underlying cardiac

diseases on short- and long-term outcome with this device. A full list of recommended additional data to be collected as part of the PMCF is provided in section 4.

## 2.5 Stakeholder information, where available

<b>Relevant information provided by stakeholders, if applicable<sup>2</sup></b>
<b>Has the Secretariat provided information from stakeholders?</b>
<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Summary of the information that was taken into account and how it was taken into account.</b>
N/A

## 2.6 Divergent positions in case no consensus was reached

<b>Please indicate how many of the experts of the panel or sub-group had divergent views</b>
Zero
<b>Summary of divergent positions</b>
N/A

END OF TEMPLATE

<sup>2</sup> According to Article 106.4 of Regulation (EU) 2017/745, expert panels shall take into account relevant information provided by stakeholders including patients' organisations and healthcare professionals when preparing their scientific opinions.