LITERATURE SEARCH

REVIEW

**{{ device\_name }}**

EU Class: {{ device\_classification }}

**Prepared Exclusively For**

**{{ company\_name }}**

{{ company\_address }}

**Prepared By**

{{preparer}}

Cite Medical, LLC

**Date**

**{{ prepared\_date }}**

**LITERATURE SEARCH**

**REVIEW**

To address the requirement for GSPR as part of the technical documentation containing information to demonstrate the conformity with the Medical Device Regulation (MDR) 2017/745

**Table of Contents**

# Overview

## Background

**{{ company\_name }}** is conducting a scientific literature search to demonstrate the performance and safety of their device, the {{ device\_name }} as well as to demonstrate its classification to the State of the Art device ({{sota\_product\_name}})

The literature search will identify data not held by the manufacturer that are needed for the

clinical evaluation. The literature search will identify potential sources of clinical data for establishing:

* Clinical data relevant to the devices under evaluation and to the similar device(s)
* Current knowledge/ the state of the art.

## Device Description

{{ device\_description }}

## Target Device

The {{ device\_name }}device or system is the intended focus of this literature search and review.

## Intended Use

{{ intended\_use }}

## Indication of Use

{{ indication\_of\_use }}

## Similar Devices

{% for device in comparator\_devices %}

1. {{ device }}

{% endfor %}

## State of the Art

{{ sota\_description }}

## Safety Claims

{{ safety\_claims }}

## Performance Claims

{{ performance\_claims }}

{%if other\_info %}

## Other Info

{{ other\_info }}

{% endif %}

# Literature Search Methodology and Selection Criteria

This review of published clinical data further provides support for the clinical evaluation of the {{ device\_name }}.

## Scope

The scope of the literature search includes a query of select adverse event report databases, as well as scientific databases within the timeframe spanning from {{start\_lit\_date\_of\_search}} to {{ lit\_date\_of\_search }}. This period of time is felt to provide sufficient clinical experience with these devices from both a safety and performance perspective. Performance assessments include reports designed to {{ scope }}

## Date of Search

{{ lit\_date\_of\_search }}

## Name of Person(s) Undertaking Search

{{preparer}}

## Period Covered by Search

Starting From {{start\_lit\_date\_of\_search}} to {{ lit\_date\_of\_search }}.

## Scientific Databases

{%p for database in lit\_search\_databases %}

### {{ database.name }}

{{ database.description }}

{%p endfor %}

## Adverse Event Databases

{%p for database in ae\_databases %}

* {{ database.name}}

{%p endfor %}

## Database Search Details

Because different databases offer different limiting options and search fields, different approaches were taken appropriate to the database. All unique circumstances are identified in the report. All searches are performed through online databases.

# Systematic Literature Review

This Systematic Literature Review searches specifically for evidence of safety and efficacy of the target device. Search terms were adapted for use in the relevant database and were guided by the suggested keywords and inclusion/exclusion criteria detailed in the protocol. In addition to single term word searches, search terms involving multiple words were evaluated using Boolean parameters such as parentheses or quotation marks.

Suggested search terms have been collected including the target and similar devices described above.

State of the Art (SOTA) search terms were included as part of the search parameters to identify devices/systems also used in similar treatments or conditions.

## Focused Search and Review Plan

The resulting number of citations (abstracts) from each database search outlined (less duplicates) is captured and reviewed electronically to determine if further review is warranted. Those articles that satisfy inclusion/exclusion criteria are “retained” for a secondary review. Each “retained” article is subsequently reviewed to assess relevancy and inclusion within the final review.

Search term relevancy criteria is established to promote the most efficient review of appropriate citations for the devices. Searches terms results with citation results in excess of 200 are considered too broad and are excluded from the review process. In contrast, search terms without citation results (i.e., zero) are considered too narrow. All search term citation results regardless of results are tabulated in the final result tables.

The search results (abstracts identified) are reviewed in detail and assessed for relevancy to target device OR target device and similar devices (modify based on the scope of the project) for clinical safety and efficacy. Similar based studies (i.e., no unique safety or efficacy results) are considered duplicate information and only referenced once. The analysis of each study reviewed is conducted based on the criteria below.

In some instances, information obtained from these reviews that fall outside the inclusion/exclusion criteria may be included within the scope of this report if the information obtained provides new or unanticipated safety or performance signals of interest within current device indications or uses.

## Handling of Duplicate Literature References

Duplicate citations found in the search results of the databases are screened and removed prior to any review. The duplicate counts are captured in the final review and summarized in search-term tables.

### How Duplicates Are Identified?

A duplicate citation is identified through electronic signatures based on a match in one of the following fields of information across the databases.

* PubMed Unique Identifier
* PubMed Central Unique Identifier
* Cochrane Library Unique Identifier
* Embase Library Unique Identifier
* Academic Citation (in APA format)

## Selection Criteria

The following criteria are used to assess the suitability of material (articles, reports, etc.) for inclusion/exclusion in the analysis stage of this report.

### Inclusion Criteria

* Citation addresses performance, risks, and/or safety of the {{ device\_name }} or similar device(s).
* Products are used in ways like indications for use of the {{ device\_name }} products.
* Any articles considered relevant to the state of the art/current knowledge identified during this search will be included in the state-of-the-art section.

### Exclusion Criteria

{%p for item in exclusion\_reasons %}

* {{ item }}

{%p endfor %}

Clinical literature were also excluded in situations where multiple papers appear to report on the same study. Consideration was given to the extent of duplication and reported safety or performance outcomes, prior to the excluding of any literature.

## Outputs

All literature citations selected for inclusion are listed as References.

## Data Selection Process

Figure 1 visually outlines the process used in assessing citations retrieved from queries of online databases for suitability for inclusion in the clinical evaluation report.

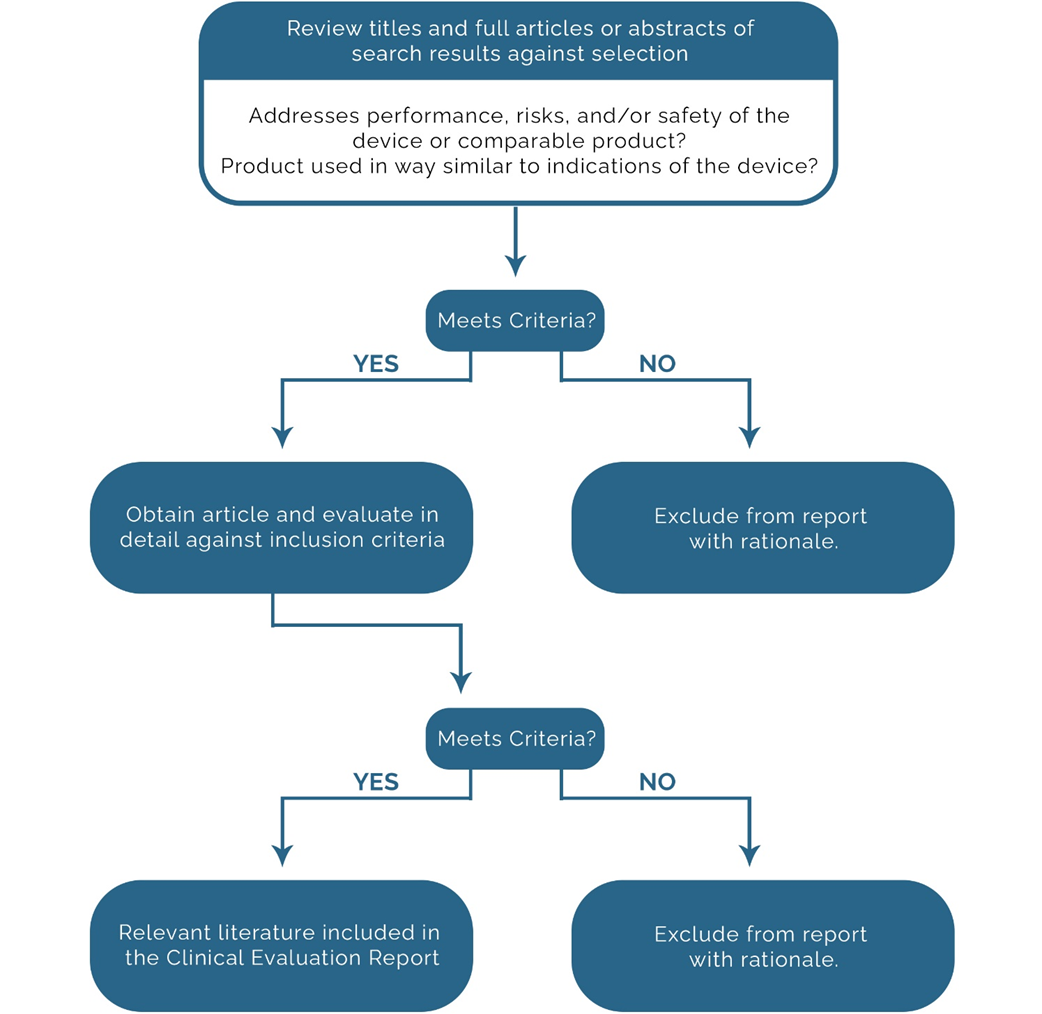


Figure 1 Citation Assessment Flowchart

## Prisma Flow Chart

Records identified through

database searching

N = {{ review.prisma.all\_reviews }}

Additional Records Identified

N = {{ review.prisma.sota\_extra\_reviews }}

Records after duplicates removed

N = {{ review.prisma.reviews\_no\_dupes }}

Records screened

N = {{ review.prisma.total\_screened }}

Full-Text Articles Assessed for

eligibility

N = {{ review.prisma.reviews\_retained }}

Full-Text Articles Excluded

N = {{ review.prisma.ft\_reviews\_excluded }}

Studies included in qualitative

Synthesis (meta-analysis)

N = {{ review.prisma.ft\_included\_synth }}

Records Excluded

N = {{ review.prisma.reviews\_excluded }}

Figure 2 Prisma Flow Chart

| Reason | Count |
| --- | --- |
| Duplicates | {{review.prisma.duplicates\_reviews}} |
| {%tr for row in review.prisma.exclusion\_reason\_counts.rows %} |  |
| {{ row[‘Reason’] }} | {{ row[‘Count’] }} |
| {%tr endfor %} |  |
| Full-Text Articles Excluded | {{ review.prisma.ft\_reviews\_excluded }} |
| Total | {{review.prisma.total\_reviews }} |

Table 1 Reasons of Excluded Articles

# Scientific Databases - SoTA

{%p for database in review.appendix\_a1 %}

## {{ database.protocol.name }}

{{ database.protocol.url }}

### Search Strategy

The following filters are to be applied in the search:

* Publication dates: Starting From {{start\_lit\_date\_of\_search}} to {{ lit\_date\_of\_search }}.

{%p for item in database.protocol.search\_strategy %}

* {{ item }}

{%p endfor %}

### Search Results Summary

{% if database.results\_summary\_table.rows %}

| ID | Search Term | Publications Yielded | Performed Date | Duplicate Results | Included | Excluded | Unclassified | Not imported  (Out of Range) |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | {%tr for row in database.results\_summary\_table.rows %} |  |  |  |  |  |  |  |
| {{ row[‘id’] }} | {{ row[‘Search Term’]}} | {{ row[‘Publications Yielded’] }} | {{ row[‘Search Performed Date’] }} | {{ row[‘Duplicate Results’ ] }} | {{ row[‘Included’] }} | {{ row[‘Excluded’] }} | {{ row[‘Unclassified’] }} | {{ row[‘Not Imported’] }} |
|  | {%tr endfor %} |  |  |  |  |  |  |  |

Table {{ 1 + database.table\_index }} Search Results Summary – {{ database.protocol.name }}

**{% else %}**

No results to display for this search/database.

**{% endif %}**

**{%p endfor %}**

{%p if report\_type == “CONDENSED\_REPORT” %}

Further details on all of the reviewed articles are provided in Appendix A.

{%p endif %}

# Scientific Databases – Device Safety Performance

{%p for database in review.appendix\_a2 %}

## {{ database.protocol.name }}

{{ database.protocol.url }}

### Search Strategy

The following filters are to be applied in the search:

* Publication dates: Starting From {{start\_lit\_date\_of\_search}} to {{ lit\_date\_of\_search }}.

{%p for item in database.protocol.search\_strategy %}

* {{ item }}

{%p endfor %}

### Search Results Summary

{% if database.results\_summary\_table.rows %}

| ID | Search Term | Publications Yielded | Duplicate Results | Included | Excluded | Unclassified | Not imported  (Out of Range) |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | {%tr for row in database.results\_summary\_table.rows %} |  |  |  |  |  |  |
| {{ row[‘id’] }} | {{ row[‘Search Term’]}} | {{ row[‘Publications Yielded’] }} | {{ row[‘Duplicate Results’ ] }} | {{ row[‘Included’] }} | {{ row[‘Excluded’] }} | {{ row[‘Unclassified’] }} | {{ row[‘Not Imported’] }} |
|  | {%tr endfor %} |  |  |  |  |  |  |

Table {{ 1 + review.appendix\_a1\_table\_count + database.table\_index }} Search Results Summary – {{ database.protocol.name }}

**{% else %}**

No results to display for this search/database.

**{% endif %}**

**{%p endfor %}**

{%p if report\_type == “CONDENSED\_REPORT” %}

Further details on all of the reviewed articles are provided in Appendix A.

{%p endif %}

# Search Results

{%p if report\_type != “CONDENSED\_REPORT” %}

## Search Results - Retained and Included

The following table outlines the articles selected based on predefined inclusion/ exclusion criteria to assist in the final clinical evaluation. The articles selected focused on the medical device or similar device, material composition, and function in order to assess risk and adverse events associated with the intended product use. Articles were also rated and appraised on the data collected and the quality of the data.

**Legend**

* S = State (Retained, Excluded, Duplicate)
* R = Retained
* I = Included
* Y = Yes
* N = No
* E = Excluded
* D = Duplicate

{%p for database in review.appendix\_b\_retinc %}

### {{ database.protocol.name }}

{% if database.results\_table.rows %}

| ID | {{ database.results\_table[‘headers’][‘Term’] }} | Citation | State | Included | Justification |
| --- | --- | --- | --- | --- | --- |
|  |  | {%tr for row in database.results\_table.rows %} |  |  |  |
| {{ row[‘Id’] }} | {{ row[‘Term’] }} | {{ row[‘Citation’] }} | {{ row[‘S’] }} | {{ row[‘I’] }} | {{ row[‘Justification’] }} |
|  |  | {%tr endfor %} |  |  |  |

Table {{ 1 + review.appendix\_a1\_table\_count + review.appendix\_a2\_table\_count + database.table\_index }} Search Results - {{ database.protocol.name }} Citations Retained and Included

{% else %}

No results found for database.

{% endif %}

{%p endfor %}

## Search Results - All

The following table outlines the articles selected based on predefined inclusion/ exclusion criteria to assist in the final clinical evaluation. The articles selected focused on the medical device or similar device, material composition, and function in order to assess risk and adverse events associated with the intended product use. Articles were also rated and appraised on the data collected and the quality of the data.

**Legend**

* S = State (Retained, Excluded, Duplicate)
* R = Retained
* I = Included
* Y = Yes
* N = No
* E = Excluded
* D = Duplicate

{%p for database in review.appendix\_b\_all %}

### {{ database.protocol.name }}

{% if database.results\_table.rows %}

| ID | {{ database.results\_table[‘headers’][‘Term’] }} | Citation | State | Included | Justification |
| --- | --- | --- | --- | --- | --- |
|  |  | {%tr for row in database.results\_table.rows %} |  |  |  |
| {{ row[‘Id’] }} | {{ row[‘Term’] }} | {{ row[‘Citation’] }} | {{ row[‘S’] }} | {{ row[‘I’] }} | {{ row[‘Justification’] }} |
|  |  | {%tr endfor %} |  |  |  |

Table {{ 1 + review.appendix\_a1\_table\_count + review.appendix\_a2\_table\_count + review.appendix\_b\_retinc\_table\_count + database.table\_index }} Search Results - {{ database.protocol.name }} All Citations

{% else %}

No results found for database.

{% endif %}

{%p endfor %}

{%p else %}

Please check Appendix A for a list of Search Results.

{%p endif %}

# Clinical Literature Appraisal

The following section outlines the criteria for suitability and data contribution used to appraise the literature to be included in this clinical evaluation (adapted from MEDDEV 2.7/1, Rev.4).

|  |  |
| --- | --- |
| Criteria | Description |
| CK0 | No SoTA information. |
| CK1 | Establishment of current knowledge/ the state of the art on the medical condition |
| CK2 | Establishment of current knowledge/ the state of the art on alternative therapies/treatments |
| CK3 | Determination and justification of criteria for the evaluation of the risk/benefit relationship |
| CK4 | Determination and justification of criteria for the evaluation of the acceptability of undesirable side-effects |
| CK5 | Determination of equivalence |
| CK6 | Justification of the validity of surrogate endpoints |

Table {{ 2 + review.dynamique\_tables\_count }} Criteria for State of the Art

|  |  |  |
| --- | --- | --- |
| Contribution Criteria | Description | Grading System |
| Appropriate device | Were the data generated from the device in question? | D1 Actual Device  D2 Comparable Device  D3 Other Device |
| Appropriate device application | Was the device used for the same intended use (e.g., methods of deployment, application, etc.)? | A1 Same use  A2 Minor deviation  A3 Major deviation |
| Appropriate patient group | Were the data generated from a patient group that is representative of the intended treatment population (e.g., age, sex, etc.) and clinical condition (i.e., disease, including state and severity)? | P1 Applicable  P2 Limited  P3 Different |
| Acceptable report/data collation | Do the reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment? | R1 High quality  R2 Minor deficiencies  R3 Insufficient information |

Table {{ 3 + review.dynamique\_tables\_count }} Criteria for Data Suitability

|  |  |  |
| --- | --- | --- |
| Accountability Level | Description | Grading |
| Data source type | Was the design of the study appropriate? | T1 Yes  T2 No |
| Outcome measures | Do the outcome measures reported reflect the intended performance of the device? | O1 Yes  O2 No |
| Appropriate follow-up | Is the duration of follow-up long enough to assess treatment effects and identify complications? | F1 Yes  F2 No |
| Statistical significance | Has a statistical analysis of the data been provided and is it appropriate? | S1 Yes  S2 No |
| Clinical significance | Was the magnitude of the treatment effect observed clinically significant? | C1 Yes  C2 No |

Table {{ 4 + review.dynamique\_tables\_count }} Criteria for Data Contribution

|  |  |  |
| --- | --- | --- |
| Rank | Types of clinical data and evidence | Considerations / comments |
| 1 | Results of high quality 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 | Is there sufficient evidence of the quality of the data collected by the registry? 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 | 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. |
| 5 | Equivalence data (reliable / quantifiable) | Equivalence must meet MDR criteria. It is normally expected that manufacturers should gather data on their own devices in the post-market phase, therefore reliance on equivalence should be duly justified, and linked to appropriate PMCF or proactive PMS. |
| 6 | Evaluation of state of the art, including evaluation of clinical data from similar devices as defined in Section 1.2 of 'MDCG 2020-6' | This is not considered clinical data under the MDR, but for well-established technologies only can be considered supportive of confirmation of conformity to the relevant GSPRs. Data from similar devices may be also important to establish whether the device under evaluation and similar devices belong to the group of devices considered as “well established technologies” (WET). See section 1.2 in 'MDCG 2020-6' for the criteria for WET. Data from similar devices may be used, for example, to demonstrate ubiquity of design, lack of novelty, known safety and performance profile of a generic group of devices, etc. |
| 7 | Complaints and vigilance data; curated data | data; curated data This falls within the definition of clinical data under MDR Article 2(48), but is not generally considered a high quality source of data due to limitations in reporting. It may be useful for identifying safety trends or performance issues. High volume data collected within a robust quality system may provide supportive evidence of device safety. |
| 8 | Proactive PMS data, such as that derived from surveys | This falls within the definition of clinical data under MDR Article 2(48), but is not generally considered a high quality source of data due limitations associated with sources of bias and quality of data collection. It may be useful for Page 22 of 22 identifying safety concerns or performance issues. |
| 9 | Individual case reports on the subject device | This falls within the definition of clinical data under MDR Article 2(48), but is not considered a high quality source of data due to limitations in generalising findings to a wider patient population, reporting bias, etc. It may provide supportive or illustrative information with respect to specific claims. |
| 10 | Compliance to non-clinical elements of common specifications considered relevant to device safety and performance | Common specifications which address clinical investigation or data requirements directly would rank higher in this hierarchy. Common specifications may address clinically relevant endpoints through non-clinical evidence such as mechanical testing for strength and endurance, biological safety, usability, etc. |
| 11 | Simulated use / animal / cadaveric testing involving healthcare professionals or other end users | This is not clinical data, but may be considered evidence of confirmation of conformity to relevant GSPRs, particularly in terms of usability, such as for accessories or instruments. |
| 12 | Pre-clinical and bench testing / compliance to standards | Pre-clinical and bench testing may address clinically relevant endpoints through non-clinical evidence such as mechanical testing for strength and endurance, biological safety, usability, etc |

Table {{ 5 + review.dynamique\_tables\_count }} MDCG Ranking

## Criteria For State of the Art

{% if review.appendix\_c.sota\_table.rows %}

| ID | Citation | {%tc for header in review.appendix\_c.sota\_table.rows[“headers”]%} | {{header}} | {%tc endfor %} |
| --- | --- | --- | --- | --- |
|  |  |  | {%tr for content\_row in review.appendix\_c.sota\_table.rows.content%} |  |
| {{content\_row.id}} | {{content\_row.citation}} | {%tc for item in content\_row.cols %} | {{ item }} | {%tc endfor %} |
|  |  |  | {%tr endfor %} |  |

Table {{ review.appendix\_c.sota\_table.table\_index + 5 + review.dynamique\_tables\_count }} Classifications for State of the Art

**{% else %}**

No SoTA results to display.

**{% endif %}**

## Criteria for Data Suitability - Retained and Included Citations

The following tables summarize the suitability of the clinical literature on the criteria described above.

The articles selected in this table were both Retained for evaluation AND Included for the full review.

{% if review.appendix\_c.suitability\_retinc\_table.rows %}

| ID | Citation | {%tc for header in review.appendix\_c.suitability\_retinc\_table.rows[“headers”]%} | {{header}} | {%tc endfor %} |
| --- | --- | --- | --- | --- |
|  |  |  | {%tr for content\_row in review.appendix\_c.suitability\_retinc\_table.rows.content  %} |  |
| {{content\_row.id}} | {{content\_row.citation}} | {%tc for item in content\_row.cols %} | {{ item }} | {%tc endfor %} |
|  |  |  | {%tr endfor %} |  |

Table {{ review.appendix\_c.suitability\_retinc\_table.table\_index + 5 + review.dynamique\_tables\_count }} Criteria for Suitability - Retained and Included Citations

**{% else %}**

No retained and included citations to display.

**{% endif %}**

## Criteria for Data Suitability Level - All Retained Citations

The following table summarizes the suitability of the clinical literature on the criteria described above.

{% if review.appendix\_c.suitability\_all\_table.rows %}

| ID | Citation | {%tc for header in review.appendix\_c.suitability\_all\_table.rows[“headers”]%} | {{header}} | {%tc endfor %} |
| --- | --- | --- | --- | --- |
|  |  |  | {%tr for content\_row in review.appendix\_c.suitability\_all\_table.rows.content  %} |  |
| {{content\_row.id}} | {{content\_row.citation}} | {%tc for item in content\_row.cols %} | {{ item }} | {%tc endfor %} |
|  |  |  | {%tr endfor %} |  |

Table {{ review.appendix\_c.suitability\_all\_table.table\_index + 5 + review.dynamique\_tables\_count }} Criteria for Data Suitability Level - All Retained Citations

**{% else %}**

No Device Related Citations to display.

**{% endif %}**

## Criteria for Data Contribution - Retained and Included Citations

The following table summarizes the suitability of the clinical literature on the criteria described above.

The citations selected in this table were both Retained for evaluation AND Included for the full review.

{% if review.appendix\_c.data\_contribution\_retinc\_table.rows %}

| ID | Citation | {%tc for header in review.appendix\_c.data\_contribution\_retinc\_table.rows[“headers”]%} | {{header}} | {%tc endfor %} |
| --- | --- | --- | --- | --- |
|  |  |  | {%tr for content in review.appendix\_c.data\_contribution\_retinc\_table.rows.content %} |  |
| {{content.id}} | {{content.citation}} | {%tc for item in content.cols %} | {{ item }} | {%tc endfor %} |
|  |  |  | {%tr endfor %} |  |

Table {{ review.appendix\_c.data\_contribution\_retinc\_table.table\_index + 5 + review.dynamique\_tables\_count }} Criteria for Data Contribution - Retained and Included Citations

**{% else %}**

No Device Related and Included Citations to display.

**{% endif %}**

## Data Extraction Results – Detailed

The following section contains expanded detail on extracted data of all Retained and Included citations.

{% if review.appendix\_c.extraction\_detail\_table.rows %}

| S. No | Bibliography | Study design/Objective | Treatment Modality/ Indication/Comparator (I/O) | Study Result/Conclusion (O) |
| --- | --- | --- | --- | --- |
|  | {%tr for row in review.appendix\_c.extraction\_detail\_table.rows %} |  |  |  |
| {{ row[‘id’] }} | {{ row[‘Citation’] }}  **Data Suitability**  {{ row[‘Grade 01’] }}  **Data Contribution**  {{ row[‘Grade 02’] }}  **MDCG Ranking**  {{ row[‘Rank’] }} | {%p for field in row[“extra\_fields”] %}  {%p if field.category == “ST” %}  **{{field.name}}**  {{field.value}}  {%p endif %}  {%p endfor %} | {%p for field in row[“extra\_fields”] %}  {%p if field.category == “T” %}  **{{field.name}}**  {{field.value}}  {%p endif %}  {%p endfor %} | {%p for field in row[“extra\_fields”] %}  {%p if field.category == “SR” %}  **{{field.name}}**  {{field.value}}  {%p endif %}  {%p endfor %} |
|  | {%tr endfor %} |  |  |  |

Table {{ review.appendix\_c.extraction\_detail\_table.table\_index + 5 + review.dynamique\_tables\_count }} Data Extraction Results – Detailed

**{% else %}**

No Device Related Retained and Included Citations to display.

**{% endif %}**

## Retained Citations Not Appraised (Device)

### {% if review.appendix\_c.excluded\_table.rows %}

| Citation | Justification |
| --- | --- |
| {%tr for row in review.appendix\_c.excluded\_table.rows %} |  |
| {{ row[‘Citation’] }} | {{ row[‘Justification’] }} |
| {%tr endfor %} |  |

### Table {{ review.appendix\_c.excluded\_table.table\_index + 5 + review.dynamique\_tables\_count }} Retained Citations Not Appraised (Device)

### {% else %}

All retained citations were appraised.

### {% endif %}

# References for Retained and Included Citations

{% if review.appendix\_d.all\_retained\_table.rows %}

|  |  |
| --- | --- |
| ID | Citation |
|  | {%tr for row in review.appendix\_d.all\_retained\_table.rows %} |
| {{ row[‘Index’] }} | {{ row[‘Citation’] }} |
|  | {%tr endfor %} |

Table {{ 1 + review.dynamique\_tables\_count\_two }} References for Retained and Included Citations

{% else %} No retained and included citations to display.{% endif %}

# Adverse Event Databases / Recalls

## US FDA MAUDE (USA)

<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm>

{{ review.appendix\_e.maude\_tables.maude\_aes.protocol.url }}

### Date Range

Starting from {{ ae\_start\_date\_of\_search }} to {{ae\_date\_of\_search}}.

### Search Strategy

The safety database and recall search will be based on the 3-letter FDA product code and represents all similar medical devices classified within the device type.

If the number of safety event results exceeds the download limitation of 500 for the range of years searched, a year-by-year download of the events will be captured and reviewed to assess relevance or new events related to the current medical device class.

### Search Terms

{%p for term in review.appendix\_e.maude\_tables.maude\_aes.protocol.terms %}

* {{ term }}

{%p endfor %}

### Adverse Event Summary

Devices and other related devices are associated with the same code (listed above). A summary of the associated deaths, injuries, malfunctions, or other reported incidents is expressed in the table below for the specified date range. (Table {{ 1 + review.dynamique\_tables\_count\_three }} )

Summary of MAUDE Reported Events for date range. If more than 500 events are reported, the searches will be conducted by year.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Date Range | Death | Injury | Malfunction | Other/NA | Excluded |
| {{ review.appendix\_e.maude\_tables.maude\_aes.single\_row\_summary[‘Date End’] }} - {{ review.appendix\_e.maude\_tables.maude\_aes.single\_row\_summary[‘Date of Search’] }} | {{ review.appendix\_e.maude\_tables.maude\_aes.single\_row\_summary[‘Death’] }} | {{ review.appendix\_e.maude\_tables.maude\_aes.single\_row\_summary[‘Injury’] }} | {{ review.appendix\_e.maude\_tables.maude\_aes.single\_row\_summary[‘Malfunction’] }} | {{ review.appendix\_e.maude\_tables.maude\_aes.single\_row\_summary[‘Other/NA’] }} | {{ review.appendix\_e.maude\_tables.maude\_aes.single\_row\_summary[‘Excluded’] }} |

Table {{ 1 + review.dynamique\_tables\_count\_three }} Summary of MAUDE Reported Events

Death: {{ review.appendix\_e.maude\_tables.maude\_aes.single\_row\_summary[‘Death’] }} deaths were reported. None of the deaths were associated with the target device or system.

Injuries: {{ review.appendix\_e.maude\_tables.maude\_aes.single\_row\_summary[‘Injury’] }} injuries were reported. None of the injuries were associated with the target device or system

Malfunctions: {{ review.appendix\_e.maude\_tables.maude\_aes.single\_row\_summary[‘Malfunction’] }} malfunctions were reported. None of the malfunctions were associated with the target device or system.

A more detailed review of these events was conducted based on the target device or system ({{ device\_name }} devices) reviewed and the associated device or system ({{ comparator\_devices }}) for each of the past years reviewed included in the search range starting from {{ ae\_start\_date\_of\_search }} to {{ae\_date\_of\_search}}.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Year | Death | Injury | Malfunction | Other/NA |
| {%tr for row in review.appendix\_e.maude\_tables.maude\_aes.maude\_by\_year.rows %} |  |  |  |  |
| {{ row[‘Year’] }} | {{ row[‘Deaths’] }} | {{ row[‘Injuries’] }} | {{ row[‘Malfunctions’] }} | {{ row[‘Other/NA’] }} |
| {%tr endfor %} |  |  |  |  |

Table {{ review.appendix\_e.maude\_tables.maude\_aes.maude\_included\_events.table\_index + 1 + review.dynamique\_tables\_count\_three }} Summary of MAUDE Reported Events by Year

{{ review.appendix\_e.maude\_tables.maude\_aes.summary }}

{% if review.appendix\_e.maude\_tables.maude\_aes.maude\_included\_events.rows %}

The following events were reviewed and marked as ‘Included’ and relevant to the {{ device\_name }}.

|  |  |  |  |
| --- | --- | --- | --- |
| Manufacturer | Term | Event Type | Description |
| {%tr for row in review.appendix\_e.maude\_tables.maude\_aes.maude\_included\_events.rows %} |  |  |  |
| {{ row[‘Manufacturer’] }} | {{ row[‘Term’] }} | {{ row[‘Event Type’] }} | {{ row[‘Description’] }} |
| {%tr endfor %} |  |  |  |

Table {{ review.appendix\_e.maude\_tables.maude\_aes.maude\_included\_events.table\_index + 2 + review.dynamique\_tables\_count\_three }} Included (Relevant) MAUDE Reported Events

{% endif %}

## Maude Recall Event Summary

### Date Range

Starting from {{ ae\_start\_date\_of\_search }} to {{ae\_date\_of\_search}}.

### Search Strategy

The safety database and recall search will be based on the 3-letter FDA product code and represents all similar medical devices classified within the device type.

The product RECALL database is also organized by product codes, and other related devices are associated with this code. The following recall classifications are defined as:

Class 1 - a situation in which there is a reasonable probability that the use of, or exposure to, a violative product will cause serious adverse health consequences or death.

Class 2 - a situation in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.

Class 3 - a situation in which use of, or exposure to, a violative product is not likely to cause adverse health consequences.

### Search Terms

{%p for term in review.appendix\_e.maude\_tables.maude\_recalls.protocol.terms %}

* {{ term }}

{%p endfor %}

### Recalls Results

{% if review.appendix\_e.maude\_tables.maude\_recalls.by\_year.rows %}

|  |  |  |  |
| --- | --- | --- | --- |
| Year | Class 1 | Class 2 | Class 3 |
| {%tr for row in review.appendix\_e.maude\_tables.maude\_recalls.by\_year.rows %} |  |  |  |
| {{ row[‘Year’] }} | {{ row[‘Recall Class 1’] }} | {{ row[‘Recall Class 2’] }} | {{ row[‘Recall Class 3’] }} |
| {%tr endfor %} |  |  |  |

Table {{ review.appendix\_e.maude\_tables.maude\_recalls.by\_year.table\_index + 2 + review.dynamique\_tables\_count\_three }} Summary of MAUDE Recalls Reported Events by Year

{{ review.appendix\_e.maude\_tables.maude\_aes.recalls\_summary }}

{% else %}

No recall data by year to display.

{% endif %}

{% if review.appendix\_e.maude\_tables.maude\_recalls.included.rows %}

The following recalls were marked as ‘Included’ or relevant to {{ device\_name }}

|  |  |  |  |
| --- | --- | --- | --- |
| Term | Date Posted | Recall Class | Recall Reason |
| {%tr for row in review.appendix\_e.maude\_tables.maude\_recalls.included.rows %} |  |  |  |
| {{ row[‘Term’] }} | {{ row[‘Event Date’] }} | {{ row[‘Recall Class’] }} | {{ row[‘Recall Reason’] }} |
| {%tr endfor %} |  |  |  |

Table {{ review.appendix\_e.maude\_tables.maude\_recalls.included.table\_index + 2 + review.dynamique\_tables\_count\_three }} Summary of Included MAUDE Recalls

{% else %}

{{ device\_name }} products were not associated with any recalls.

{% endif %}

{%if review.appendix\_e. faers\_tables %}

## US FDA Adverse Event Reporting System (FAERS) USA

<http://www.fdable.com/basic_query/aers>

### Date Range

[xx years (20xx – 20xx) Prior to the Date of Search.

### Search Strategy

The FAERS safety database search is based on the FDA manufacturer**.**

### Adverse Event Summary

FAERS provides safety information related to medications. The [[product name used to [[xx The FAERS Database (US) was reviewed for events related to {{device\_name}}. Since [[20xx there were [[xx events reported [[(all non-serious).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Date Range | Death | Injury | Malfunction | Other/NA | Excluded |
| [[20xx-20xx |  |  |  |  |  |

Table {{ review.appendix\_e.maude\_tables.maude\_recalls.included.table\_index + 3 + review.dynamique\_tables\_count\_three }} Summary of FAERS Reported Events

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Date Range | Death | Injury | Malfunction | Other/NA | Excluded |
| [[2021-2022 |  |  |  |  |  |
| 2020-2021 |  |  |  |  |  |
| 2019-2020 |  |  |  |  |  |
| 2018-2019 |  |  |  |  |  |
| 2017-2018 |  |  |  |  |  |
| 2016-2017 |  |  |  |  |  |
| 2015-2016 |  |  |  |  |  |
| 2014-2015 |  |  |  |  |  |

Table {{ review.appendix\_e.maude\_tables.maude\_recalls.included.table\_index + 4 + review.dynamique\_tables\_count\_three }} Summary of FAERS Reported Events by year

Death: [[xx deaths were reported using the device/ system.

Injuries: [[xx injuries were reported on the use of a device or system. None of the injuries were serious or related to device or system

Malfunctions: [[xx device malfunctions were reported. The following events could be associated with the device that include product leakage and incorrect dose administration

| Case ID | Suspect Product Names | Suspect Product Active Ingredients | Reason for Use | Reactions | Serious | Outcomes | Sex | Event Date | Latest FDA Received Date | Case Priority | Patient Age | Patient Weight | Sender | Reporter Type | Report Source | Concomitant Product Names | Latest Manufacturer Received Date | Initial FDA Received Date | Country where Event occurred | Reported to Manufacturer? | Manufacturer Control Number |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |

Table {{ review.appendix\_e.maude\_tables.maude\_recalls.included.table\_index + 5 + review.dynamique\_tables\_count\_three }} Summary of FAERS Reported Events

{% endif %}

{%p for database in review.appendix\_e.ae\_dbs %}

## {{ database.protocol.name }}

{{ database.protocol.url }}

### Date Range

Starting from {{ ae\_start\_date\_of\_search }} to {{ae\_date\_of\_search}}.

Searches included Device Safety Information reports in all medical specialties.

### Search Strategy

{%p for strategy in database.protocol.search\_strategy %}

{{ strategy }}

{%p endfor %}

### Search Terms

### {%p for term in database.protocol.terms %}

* {{ term }}

{%p endfor %}

### Search Results

{% if database.included.rows %}

The following terms yielded Adverse Events, Product Alerts, or Field Alerts.

| Term | Date | Type | Severity |
| --- | --- | --- | --- |
| {%tr for row in database.included.rows %} |  |  |  |
| {{ row[‘Term’] }} | {{ row[‘Date’] }} | {{ row[‘Type’] }} | {{ row[‘Severity’] }} |
| {%tr endfor %} |  |  |  |

Table {{ database.included.table\_index + review.dynamique\_tables\_count\_four }} Summary of UK Adverse Events, Product Alerts, or Field Alerts

{% else %}

No adverse events, product alerts, or field reports related to {{ device\_name }} or comparative state-of-the-art devices were identified from these searches.

{% endif %}

{%p endfor %}

## {%p for database in review.appendix\_e.recall\_dbs %}

## {{ database.protocol.name }}

{{ database.protocol.url }}

### Date Range

Starting from {{ ae\_start\_date\_of\_search }} to {{ae\_date\_of\_search}}.

Searches included Device Safety Information reports in all medical specialties.

### Search Strategy

{{ database.protocol.search\_strategy }}

### Search Terms

### {%p for term in database.protocol.terms %}

* {{ term }}

{%p endfor %}

### Search Results

{% if database.included.rows %}

The following terms yielded Adverse Events, Product Alerts, or Field Alerts.

| Term | Number | Description |
| --- | --- | --- |
| {%tr for row in database.included.rows %} |  |  |
| {{ row[‘Term’] }} | {{ row[‘Number’] }} | {{ row[‘Description’] }} |
| {%tr endfor %} |  |  |

Table {{ database.included.table\_index + review.dynamique\_tables\_count\_five }} Summary of UK Adverse Events, Product Alerts, or Field Alerts

{% else %}

No adverse events, product alerts, or field reports related to {{ device\_name }} or comparative state-of-the-art devices were identified from these searches.

{% endif %}

Summary {{ database.summary }}

{%p endfor %}

# Technical Sheets

All Technical Sheets will be attached via Zip file and included with this submission.

# Search Verification

All search results have been exported from each relevant Database and included via Zip file for verification purposes.

An extensive verification process is conducted to ensure the validity of all search results. Results are validated on an individual search basis and are recorded in such a way that any other party could easily duplicate results.

All searches are conducted on 3rd party databases that are subject to change in their literature availability. We are not responsible for future changes/modifications to a public database that could affect previously conducted searches.

|  |  |  |  |
| --- | --- | --- | --- |
| Scientific Databases | Searches Verified  Yes / No | Method of Verification | Backup Files |
| {%tr for database in lit\_search\_databases %} |  |  |  |
| {{ database[‘name’] }} | Yes | Export Files and Exact Search URL | Full Results Attached (Zip File) |
| {%tr endfor %} |  |  |  |

Table {{ 1 + review.dynamique\_tables\_count\_six }} Search Verification

# Acknowledgment and Agreement

SEARCH PERFORMED AND WRITTEN

By:

Name: {{preparer}}

Title: Medical Writer (CV Attached)

Date:

CITE MEDICAL, LLC

By:

Name: {{preparer}}



Date:

{{ company\_name }}

By: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Name:

Title:

Date: