WHITEPAPER

Boost the Success of Medical Device Development With Systematic Literature Reviews

BIOMEDICAL LITERATURE SUPPORTS MEDICAL DEVICE DEVELOPMENT

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ELSEVIER

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MEDICAL DEVICE DEVELOPMENT — A CHALLENGING FIELD

Medical device manufacturers face numerous challenges during device development and postmarket surveillance. Their required expertise goes beyond engineering and medicine, and includes medical regulation, insurance law and research informatics. Whether engaged in developing and marketing new medical devices or repurposing and re-marketing existing ones, a number of critical hurdles must be overcome. Before the ideation and creation of a novel prototype device — or the establishment of a new purpose for an existing one — medical device manufacturers must be confident that the device will serve a real need in the market. They must also establish that the device has unique value and will be effective and safe. Such concerns are similar for all device manufacturers, whether they are designing a simple tongue depressor or invasive implant.

Beyond that, the medical device story becomes increasingly complicated. No medical device will ever succeed without a solid reimbursement strategy that requires knowledge of the intricacies of health insurance. Furthermore, companies must go through the complex process of regulatory approval, which includes performing the appropriate clinical trials or demonstrating safety through systematic review of the scientific literature. Even after a device has been approved and released to market, the manufacturer's job is not over. Comprehensive post-market safety monitoring is mandatory — missing a mention of an adverse event or not having an auditable search strategy can have serious consequences for the manufacturer.

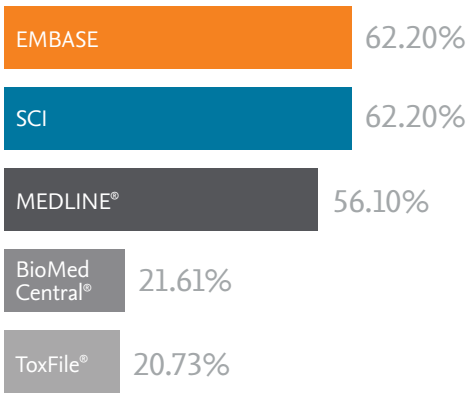


Figure 1. The top five research informatics solutions for medical device literature. In this case study, a search was done for all publications known to mention a specific medical device. The percentage retrieved by each of the top five research informatics solutions is shown (Ref. 1). SCI – Science Citation Index.

BIOMEDICAL LITERATURE — AN ESSENTIAL RESOURCE

Modern regulatory requirements have made biomedical literature research an essential part of the medical device life cycle. A solid literature research strategy strengthens every stage of this process, from concept and design through clinical trials to release and reimbursement. In addition, medical device companies are required to screen the literature to comply with regulatory authorities during the approval process and for post-market surveillance.

Literature reviews are not just a wise investment — they are crucial to the success of a medical device.

THE ROLE OF LITERATURE

Systematic reviews of the biomedical literature support multiple aspects of the development process:

1. Identifying user needs
2. Determining the market potential of the device
3. Gaining competitive knowledge
4. Demonstrating value, effectiveness and safety
5. Calculating cost-effectiveness
6. Calculating reimbursement potential
7. Preparing marketing strategies

Systematic reviews also help manufacturers meet strict regulatory requirements:

1. Designing an effective clinical trial
2. Submission of complete regulatory documents
3. Establishing a comprehensive post-marketing safety surveillance plan

WHAT IS A SYSTEMATIC LITERATURE REVIEW?

Systematic literature reviews are far more than text-based searches of literature databases. Medical device manufacturers need to plan and execute a dedicated strategy for literature monitoring, triage and analysis, and the results of the analysis must translate into decisions that minimize risk.

The key is to select a research informatics solution that includes a literature database with appropriate medical device coverage, in terms of content and indexing. In a case study reviewing literature about a particular medical device, the top research informatics solutions were Embase and Science Citation Index® (Figure 1).

The search strategy used for monitoring literature must be broad enough to ensure that no essential information is missed, but still allow precise identification of relevant results. This can involve the use of search features such as filters to narrow down the result set, subheadings based on key concepts such as device adverse effects or device comparison and triage and analysis methods to identify the most relevant literature.

The results themselves are generally in the form of a list of citations or data with descriptive indexing tags and other key information. If a citation is deemed useful, the full-text article can be obtained for detailed analysis. Good research informatics solutions allow both flagging of the citation and annotation of the full text article so that teams can work closely on individual items.

Ideally, post-market surveillance searches should be automated to check for new results that meet the user's criteria at regular intervals. Email alerts and/or RSS feeds inform the user of new items, ensuring that no adverse events are missed.

Such systematic literature review facilitates rapid analysis and confident decision-making, enabling effective medical device development and go to market plans, and compliance in post-market surveillance.

For more on systematic literature reviews, see Ref. 2.

SYSTEMATIC LITERATURE REVIEWS FOR MEDICAL DEVICES

As mentioned, systematic reviews of the biomedical literature facilitate a wide range of tasks that are intrinsic to medical device development, from basic design to identification of how the device will be an improvement over what's currently available on the market.

User needs and market potential

Essential questions during the creation of the basic design for a medical device pertain to its use.

- What is the problem that needs solving and what is the most effective design to solve the problem?
- Do we have an innovative solution to the problem?
- Will it improve the lives of patients?
- Is there a user requirement that could be met with an innovation to an existing device or is a new device needed?
- Do existing processes or technologies already serve the market?
- How is this medical device better than existing devices that meet similar needs?

Reviewing the biomedical literature can reveal how medical practitioners and patients use existing devices and where there are unmet needs. Analyzing results of searches on medical conditions can give insight into aspects of treatment that a device could support.

Competition is naturally an important consideration for any manufacturer.

How a medical device compares to others with the same or similar functions can inform design choices and marketing strategies. Most crucially, reviewing the biomedical literature, including adverse events reported in the literature, reveals much about the safety profiles of existing medical devices and the ways in which designs can be improved.

For more on the role of research in product development, see Ref. 3.

Demonstrating measurable benefit for successful reimbursement strategies

Researching both the cost-effectiveness and reimbursement potential of a new, updated or repurposed medical device is essential. Reviewing the biomedical literature for cost analysis, treatment outcome and quality of life studies, and to identify the medical benefits of similar devices, enables comprehensive estimations of how a new or repurposed device adds value. If a new device can be shown to have greater value or to provide new benefits, there will be increased likelihood of adoption.

In terms of reimbursement, there are certain basic considerations that relate purely to health insurance law. If the device is new, does it fall within existing insurance categories? And if the device is to be used for new purposes, will that affect reimbursement? Reimbursement policies should be taken into account during medical device development because the sale and use of devices are also dependent on insurance companies being prepared to pay for the device.

Therefore, a device must compete not only for the interest of medical practitioners, but also that of the insurance companies themselves. Competitive analyses that allow the manufacturer to reliably demonstrate benefit over existing devices is central to a reimbursement strategy, and it is in this area that the biomedical literature excels.

For more on reimbursement of medical device costs, see Ref. 4 and 5.

REGULATORY CLASSES FOR MEDICAL DEVICES

Figure 2 shows the regulatory classes of medical devices in the US and EU.

Medical devices have been regulated in the US for over 30 years. All manufacturers must list their devices and register all adverse events. Prior to the release of a device the manufacturer may need to perform the 510(k) process or obtain premarket approval (PMA).

In the EU, as of 2010, every medical device must have a Clinical Evaluation (CE) Report. Even devices that were already commercialized prior to 2010 must now have updated CE Reports, and clinical data are generally required.

SYSTEMATIC LITERATURE REVIEWS FOR MEDICAL DEVICES

Regulatory authorities worldwide require systematic reviews of the biomedical literature to be performed at certain stages of the development process and after release of the product. Compliance is mandatory for each territory where the device will be sold.

Regulatory authorities require literature reviews for:

1. Pre-clinical and clinical trials
2. Regulatory approval
3. Post-marketing safety surveillance

For examples of such regulatory requirements, see Ref. 6, 7 and 8.

Trials and approval

Literature reviews can play a number of roles in the trials and approvals phase.

Regulatory authorities require clinical evaluation reports to be submitted during device development. These include literature on clinical trials for similar medical devices, with relevant data sorted by device performance, device safety and device comparability. Additionally, the reasons why certain literature items were excluded may also be required. Thus, there is a workflow for literature review required as part of the clinical evaluation of a medical device (Figure 3).

It can also be possible to forego a full clinical investigation and instead present a detailed review of the literature, showing how the device meets the criteria to pass approval.

Furthermore, the manufacturer must indicate, with appropriate evidence, if the materials used in the device are clinically safe. It is essential to show that similar designs have been deemed clinically safe, and if any adverse events have been reported for similar designs, these must be described.

Post-marketing safety surveillance

Identifying adverse events for a medical device is not just a measure to protect the reputation of the manufacturer. It's a matter of patient safety and it is required by law in most countries. Thorough monitoring of adverse event reports in the literature, along with comprehensive strategies for literature triage and analysis, is critical to ensure that nothing is missed.

Reporting of adverse device events is on the rise. Less than 100 thousand were reported in the US in 2003, whereas close to half a million such events were reported in 2012 (Figure 4). Every device manufacturer has to confront the task of literature monitoring.

Class	Definition	US Legislation	EU Legislation
Class I Devices: –Require PMA 55% of devices	Non-life sustaining Present minimal potential for harm to the user Examples: tongue depressors, manual wheelchairs, and bandages	Manufacturer registration, proper labeling, and general reporting procedures required 510(k) required in some cases	Further divided into sterile and non-sterile Class I devices Manufacturer registration, proper labeling, and CE Report required
Class II Devices: –Usually 510(k) clearance 40% of devices	Non-life sustaining but more complex and may present harm to the user Examples: powered wheelchairs, and infusion pumps	Special labeling, mandatory performance standards, and post-market surveillance may be required in addition to the above 510(k) required in most cases	Further divided into Class IIa and Class IIb devices Manufacturer registration, proper labeling, and CE Report required, including clinical data
Class III Devices: –3% of devices	Supporting or sustaining human life, important in preventing impairment of human health, or presenting a potential, unreasonable risk of illness or injury Example: replacement heart valves, and implanted cerebellar stimulators, intra-bone dental implants	Premarket approval (PMA), scientific review of safety and effectiveness, special labeling, mandatory performance standards, and post-market surveillance required	Manufacturer registration, proper labeling, and CE Report required, including clinical data

Risk

Figure 2. The general classes of medical device in the US and EU. Based on information from Ref. 7 and 9.

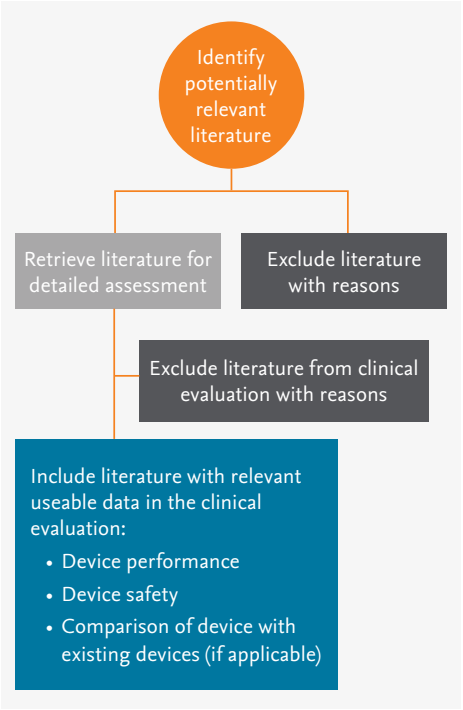


Figure 3. The workflow for literature review in the clinical evaluation of a medical device (Ref. 6).

This massive task of literature monitoring can be streamlined with the right research informatics solutions. Using a solution that performs automated searches and notifies the user of relevant new data via email alerts or RSS feeds saves considerable time. If the tool has the appropriate indexing and tagging, this will simplify literature triage. More importantly, a comprehensive biomedical literature database and thorough indexing dramatically reduce the risk of missing adverse event reports.

Ultimately, without such automation and streamlining, the daily task of monitoring the literature would become a monumental one. Since regulatory authorities expect adverse event reports and safety reports to be filed within a certain period of time, there is no room for a slow or inefficient process or one that might miss essential information.

For more information on adverse event reporting for medical devices, see Ref. 8 and 10.

HOW EMBASE AND QUOSA ARE AN INTEGRAL PART OF YOUR MEDICAL DEVICE DEVELOPMENT AND POST-MARKET SURVEILLANCE STRATEGIES

Embase provides a highly indexed and comprehensive biomedical literature database, including over 8,500 journals and over 1.75 million conference records from more than 5,500 conferences. The total coverage is currently over 29 million records dating back to 1947, and it has significantly more drug, device and disease coverage than MEDLINE.

Also, thanks to regular updates, Embase content is continually growing.

Embase is recognized by regulatory authorities, and is named as a source for literature in European Union guidelines on pharmacovigilance and post-market medical device surveillance. As shown in Figure 1, Embase is a top literature database for medical device information (Ref. 1).

The Embase content is indexed with terms relevant for all the literature-monitoring tasks mentioned in this paper. These terms include trade and generic names for medical devices, manufacturer names, medical conditions and adverse event types. In addition, easy-to-use automated search functions with email alerts streamline the monitoring process and ensure that users are aware of all new information matching their search criteria.

Embase also has a dedicated search form for medical device information, supporting precise searching for the most relevant information.

QUOSA is an end-to-end solution for scientific literature management. It enables life sciences institutions to meet regulatory reporting requirements, address medical inquiries and maintain awareness of topics or authors. Embase and QUOSA are fully compatible and have been optimized to support medical device development workflows.

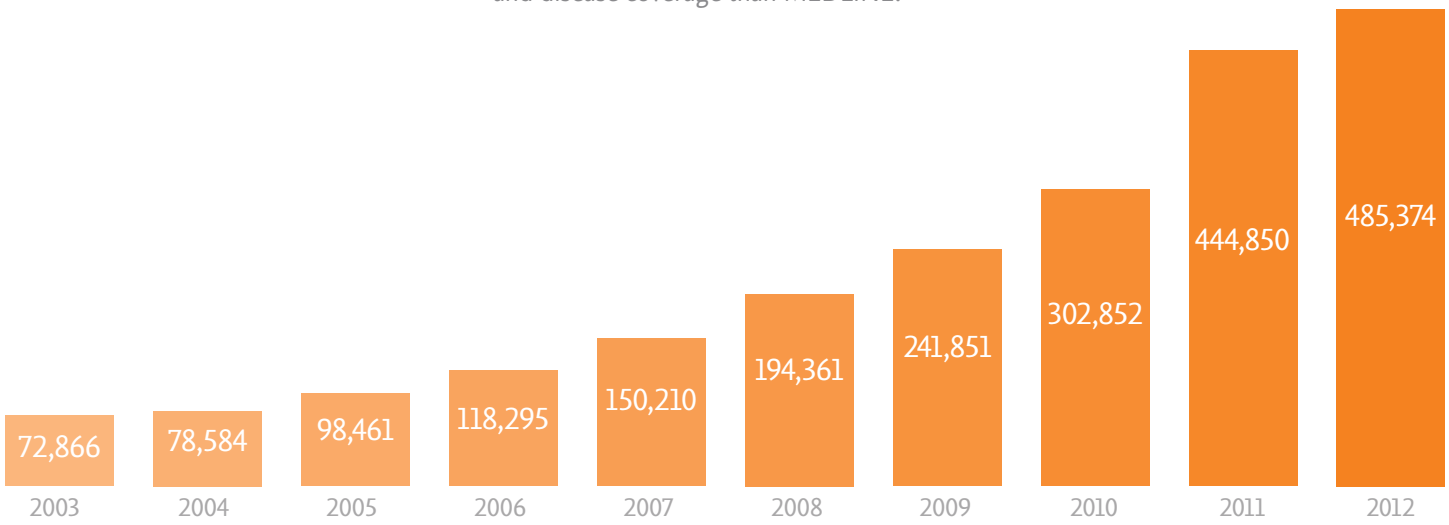
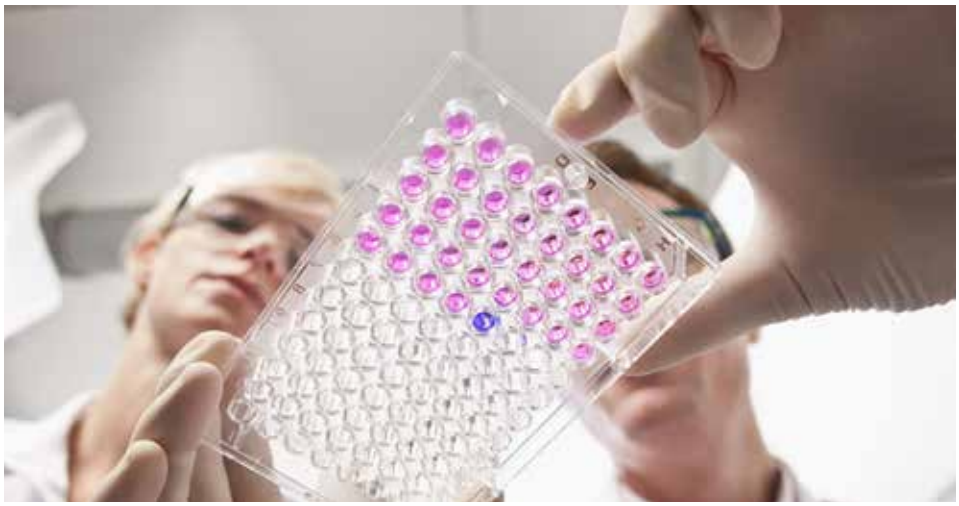


Figure 4. The number of adverse events reports for medical devices has risen rapidly in recent years (Ref. 10 and 11).

The wealth of biomedical literature remains an untapped resource for many medical device manufacturers.



CONCLUSION

The wealth of biomedical literature remains an untapped resource for many medical device manufacturers. A comprehensive literature monitoring strategy has enormous potential for development and marketing and is crucial for regulatory compliance. Working with a trusted partner to navigate the increasingly large volumes of scientific literature is key to ensure the success of medical device development.

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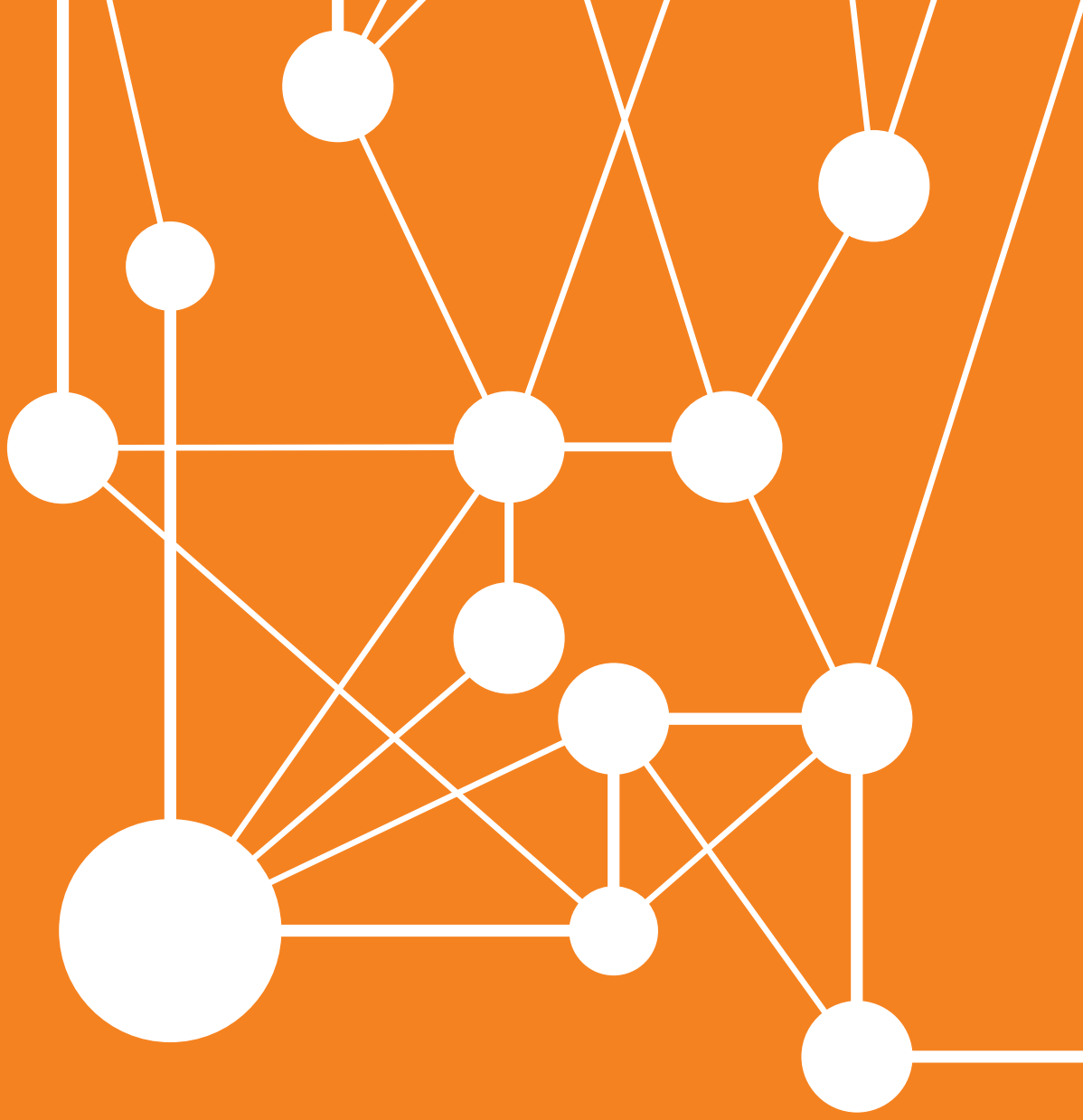

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EUROPE, MIDDLE EAST AND AFRICA
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