Post market surveillance in the german medical device sector – current state and future perspectives

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Post market surveillance in the german medical device sector –
current state and future perspectives

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ABSTRACT

Medical devices play a central role in the diagnosis and treatment of diseases but also bring the potential for adverse events, hazards or malfunction with serious consequences for patients and users. Medical device manufacturers are therefore required by law to monitor the performance of medical devices that have been approved by the competent authorities (post market surveillance). Conducting a nationwide online-survey in the German medical device sector in Q2/2014 in order to explore the current status of the use of post market instruments we obtained a total of 118 complete data sets, for a return rate of 36%. The survey included manufacturers of different sizes, producing medical devices of all risk classes. The post market instruments most frequently reported covered the fields of production monitoring and quality management as well as literature observation, regulatory vigilance systems, customer knowledge management and market observation while Post Market Clinical Follow-up and health services research were being used less for product monitoring. We found significant differences between the different risk classes of medical devices produced and the intensity of use of post market instruments. Differences between company size and the intensity of instruments used were hardly detected. Results may well contribute to the development of device monitoring which is a crucial element of the policy and regulatory system to identify device-related safety issues.

Keywords:
Medical devices; Post marketing; Product surveillance; European Union; Medical device regulation (MDR); In vitro diagnostic regulations (IVDR)

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INTRODUCTION

Background

Medical devices provide healthcare benefits to millions of people but can also lead to adverse events and incidents with serious consequences for the affected patients and users [1–3]. In order to reduce medical device associated risks, manufacturers are obliged by law to observe systematically the safety and performance of those medical devices which have already been approved and are now being used in clinical care. This applies to Europe, but also to other markets such as the USA or Japan [4–6]. According to European law, medical device companies have to implement a quality system that shall include "an undertaking by the manufacturer to institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase" [7]. This has to be verified and approved by a notified body. The implementation and operation of such a post market surveillance system can also be found in the directives for active implantable medical devices (AIMD) [8] and in vitro diagnostics (IVD) [9]. In this way, the medical device companies should receive structured information both on device-related adverse events and equipment defects and on rare problems, outcomes and complications occurring through-out the whole product lifecycle. This information can then be analyzed, evaluated and used for risk prevention. Some high-profile device recalls in recent years – such as artificial metal-on-metalhip implants [10,11], breast implants [12–14] or implantable cardioverter/defibrillators (ICD) [15–17] – illustrate the importance of this regulatory measure both for the risk management of the manufacturer and for a stronger patient and user safety.

Although regulation for medical devices has been discussed in literature for a long time [18–23] and despite the broad consensus on the importance of post market surveillance activities to collect safety-related information on medical devices and processes [5,6,24], we discovered a lack of empirical data so far. Our aim was to find out how medical device companies which are engaged in the German market perform their post market activities in daily practice.

Objectives

The present study had two objectives:

(i) To evaluate and analyze the intensity of use of post market surveillance instruments and measures in the German medical device sector.

(ii) To check whether the intensity of use of post market activities is associated with the company size or the risk class of the medical devices produced, as we assumed that this is mainly influenced by the manufacturer's resources or the device-related risk.

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MATERIAL AND METHODS

Study sample

We first considered manufacturers organized in one of the following trade associations for medical technology in Germany: German Medical Technology Association (BVMed), German Hightech Industry Association (SPECTARIS) and Association of the Diagnostics Industry (VDGH) (total n = 466, Date: 03/31/2014). This allowed to include in the study sample manufacturers with different company sizes from all over the country. Moreover, we considered companies with medical devices of all risk classes as well as AIMD and IVD. Device risk classes and IVD groups are as defined by the European Commission (see Table 1, [9,25]). Companies only distributing or repairing medical devices or having an authorized representative on the German market etc. (and therefore not subject to post market requirements) were not included. As a result, there was a sample of n = 324 medical device companies (as shown in the flowchart in Fig. 1).

Questionnaire design and measures

With regard to the first objective, medical device manufacturers were asked to assess how often they used each of a total of 24 instruments for post market surveillance. The instruments were identified on the basis of a systematic search in the legal and regulatory requirements for post market surveillance as well as the relevant international regulatory and device-related literature and then categorized into two main sections: internal and external knowledge sources. Internal sources were further subdivided into production monitoring and quality management. External sources were subdivided into customer knowledge management, market observation, literature observation, regulatory vigilance systems, Post Market Clinical Follow-Up (PMCF) and health services research. The data collection was based on a six-point Likert scale ranging from 0 (“never”) to +5 (“very often/always”).

Regarding the second objective, we were interested in company-specific characteristics. We were particularly interested in the risk class(es) and type(s) of produced medical devices as well as in the size of the company (turnover, balance sheet total and number of employees, all in 2013), company classification as defined by the European Commission for SMEs [26]. To assess the quality of data collected, respondents were asked to provide information on their position in the company and their professional work-experience in the field of post market surveillance in years. All questions could be skipped by answering “not specified”.

Prior to the final survey, six experts, each responsible for post market surveillance of medical devices, were asked to participate in a pre-test. To cover the heterogeneous spectrum of medical devices, we asked representatives of medical device manufacturers from various product areas (anaesthesia devices, intraocular lenses, artificial hip joints, surgical equipment, IVD, etc.). Based on the pre-test, the wording and layout of the questionnaire was finalized. We also added examples of knowledge sources to the different post market knowledge categories in order to achieve a uniform understanding among the participants and therewith better data quality.

Data collection and analysis

Data were collected between April and June 2014, based on a nationwide online survey. We used a two-step approach: first, telephone contact with a post market expert in each of the sampled companies and second, personalized invitation to participate in the survey via e-mail. We made up to three telephone contact attempts on different days of the week and times of day in order to avoid systematic or accidental bias in the survey. A week before the end of the survey we conducted a follow-up mailing to increase the response rate.

We analyzed data using descriptive analysis. To identify differences in the use of post market surveillance instruments regarding the company size and the highest reported risk class, we analyzed the local significance of the mean differences between company subgroups by using the two-sided non-parametric Kruskal-Wallis-Test ($p = 0.05$). This test was chosen for independent, non-parametric testing, as the manufacturer (sub-) groups we assumed to be not normally distributed. Collected data was analysed by software package SPSS® Statistics (22.0), IBM Corporation®, Armonk, New York, USA, for the operating system Windows® 7, Microsoft Corporation®, Redmond, Washington, USA.

RESULTS

Description of the survey dataset

A total of 118 medical device companies participated in the survey, for a return rate of 36% (see Table 2 for the profile of the study population).

Of these, 48 (41%) were SMEs, 45 (38%) large enterprises, 25 (21%) could not be classified because of insufficient information. Medical device companies of all risk classes participated in the survey. The sequence was as follows: Class IIa (68%), Class I (66%), Class IIb (55%), Class III (37%), IVD (all together 23%) and AIMD (2%). Among the ten most frequently reported product categories, medical electronics and electrical engineering dominated (32%) followed by Non-active implants (26%), IVD (23%), Human Medical instruments (19%), Surgical equipment and anaesthesia (17%), General health care equipment/aids (15%), Medical data processing (software) (13%), Dental products (12%) and Optics/precision mechanics and Dressing material (10% each).

Of the study participants, 63 (53%) reported to work as Senior Manager/Chief Executive in quality assurance or regulatory affairs, 36 (31%) in middle management/as quality or regulatory manager, 6 (5%) as post market surveillance expert, 4 (3%) as member of the executive board and 9 (8%) said they held another position. A total of 58 (49%) participants reported to have >10 years of professional experience in post market surveillance, 38 (32%) ≤10 years, 13 (11%) ≤5 years, 6 (5%) ≤2 years, and the remaining 3 (3%) skipped the question.

Use of post market surveillance instruments

Mean frequency and variance of the use of post market surveillance instruments are shown in Table 3. The instrument most frequently used for the collection of post market surveillance information were complaint processes [mean value (MV): 4.4; standard deviation (SD): ±1.1], followed by customer complaints (4.2; ±1.0), re-

ports of medical consultants/field service (3.7; ±1.4), product testing/quality control (3.7; ±1.4), information/feeds from national authorities/institutions (3.7; ±1.5), and product development/manufacturing process (3.6; ±1.5). The bottom quartile figured extended follow-up of patients enrolled in premarket investigations (2.3; ±1.9), information from new clinical investigations (2.2; ±1.8), review of relevant retrospective data from patients previously exposed to the device (2.0; ±1.8), information from infrastructures of health services research (1.3; ±1.5), the use of other health services research data (1.1; ±1.3), and medical device-associated critical incident reports (1.1; ±1.4).

There is a dichotomy in terms of the intensity of use between the subgroups of the external knowledge sources. Information from literature observation and regulatory vigilance systems are fairly often used (with an overall mean of 3.4 for each category), followed by customer knowledge management and market observation (both 3.3). The subgroups PMCF (2.3) and health services research (1.1), however, have a lower overall average of one to two levels on the six-point Likert scale.

Two thirds of the post market surveillance instruments show a relatively low variance (SD from ±1.0 to ±1.5). This applies equally to the instruments used frequently as well as to those of the health services research category with the overall lowest intensity of use. By contrast, every third instrument shows a higher variance (SD from ±1.6 to ±1.9). The four instruments with the highest variances all fall into the PMCF category.

Differences in company size and risk class

Table 3 also shows the statistic results broken down by company size and medical device risk class. Mean values are shown in bold if the estimate differs more than ±0.5 scaling steps from the grand mean of a post market instrument. Mean values are greyed out if the Kruskal-Wallis test showed a significant difference between the observed groups of the device manufacturers.

Company Size: Significant differences exist almost exclusively for instruments of the PMCF category. In three of the four PMCF instruments larger enterprises reported a significant higher intensity of use than SMEs.
Risk class: Significant differences between the mean values can be found in both internal and external knowledge sources. In the internal section, significant differences can be found in the subgroup of quality management. Thus, reports of medical consultants/field service play an important role for post market surveillance in companies producing AIMD and Class III devices (difference from the overall mean of the instrument: +0.6), and a less important role for manufacturers of Class IIa devices (−0.6). Medical device-associated claims are frequently used by manufacturers of AIMD/Class III devices (+1.1), while companies producing Class IIb (−1.0) and Class IIa (−0.7) devices use these below average. In the external section, nearly all subgroups (with the exception of health services research) show significant differences. Manufacturers of AIMD/Class III devices make use of many instruments above average, while manufacturers of devices with lower risk class show a significantly lower intensity of use.

DISCUSSION AND CONCLUSIONS

This is the first empirical study on the intensity of use of post market surveillance instruments reported by medical device companies. We discuss study results and place them in the context of current literature. Also discussed are selected implications and perspectives for policy and regulatory development. Finally, we address methodological limitations of the study.

Post market surveillance in the medical device sector

Our first aim was to evaluate the current state of use of post market surveillance instruments in medical device companies. As shown in Table 3, there is a wide use of the various post market instruments of the different knowledge categories. Four of the six instruments most commonly used for post market surveillance are classified as internal knowledge sources. This makes sense because this kind of information has already been collected by many medical device companies using standardized production management or quality assurance processes and can thus be transferred quickly and inexpensively for post market surveillance purposes. Instruments rarely used for post market surveillance nearly all fall into the PMCF and health services research category.

Differences according to medical device risk class

The subgroup analysis under the second objective showed that post market instruments are carried out by medical device manufacturers to different extents, in particular with respect to the medical device risk class. A statistically significant positive difference between the risk class and intensity of use of instruments can be seen in about four-fifths of the post market surveillance instruments. Again, this makes sense since – for example – a manufacturer of high-risk implants (usually inserted for a longer period) faces other opportunities and needs regarding the use of post market instruments than a manufacturer of IVD (usually of low risk and used for a short time, often by laboratory physicians).

The intensity of use varies especially with the PMCF instruments, as shown by the standard deviations and the variations in the mean values between the different groups of manufacturers. Only 22–34% of the responding manufacturers reported to use PMCF instruments “often” or “very often/always” for post market surveillance, one reason being probably the systematic collection and analysis of information from the field of PMCF, which is relatively complex from an organizational standpoint. Clinical trials for medical devices, for example, are often associated with high costs resulting from study planning, implementation, use of complex biometric methods and management of medical device-related data. Accordingly, PMCF instruments are rather used for post market surveillance by manufacturers with greater financial resources or a PMCF databank. Reasons include conformity assessment, technical documentation or clinical evaluation of medical devices. This is mainly done by manufacturers who produce high-risk AIMD or Class III devices.

PMCF is particularly important for the monitoring of high-risk medical devices like implants. This is because devices implanted in the human body and staying there for a long period of time tend to offer more medical device specific risk knowledge (e.g. studies on long-term effects, chronic complications, product performance over time) than short-lived devices. Also, clinical implant trials are often significantly shorter than the expected

time of the product in the human body [27], resulting in a surveillance gap. This is why the medical literature of recent years figures a relatively high number of implant-related post market surveillance studies, especially with a focus on cardiovascular medical devices like pacemaker or ICD [28-32].

Policy and regulatory relevance

Results in the context of the medical device regulation

As a result of the device recalls [10-17], a discussion arose on the safety and regulation of medical devices in Europe, also concerning post market surveillance and monitoring [5]. The political debate of recent years has been dominated by two proposals of the European Commission to review and revise the existing regulation legislation and framework on medical devices and IVD. In this context, an open letter from a group of European research experts headed by NEUGEBAUER was presented to the European Union in 2013, calling for stricter licensing and regulatory requirements especially for moderate and high risk medical devices [33]. After a long discussion, the European Parliament approved the final versions of the new Medical Device Regulations (MDR) and In Vitro Diagnostic Regulations (IVDR) in spring 2017 [34,35]. The new regulations will replace the existing directives after a transitional period of three to five years respectively.

The new medical device regulation strengthens the importance of post market surveillance. Examples include a revision of market surveillance with shorter reporting periods and a higher classification of certain surgically invasive medical devices. In this context, our study shows differences in the use of post market knowledge sources between the manufacturer groups, which should be taken into account by the regulatory authorities such as BfArM, FDA or the notified bodies from a health policy point of view. Also PMCF, e.g. for clinical product evaluation, is becoming more important with the MDR [34,35]. Here the study results show that the systematic collection of device-related patient data is not an integral part of all manufacturers' product surveillance system yet. Medical device manufacturers as well as regulatory authorities should therefore expand their trial expertise and capacities in order to be able to perform and assess more and more clinical trials with (high risk) devices. The pharmaceutical sector, where clinical trials have long been a component of pharmacovigilance can be considered as a role model in this aspect. Finally, health policy should focus on the surveillance of the increasing number of medicinal products that are subject to the regulatory requirements of the medical device and drug law, e.g. products with a complementary drug component (hybrid) such as drug-eluting stents.

All this should then lead to an increased use of the appropriate instruments for post market surveillance resulting in safer products and an increase in patient safety. Against this backdrop, it would have to be assumed that the activities of the medical device companies in the post market surveillance sector, in general, tend to increase over time. A follow-up study on post market activities of medical device companies, for example, after the end of the transitional period would thus be conceivable and meaningful. For now the results of this study do not only complement the regulatory publications in this field with empirical data. They also provide for the first time an insight into medical device companies on the field of post market surveillance, and thus give a point of reference for future research.

Potential of device-related health services research data

According to the results, instruments of the health services research category are used the least for post market surveillance. Only between six and 14% of the manufacturers surveyed said they "often" or "very often/always" used these instruments for medical device monitoring. About half (44–52%) of the surveyed companies do not at all use these instruments as a knowledge source for product surveillance. Accordingly, information resulting from structured collection, analysis and evaluation of medical device-related health services research data does not seem to justify the associated costs from the manufacturer's perspective.

However, we expect that medical device-related data will increasingly come from the field of health services research and this in turn will become a more and more important knowledge source for post market surveillance of medical devices. First, because an increasing number of medical devices has been applied and used in medical care in recent years; according to the OECD each year more than 300,000 artificial hip and knee joints are implanted in Germany alone [36]. Second, more information and communication technologies will be used in health care, resulting in an increasing number of clinical registries, cohort studies, HTA, etc. In this context an EU-funded working group aims to compare the activities and differences in medical device-associated HTA and presents ideas for future development at the European level [37-39]. Both lead to a better collection and availability of medical device-specific information. It can be assumed that especially manufacturers of moderate to high risk medical devices will benefit from this development. This applies, for example, to manufacturers of anaesthesia equipment which can already access and analyse medical device-associated critical incident reports [40-42], and to manufacturers of implants which can use device-specific registries. According to NIEDERLANDER ET AL. there are more than 100 registries for implantable medical devices in Europe alone [43]. One example are registries for arthroplasty which have existed in Scandinavia for a long time [44] and were initiated in Germany recently [45]. We therefore welcome the current health policy development in Germany to strengthen activities in the field of health services research by national funding programs, also from the perspective of post market surveillance. Patients and users could then benefit from a safer and more effective use of medical devices in every-day clinical care delivery.

Limitations

The results cover a wide range of medical device companies and therefore give a valuable insight into the process of post market surveillance of medical devices. Furthermore, the majority of respondents reported to have a job in senior or middle management with relevant professional experience in the field of quality management (as shown in Table 2) so that a high level of expertise of the participants and thus a high quality of data collected can be assumed.

However, a number of limitations apply. First, the study sample was deliberately chosen for data collection as shown in Fig. 1. In this way, medical device companies were excluded a priori which were not organized in any of the above mentioned trade organizations or in another German trade association for medical/diagnostic devices. Second, the study was subject to the classic limitations of an online survey. For example, it could not be checked who responded to the questionnaire. Third, it is assumed that the participants of the survey were more likely employed by a manufacturer with a higher awareness and more experience regarding post market surveil-

lance activities. This would mean that the actual intensity of use of the post market instruments in daily practice is somewhat lower among the medical device industry as a whole. Fourth, the chosen points on the Likert Scale may lead to a partly inconsistent assessment among the participants. Still the results show tendencies in the intensity of use of the post market instruments. Finally, the study was limited to manufacturers active in the German medical device market. This was mainly because regulatory requirements for medical devices differ from country to country [23,46]. Therefore it would be interesting to explore the intensity of use of post market surveillance instruments in other medical device markets, and to test if it is possible to transfer the findings of this study. For this, more research looking at medical device markets around the world is needed. It would be particularly interesting to compare the situation between the German and US markets, because these are two of the largest medical device markets in the world, and because there are considerable regulatory post market surveillance differences for manufacturers in Europe and the US [46,47].

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Conflict of interest

The authors declare that they have no conflict of interests.

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TABLES AND FIGURES

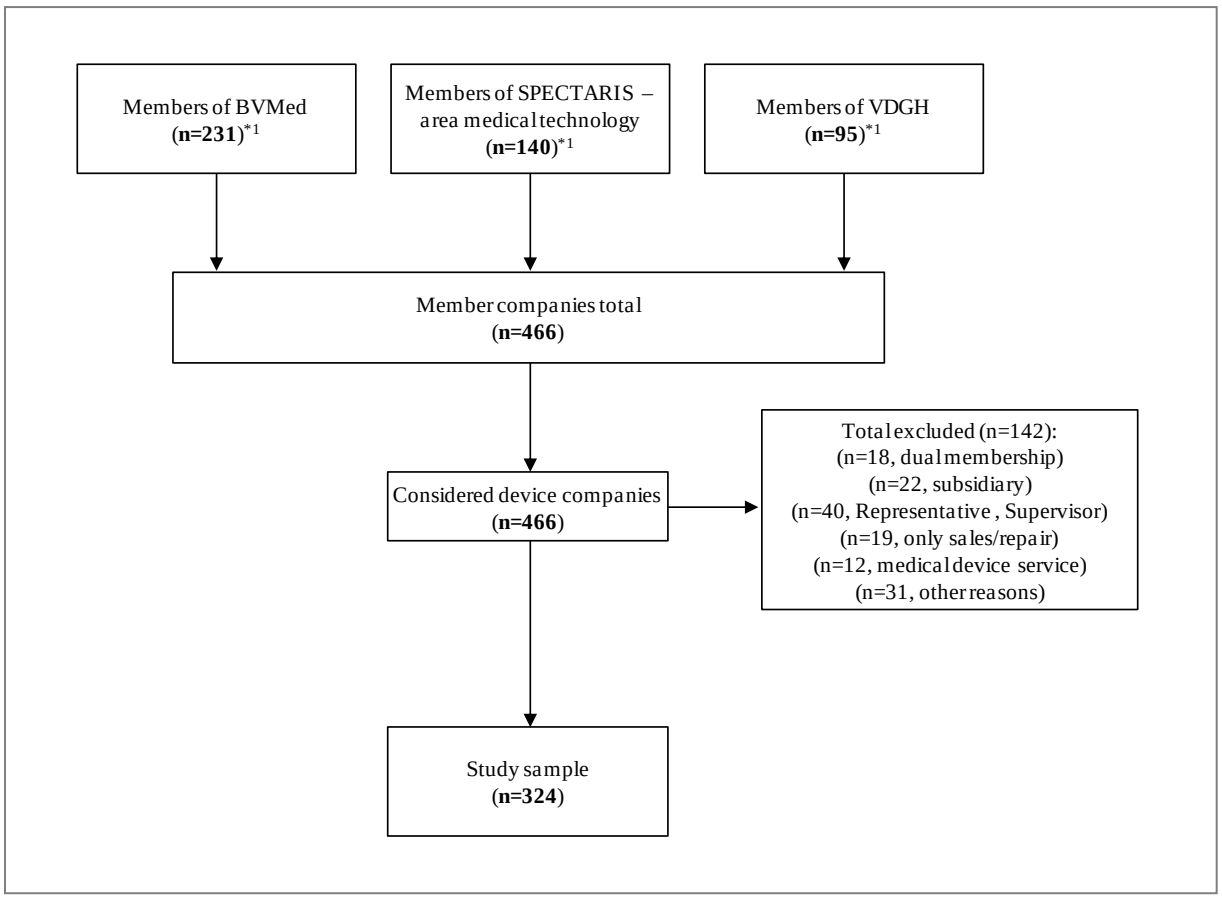

Fig. 1: Flow diagram of medical device companies selected for the study sample. *1Date 03/31/2014

Table 1: European classification system for medical devices, AIMD and IVD groups [9,25], with medical device, AIMD and IVD examples.

Risk class/ group	**Risk level**	**Medical device examples**
I	Low	reading glasses, stethoscope, wheelchair, hospital bed, dressings, scalpel
IIa	Low-moderate	hearing Aid, blood pump, ultrasound device, MRI Scanner, contact lens, Positron emission tomography, dental implant
IIb	Moderate-high	intraocular lens, ventilator, infusion Pump, anaesthetic machine, defibrillator, X-ray machine
III	High	Prosthetic heart valve, cardiac catheter, coronary stent
AIMD	High	implantable cardiac pacemaker, implantable cardioverter defibrillator
IVD group		**IVD examples**
IVD Annex II List A		blood groups of the AB0 system, blood groups of the Kell system, irregular anti-erythrocyte antibodies, markers of HIV infection, Hepatitis B, C und D
IVD Annex II List B		congentital infection with rubella or toxoplasma, hereditary diseases phenylketonuria and Down syndrome (trisomy 21), tumor marker PSA
IVD Products for self-testing		systems for measurement of blood glucose
IVD General		cholesterol, blood clotting or thyroid function tests

AIMD, Active implantable medical devices;
IVD, In vitro diagnostics;
Annex II, see IVD listed in Annex II – List of Devices referred to in Article 9(2) and 3 of the Directive 98/79/EC

Table 2: Profile of the study population, based on self-reported data (n = 118).

	absolute frequency	relative frequency (%)
Characteristics of participating medical device companies		
Company size[*1]		
SME	48	41
Large Enterprise	45	38
No information	25	21
Risk Class(es) of medical devices sold in Germany[*2;*3]		
AIMD	2	2
Class III	44	37
Class IIb	65	55
Class IIa	80	68
Class I	78	66
IVD Annex II List A	5	4
IVD Annex II List B	8	7
IVD Devices for self-testing	3	3
IVD General	25	21
Offered medical device group(s)[*2;*4]		
Medical electronics and electrical engineering	38	32
Non-active implants	31	26
IVD	27	23
Human Medical instruments	22	19
Surgical equipment and anesthesia	20	17
General health care equipment/aids	18	15
Medical data processing (software)	15	13
Dental products	14	12
Optics/precision mechanics	12	10
Dressing material	12	10
Orthopaedic and Rehabilitation Technology	11	9
Injection/Infusion/Transfusion/Dialysis	10	8
ultrasound technology	7	6
AIMD	2	2
Radiological technology	2	2
Electromagnetic fields	2	2
Physical therapy	1	1
Ophthalmologic technology	1	1
No information	2	2
Characteristics of experts responding to survey		
Position in the company		
Executive board	4	3
Senior Manager/Chief Executive	63	53
Middle Management/Quality & Regulatory Manager	36	31
Post market surveillance expert	6	5
Other	9	8
Professional experience in post market surveillance in years		
≤ 2 years	6	5
≤ 5 years	13	11
≤ 10 years	38	32
> 10 years	58	49
No information	3	3

SME, Small and Medium-sized Enterprises;
AIMD, Active implantable medical devices;
IVD, In vitro diagnostics;
[*1] Company size according to the criteria of the European Commission Recommendation concerning the definition of micro, small and medium-sized enterprises [26]; classification based on reported annual turnover, balance sheet total and number of employees (all in 2013)
[*2] Multiple answers possible
[*3] Risk class according to the European risk classification for medical devices, AIMD and IVD
[*4] Medical device groups according to the classification system used by the German Federal Institute for Drugs and Medical Devices

Table 3: Total evaluation of the intensity of self-reported use of post market surveillance instruments by knowledge category, broken down by company size and highest risk class; large significant differences[*1] are visually highlighted; *p*-values of Kruskal-Wallis-Tests.

	Post market surveillance of medical devices Knowledge sources by knowledge category[*2]	**Total**	**Manufacturer group**								
			Company size			**Risk class**					
			SME	Large enterprise	asymptotic significance	AIMD/ Class III	Class IIb	Class IIa	Class I	IVD	asymptotic significance
		n=118 MV (±SD)	n=48 MV (±SD)	n=45 MV (±SD)	Kruskal-Wallis-Test[*3]	n=44[*4*5] MV (±SD)	n=27[*4] MV (±SD)	n=16[*4] MV (±SD)	n=9[*4] MV (±SD)	n=22[*4*6] MV (±SD)	Kruskal-Wallis-Test[*4]
Internal knowledge sources	**Production monitoring**										
	Product development/manufacturing process *[e.g. rejection rates/faults detected at final medical device checks]*	3.6 (1.5)	3.8 (1.4)	3.7 (1.5)	0.933	3.7 (1.6)	3.5 (1.5)	3.3 (1.6)	4.0 (1.3)	3.7 (1.6)	0.608
	Product testing/quality control *[e.g. information from material testing, device inspections]*	3.7 (1.4)	4.0 (1.2)	3.8 (1.4)	0.616	3.9 (1.4)	3.5 (1.4)	3.3 (1.5)	4.0 (1.1)	3.8 (1.5)	0.276
	Quality management										
	Complaints processes/trend curves *[e.g. information on guarantee claims, problem complaints]*	4.4 (1.1)	4.4 (1.1)	4.4 (1.0)	0.784	4.8 (0.5)	4.3 (1.2)	**3.8** (1.4)	4.6 (1.0)	4.1 (1.2)	**< 0.01**
	Reports of medical consultants/field service *[e.g. service repair, maintenance]*	3.7 (1.4)	3.7 (1.3)	4.1 (1.1)	0.154	**4.3** (1.1)	3.3 (1.6)	**3.1** (1.4)	3.9 (1.4)	3.4 (1.2)	**< 0.01**
	Information on material consumption *[e.g. replacement deliveries, required spare parts, defects on arrival]*	2.8 (1.7)	2.8 (1.6)	3.1 (1.6)	0.296	2.9 (1.7)	3.2 (1.8)	**2.3** (1.5)	**2.1** (1.6)	2.8 (1.7)	0.304
	Medical device-associated claims *[e.g. from the company's internal vigilance system, insurers]*	3.5 (1.7)	3.1 (1.9)	3.8 (1.5)	0.074	**4.6** (0.9)	**2.5** (1.9)	**2.8** (1.6)	3.8 (1.3)	3.2 (2.0)	**< 0.001**
External knowledge sources	**Customer knowledge management**										
	Customer feedback *[e.g. from device instructions, user training, product/design tests]*	3.6 (1.2)	3.6 (1.3)	3.7 (1.2)	0.572	4.1 (1.1)	3.5 (1.1)	**3.0** (0.9)	3.3 (1.5)	3.5 (1.4)	**< 0.01**
	Customer complaints *[e.g. from complaints management, customer/product workshops]*	4.2 (1.0)	4.1 (1.1)	4.4 (0.7)	0.263	4.6 (0.6)	4.1 (1.0)	**3.5** (1.2)	4.3 (1.3)	4.1 (1.0)	**< 0.01**
	Customer surveys *[e.g. WebQuery]*	2.4 (1.5)	2.2 (1.7)	2.6 (1.3)	0.118	2.6 (1.5)	2.2 (1.2)	2.4 (1.3)	2.4 (1.8)	2.2 (1.8)	0.633
	Cooperation with advanced users *[e.g. lead user-method, innovation portal]*	2.9 (1.6)	2.6 (1.6)	3.1 (1.6)	0.209	**3.4** (1.6)	2.7 (1.6)	2.6 (1.2)	**1.9** (1.7)	2.6 (1.5)	**< 0.05**
	Feedback/experiences of other stakeholders *[e.g. device/product suppliers, co-operation partners]*	3.2 (1.3)	3.2 (1.3)	3.4 (1.3)	0.600	**3.8** (1.2)	3.1 (1.0)	2.8 (1.2)	2.8 (1.6)	**2.6** (1.5)	**< 0.01**
	Market observation										
	Information about similar medical devices	3.4 (1.3)	3.2 (1.3)	3.5 (1.3)	0.186	**4.1** (1.1)	3.4 (1.2)	**2.8** (1.1)	3.0 (1.7)	**2.8** (1.3)	**< 0.001**
	Manufacturers of similar medical products *[e.g. at industrial exhibition/trade fair, through patent research]*	3.1 (1.4)	2.9 (1.5)	3.3 (1.4)	0.248	**3.8** (1.2)	3.0 (1.2)	**2.6** (1.3)	2.7 (1.8)	**2.6** (1.5)	**< 0.01**

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Post market surveillance of medical devices Knowledge sources by knowledge category[*2]	**Total**	**Manufacturer group**								
		Company size			**Risk class**					
		SME	Large enterprise	asymptotic significance	AIMD/ Class III	Class IIb	Class IIa	Class I	IVD	asymptotic significance
	n=118 MV (±SD)	n=48 MV (±SD)	n=45 MV (±SD)	Kruskal-Wallis-Test[*3]	n=44[*4*5] MV (±SD)	n=27[*4] MV (±SD)	n=16[*4] MV (±SD)	n=9[*4] MV (±SD)	n=22[*4*6] MV (±SD)	Kruskal-Wallis-Test[*4]
Literature observation										
Studies/Publications *[e.g. in scientific journals, databases]*	3.6 (1.3)	3.4 (1.3)	3.6 (1.3)	0.587	**4.4** (0.9)	3.3 (1.2)	**2.9** (1.3)	**2.4** (1.2)	3.2 (1.3)	< **0.001**
Other written documents *[e.g. on the internet, conference reports]*	3.2 (1.2)	3.1 (1.2)	3.2 (1.2)	0.898	**3.9** (1.0)	2.9 (1.2)	**2.6** (1.2)	**2.4** (1.4)	3.1 (1.1)	< **0.001**
Regulatory vigilance systems										
Information/feeds of national authorities/ institutions *[e.g. on incidents, recalls, field safety notices]*	3.7 (1.5)	3.8 (1.5)	3.7 (1.4)	0.658	**4.5** (1.0)	3.7 (1.3)	**2.5** (1.6)	3.7 (1.4)	**3.0** (1.8)	< **0.001**
Information/feeds of international authorities *[e.g. from FDA, MHRA, Health Canada]*	3.1 (1.7)	2.9 (1.8)	3.3 (1.5)	0.260	**4.0** (1.4)	3.0 (1.6)	**2.1** (1.7)	2.8 (1.4)	**2.2** (1.7)	< **0.001**
Post Market Clinical Follow-Up (PMCF)										
Extended follow-up of patients enrolled in premarket investigations	2.3 (1.9)	**1.7** (1.7)	2.7 (2.0)	< **0.05**	**3.2** (1.9)	2.0 (1.8)	1.9 (1.7)	**1.4** (1.3)	**0.9** (1.5)	< **0.01**
New clinical investigation *[e.g. from (inter-) national register data]*	2.2 (1.8)	1.7 (1.5)	**2.7** (1.8)	< **0.05**	**3.3** (1.8)	1.7 (1.4)	**1.5** (1.2)	**1.3** (1.3)	**1.3** (1.7)	< **0.001**
Review of data derived from a device registry	2.6 (1.8)	2.2 (1.8)	3.0 (1.8)	< **0.05**	**3.6** (1.6)	2.2 (1.8)	**1.8** (1.1)	**1.8** (1.7)	**1.8** (2.0)	< **0.001**
Review of relevant retrospective data from patients previously exposed to the device	2.0 (1.8)	1.7 (1.7)	2.0 (1.8)	0.440	**3.2** (1.8)	**1.4** (1.3)	**1.5** (1.2)	**0.9** (1.1)	**0.9** (1.6)	< **0.001**
Health services research										
Infrastructure of health services research *[e.g. medical device-related databases, HTA reports]*	1.3 (1.5)	1.0 (1.3)	1.5 (1.6)	0.197	1.7 (1.7)	1.3 (1.4)	0.9 (1.1)	**0.8** (0.8)	0.9 (1.7)	0.271
Medical device-associated critical incident reports *[e.g. from hospital critical incident report systems]*	1.1 (1.4)	0.7 (1.1)	1.3 (1.4)	< **0.05**	1.3 (1.6)	1.3 (1.6)	0.6 (0.7)	0.8 (0.8)	0.6 (1.3)	0.269
Other health services research data *[e.g. from health services research networks]*	1.1 (1.3)	0.8 (1.0)	1.3 (1.4)	0.156	1.3 (1.5)	1.0 (1.2)	0.9 (1.2)	1.1 (0.8)	1.1 (1.4)	0.859

MV, mean value;
SD, standard deviation;
AIMD, Active implantable medical devices;
IVD, in vitro diagnostics;

[*1] MVs are shown in **bold** if the estimate differs more than ±0.5 scaling steps from the grand mean of a post market instrument, measured on a six-point Likert scale, denoting "unavailable" (0), "very rare" (1), "seldom" (2), "sometimes" (3), "often" (4), "very often/always" (5) respectively
[*2] Rank of knowledge source for post market surveillance according to the self-estimated frequency of use (MV) in parentheses
[*3] Mean values are greyed out if the two-sided Kruskal-Wallis test shows a significant difference between the groups of medical device manufacturers; statistical significance levels: p <0.05 ; p < 0.01 ; p <0.001
[*4] The highest self-reported risk class of the manufacturer has been decisive for the grouping
[*5] AIMD and Class III-manufacturers evaluated in one group because both product groups are high risk devices (see table 1) and the AIMD manufacturers reported also the distribution of Class III products
[*6] In this category, the manufacturers of all IVD groups are summarized (IVD Annex II List A, IVD Annex II List B, IVD Devices for self-testing, IVD General; see table 2)

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