MDR PILOT

Use of a registry to perform MDR post-market clinical follow-up for trauma implants — a pilot study

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Photos & illustrations
Shutterstock.com:
Spotmatik Ltd (p. 3)
Adobe Stock:
wladimir1804 (p. 8), BillionPhotos.com (p. 9),
niroworld (p. 10), megaflopp (p. 19),
Gorodenkoff (p. 21), Drobot Dean (p. 22),
Worawut (p. 31)
All unmarked illustrations: Anne Mayer-Tasch

Published in February 2019

Lead partner & publisher
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BFCC—BALTIC FRACTURE COMPETENCE CENTRE

The Baltic Fracture Competence Centre (BFCC) is a pan-Baltic fracture cooperation network fostering innovation within fracture management. The project consortium consists of a transnational cross-sector partnership involving five hospitals, three companies from the medical technology industry, a university, three clusters and one technology transfer organization.

Due to an ageing society, the need for innovative products and clinical procedures for fracture treatment is increasing as a response to age-related fractures and co-morbidities such as osteoporosis, infections and non-unions. Innovations in fracture management must reduce the cost of care or clearly improve quality of care.

Clinicians will support the innovation process by identifying the clinical needs to ensure user-oriented product development. The collaboration between hospitals across countries will foster the innovation of clinical procedures through the exchange of best practice in fracture management influenced by different national, organizational and regulatory conditions.

However, clinicians and companies often lack insight information about total cost and effectiveness of fracture management and causes of adverse health outcomes in the hospitals. To overcome this information gap, the BFCC will develop and implement a transnational fracture registry with five hospitals from Estonia, Germany, Lithuania, Poland, and Sweden, respectively, providing evidence about fracture treatment in the clinical »real world« and reveal clinical needs as well as potentials for innovation.

The BFCC will publish two innovation reports. The Innovation Report No 1 deals with trends in the surgical treatment methods of proximal femur fractures. The Innovation Report No 2 based on results and findings from registry data analysis will identify innovation needs and potentials.

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1. MANAGEMENT SUMMARY

This document describes the pilot study regarding the use of the BFCC Fracture Registry to produce Post-Market Clinical Follow-up (PMCF) study of CE marked medical products in fracture treatment in the context of manufacturers' responsibilities according to the new Medical Device Regulations (MDR) of the EU.

The theoretical framework, embedding regulatory necessities and requirements including data safety and ethical issues, was created. In a test environment of a large university hospital in Lübeck/Germany, different test runs of a PMCF study were accomplished.

With this report, we could show, that Post-Market Clinical Follow-up is successfully possible in a registry environment. For vigilance procedures, the information gained regarding the implants and their failure modes does not yet seem to be precise enough.

Non-sterile pre-packed implants can at the moment not be tracked and traced sufficiently, at least at the chosen hospital. This will require further modifications in the future.

2. RATIONALE OF THE PILOT PROJECT

The BFCC establishes a transnational collaboration platform between hospitals and industry, which will be tested in three transnational pilots, with five hospitals and three companies involved. Hospitals generally store a large amount of clinical data for each treatment case. This nowadays includes details of medical devices used in the treatment. If these devices are implanted, the identifying serial number is stored in context of the case.

Manufacturers of medical devices are in general interested in the performance of their product. The implementation of the EU medical device regulation legislation makes it from 2020 (at the latest) on a legal requirement to sample clinical data in conjunction with their medical products over the whole life cycle of such products. This is in addition to the general vigilance procedures that manufacturers have to fulfil in their Post-Market Surveillance (PMS) process.

According to EU MDR, the PMCF plan is product specific and so it is required to have a separate plan for each product in the company portfolio.

PMCF is a continuous process that updates the clinical evaluation, which is the assessment and analysis of clinical data pertaining to a medical device to verify the clinical safety and performance of the device when used as intended by the manufacturer.

When conducting PMCF, the manufacturer should proactively collect and evaluate clinical data from the use in or on humans of a device which bears the CE marking and is placed on the market with the aim of confirming the safety and performance throughout the expected lifetime of the device, of ensuring the continued acceptability of identified risks and of detecting emerging risks on the basis of factual evidence.

PMCF shall be performed pursuant to a documented method laid down in a PMCF plan.

Rationale of this feasibility study was thereby to establish if this process could be performed on a register using automatic or semi-automatic data acquisition from a hospital information system (HIS) including the specified implants for each patient.

3. BACKGROUND

3.1. MDR changes

The recently released Medical Device Regulation (MDR) will replace the former EU's current Medical Device Directive MEDDEV (93/42/EEC) and the EU's Directive on active implantable medical devices (90/385/EEC).

Besides other changes, the MDR will newly regulate the classification of certain medical devices and will renew the requirements for device identification (UDI) and reporting (e. g. Post-Market Surveillance Plan / Report [PMS], Post-Market Clinical Follow-up Report, Periodic Safety Update Report [PSUR], and Summary of Safety and Clinical Performance [SSCP]). Additionally, the requirements for clinical data will be uplifted with the consequence that more pre- and post-market clinical data will be needed for new and legacy products. Therefore, the MDR study aims to support the collection of relevant clinical data in perfect amendment to the complication pilot. Moreover, this approach within the BFCC project may help to identify yet unknown complications in fracture treatment. Companies could utilize such data as additional input to develop products that fulfill the patients' and surgeons' user needs.

Generating clinical trials requires time, resources and budget. Also the MDR expects a timely implementation of the new requirements, as shown in Figure 1. To overcome those challenges, an effective way to generate clinical data needs to be developed. Utilizing a registry such as BFCC, may be an efficient way to collect clinical data with an overall reduced burden for the healthcare system.

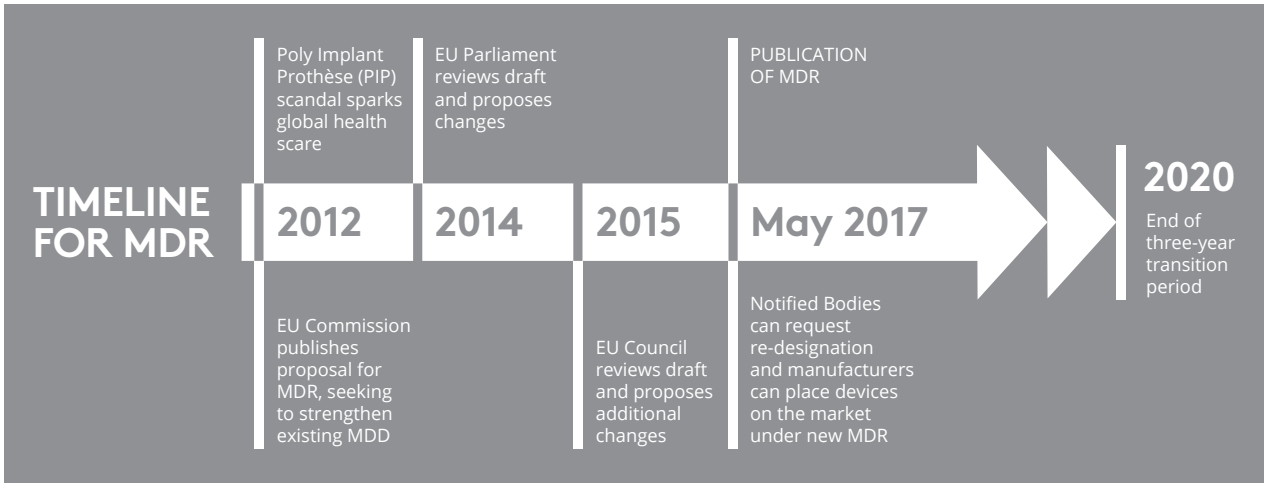


Figure 1: Estimated timelines for the MDR based on current assumptions (taken from: http://www.lrqa.co.uk/)

The BFFC consortium compiles experts from the clinical side, data management and industry and, hence, is well positioned to take on the above mentioned challenges. Moreover, with the project running now for more than 1.5 years, the consortium has grown to an effective team and with recent changes in the group it appears feasible to add a respective pilot program even within the running project. The proposed scope of the pilot has been reviewed and agreed upon in the last steering group meeting.

If these alterations succeed, it can be applied to many hospitals in the Baltic Sea Region and beyond. For the hospitals, an upscaling to other areas should be easily, so that also many different other registers can be handled this way, allowing significant reduction in effort used for data sampling at the moment.

The MDR pilot study will be integrated mainly in GoA 5.5 Demonstration Pilot 3 — Complications, but, as mentioned earlier, also GoA 5.2 Evaluation and case studies of demonstration pilots will benefit by this additional and innovative approach. With this valuable evaluation of the new BFCC MDR study obviously different stakeholder groups from industry, hospitals (clinicians) and researchers will benefit.

PHOTO: Adobe Stock

4. VIGILANCE OR PMCF? OR BOTH?

The term »vigilance report« encompasses Incident Reports and Field Safety Corrective Action (FSCA) reports. According to MEDDEV 2.12/1, an incident report must be filed if a device malfunction, deterioration in device performance, inadequate instructions, or inadequate labeling results in death, serious injury, or may lead to death or serious deterioration in state of health if it were to recur. The incident must be reported to the Competent Authority (CA) of the member state where the incident occurred. In Germany that implies a report to the Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) by the physician involved in the case.

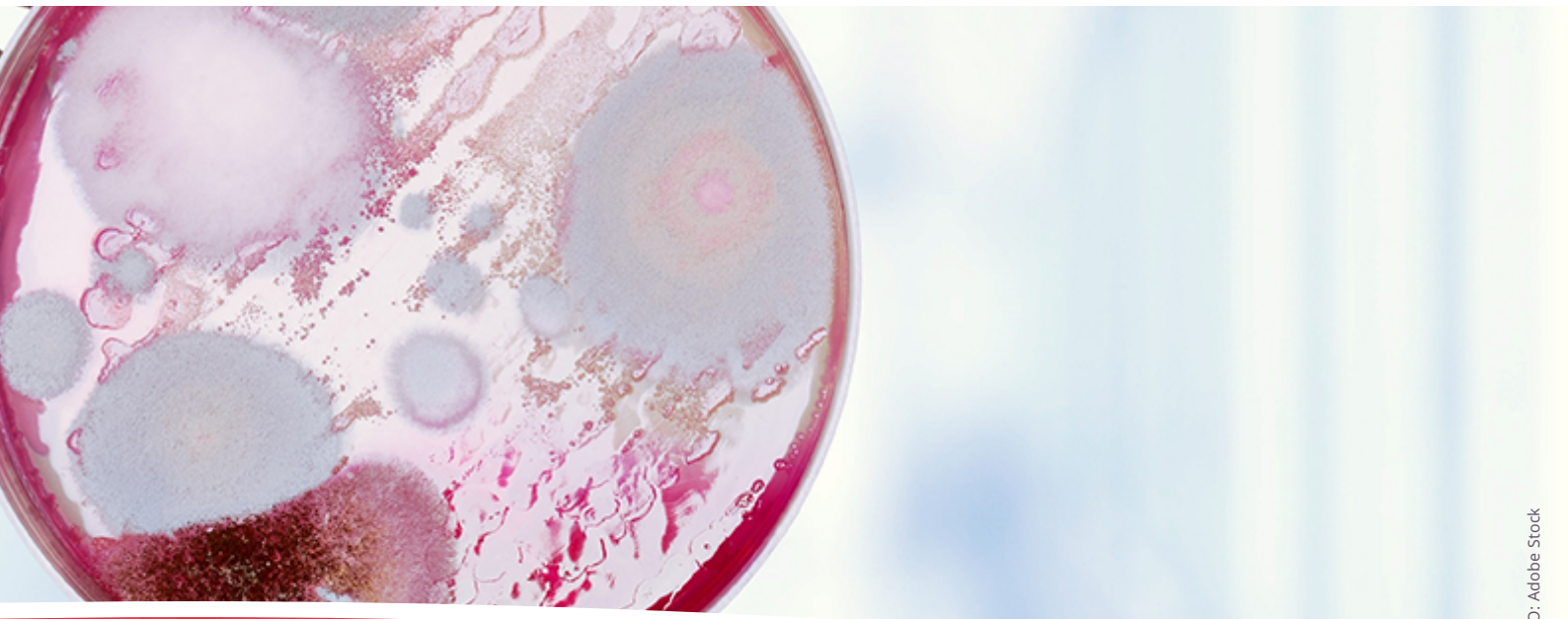
The »Post Marketing Clinical Follow-Up« is a continuous process that updates the clinical evaluation of a whole case series which is the assessment and analysis of clinical data pertaining to a medical device to verify the clinical safety and performance of the device when used as intended by the manufacturer. In a PMCF, it is crucial, that not only patient data of cases with incidents are reported but full case series. Only by this, the extent of a problem can be evaluated.

Both are important parts of the »Post-Market Surveillance« process but require different access pathways to the problem.

Whilst in a vigilance case, a swift reporting and a detailed analysis of the involved implant, (sometimes including in-vitro biomechanical tests etc.) are of crucial importance, in a PMCF study the reality in use of a medical device is documented with a focus on a high number of cases involved in a study. Also, adverse events that are not obviously connected to the medical device in question are observed, to ensure to find indirect negative influence in the treatment of injuries or illnesses.

Currently, reporting of specific incidents requires significant workload from the treating physicians. Although these are certainly interested in good and safe medical products, time constraints in nowadays hospital workplaces make a heavy under-reporting quite likely. In Germany, the physicians have to file a report to the BfArM every time a suspected incident occurs.

As the strength of a medical registry is clearly the sampling of large series of patients as a consecutive series, it was decided to focus on the aspects important for a PMCF in this feasibility study but keeping the requirements of incident reporting in mind as it is important both for manufacturer and physicians.



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5. OBJECTIVES AND ACTIVITIES OF THE MDR PILOT

With the currently known information, it became clear that a successful MDR-PMCF project must take a series of rules, regulations and guidelines into consideration:

- EU MDR 2017/745
- EN ISO 13485: 2012 clauses 8.2.1 and 8.5.1
- MEDDEV 2.12/1 Rev. 8, Medical devices vigilance systems
- MEDDEV 2.7/1 Rev. 4, Clinical evaluations
- MEDDEV 2.12/2 Rev. 2, Guidelines on Post-Market Clinical follow-up
- PMS Sources NBMED 2.12 rec 1

The following goals were followed during the feasibility project:

- collect device-specific clinical data continuously
- identify medical devices unambiguously
- allow for immediate awareness for Adverse Device Events (ADEs)
- provide clinical data that fulfils the MEDDEV/MDR requirements
- possibly be an effective source to generate periodic reports (e. g. PSUR, SSCP)
- is applicable in daily clinical practice
- automatically performs reporting of device related complications in clinical practice to the relevant authorities (e. g. BfArM in Germany)

The clear intention of our project is, that the MDR-PMCF system should be running inside the framework of a multinational registry of fracture treatment and that all data generated for a PMCF should be included in the registry anyway or should be added automatically.

Objectives of the MDR pilot:

- Develop a device-specific minimal data subset translation to fulfil the above requirements
- Develop and test run a data input process, with focus on medical devices clinical data, e. g. via barcode-scanner
- Apply legal, ethical and data privacy requirements
- Develop IT infrastructure on the registry side (UMG) and hospitals side (UKSH, Orbis)
- Adapt the electronic Case Report Forms (eCRF) of the pilot study for data collection (UKSH, UMG)
- Apply pilot to first patient data

On work package level, these activities lead to the following list of sub-activities that were completed in the course of the pilot project:

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WP	CONTENTS
1.a	Translate Post-Market Surveillance Terms to Items in the BFCC Registry and Complication Classification
1.b	Clarify MDR requirements
1.c	Assemble minimally required Dataset for MDR Pilot
2.a	Identification of Data in HIS
2.b	Identification of Data Safety Issues of Patient Data
2.c	Identification of Data Safety Issues of Employees Data
2.d	Data Safety Concept
3	Translate ADE/SADE etc. into Complications (Grading & Items)
4.a	Identify of the universal one-to-one barcode
4.b	Identify Scannable Implants & Problem cases
5	Generate Clinical Test Data
6	Hip Registry Data Output Identification (AT Register)
7	Define Data Pathway
8.a	Concept for Data Output to Industry (format, on the fly?)
8.b	Concept for Data Output to Registers (e. g. Alterstrauma, FFN; Monthly?)
8.c	Concept for Data Output to Medical Staff
8.d	Draft Style/Contents of Reports for 8 a–c
9.a	Acquire test Data
9.b	Validate test data against Case notes (Define Parameters of Interest!)
9.c	Formulate Follow-up plan to detect complications
10	Test Run of follow-up (Mailing)
11	Final Report

Table 1: List of sub-activities

6. SCOPE FOR MDR FEASIBILITY

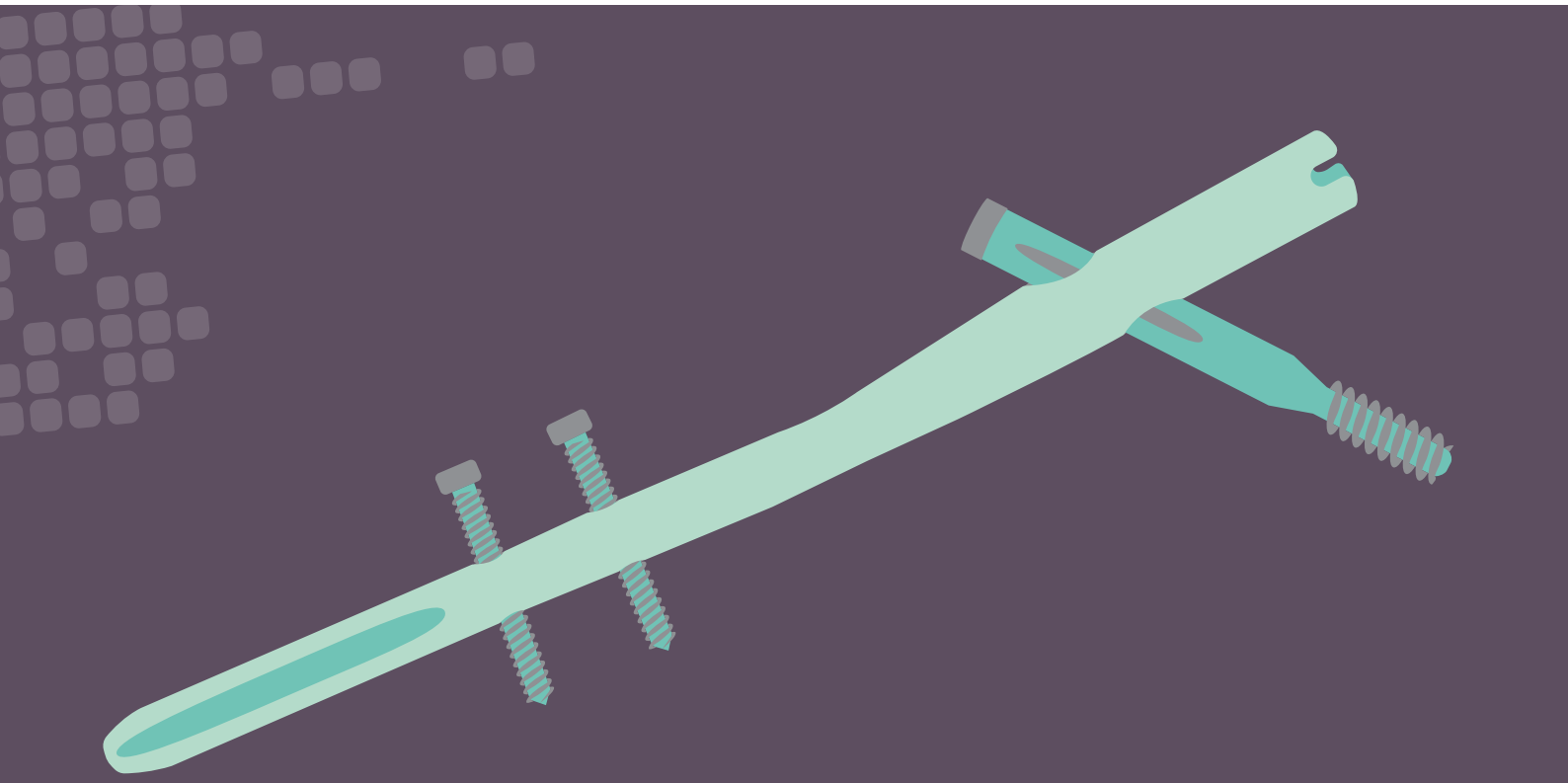
6.1. Current requirements

UKSH determined the scope of implant data already recorded in the clinical documentation process. As part of the legally required disclosure and information obligations to patients already fundamental information on implants used must be recorded and handed over to the patient (»Implantatpass«). In addition, UKSH has an obligation to document unused implants even if they have not been used due to product defects (defective implant, non-sterile implant, etc.). Finally, UKSH aims for a way to electronically transfer the information collected in the HIS to the BFCC registry.

6.2. Selected medical devices

For the purpose of the feasibility study and for the specification of device related adverse events, a specific implant system was chosen. It could thereby be assured that all necessary information (full set of Global Trade Item Number [GTIN] etc.) was available to conduct the feasibility.

In the UKSH hospital sterilization unit, only sterile pre-packed implants and instruments are fed into the hospital database. Large tools or implants that are delivered non-sterile are currently noted in an excel file that is not connected. Small non-sterile implants like screws that contain a micro-lasered GTIN number are not recorded at all.



6.3. Medical device specific data

6.3.1. Clinical complications

For a PMCF, all types of adverse events occurring during the treatment period observed have to be noted. The BFCC Fracture Registry is capable of doing so. To cluster device related complications into groups meaningful for the MDR Pilot Study, an export file translating the BFCC complication items into terms used in PMCF studies was formulated (see Figure 2). In the active system of the BFCC Fracture Registry, clinical complications are subdivided into 9 groups of which one is called »Implant and Device«. This subgroup has 13 items describing the complication related to a device. To distinguish between an »adverse device event« (ADE) and a »severe adverse device event« (SADE) a grading is mandatory to be filled in as a complication has been selected. Grade A and B relate to ADE and grade C, D and E relate to SADE. The device used during the procedure can be found in the »treatment« section. To more specifically relate a device to a complication, the comment section in the complication chapter can be used.

The output of a complication can either be numerical (0 to n) or descriptive (broken implant, postoperative, reoperation).

The following example represents a SADE in form of a broken implant nail with the descriptive parameter followed by the numerical code:

1 Compl_occurance = yes [1]
2 Compl_event = implant_device [02]
  a. Implant breakage [02.03.03]
  ← *note: this is the detailed description of the advice related complication*
3 Compl_grading = severe [C]
  ← *note: reoperation was necessary*
4 Compl_timing = postoperative [4]

To search for any SADE in the registry, one could filter this event by the following method in R statistics: filter (UKSH_all_data_final, compl_occurance == »yes« & compl_event_02 != »NA« & compl_grading == »C«). This can be further linked to a specific medical device by adding ([...] & device == »x«).

If it is wanted to know whether the patient was re-operated due to a broken implant, one would have to look into the treatment section of the registry:

5 treat_type = re-operation [2]
6 treat_reasonreop = broken_implant [5]

All these parameters linked to a patient can be independently filtered from the registry. This is necessary to allow complication identification via proxy methods. It is important to note, that the specific complication in case of a direct advice related complication has to be linked to at least one of all registered/implanted devices of the medical case.

Within the test system of the registry, a novel mask has been set up under the name of »Medical Device Regulation«. It basically resembles a fusion of the two sections named above. Instead of a comment section to relate devices to complications, a direct description of the ADE is possible. The adverse events are rather related to technical aspects of the device than medical complications.

ADE should not be up to the data entering person but rather a result of a clinical status. For that reason, a classification for complications was developed to draw clear margins between SADE and ADE. To solve this issue, technical adjustments to the complication section would be recommendable to integrate the mask from the test system into the BFCC registry. These would involve additional complication events as well as a copied mask from the treatment section to the complication department with all used medical devices to indicate which items were related to complications.

	ITEMNO SHORTNAME	VALID_VALUES	VALUDE_CODE
ADE — ADVERSE DEVICE EFFECT	43 treat_type	conservative, rehabilitation	1, 3
	46 treat_material	titanium, stainless steel, PEEK, other	0, 1, 2, 3
	47 treat_implant_type	implant type 0	0–17
	48 treat_manufacturer	company A–F	0–5
	85 treat_implant_identifier		
	73 compl_occurance	yes	1
	86 compl_timing	intraoperative, postoperative	2, 3
	88 compl_event equals 2	Loss of correction, Complications with endoprosthesis, Loosening of endoprosthesis, Dislocation of endoprosthesis, Fracture of endoprosthesis, Complications with implants, Implant loosening, Implant migration, Implant breakage, Implant exposure, Implant bending, Secondary dislocation, Other complication with implants or devices	02.01.00, 02.02.00, 02.02.01, 02.02.02, 02.02.03, 02.03.00, 02.03.01, 02.03.02, 02.03.03, 02.03.04, 02.03.05, 02.05.00, 02.06.00
	77 compl_grading	A — No Treatment required B — Minor Treatment but no prolongation of or no extra Hospital Treatment	0, 1

	ITEMNO SHORTNAME	VALID_VALUES	VALUDE_CODE
SADE — SERIOUS ADVERSE DEVICE EFFECT	43 treat_type	surgery, conservative, re-operation, rehabilitation	
	46 treat_material	titanium, stainless steel, PEEK, other	0, 1, 2, 3
	47 treat_implant_type	implant type 0–17	0–17
	48 treat_manufacturer	company A–F	0–5
	85 treat_implant_identifier		
	73 compl_occurance	yes	1
	86 compl_timing	intraoperative, postoperative	2, 3
	88 compl_event equals 2	Loss of correction, Complications with endoprosthesis, Loosening of endoprosthesis, Dislocation of endoprosthesis, Fracture of endoprosthesis, Complications with implants, Implant loosening, Implant migration, Implant breakage, Implant exposure, Implant bending, Secondary dislocation, Other complication with Implants or devices	02.01.00, 02.02.00, 02.02.01, 02.02.02, 02.02.03, 02.03.00, 02.03.01, 02.03.02, 02.03.03, 02.03.04, 02.03.05, 02.05.00, 02.06.00
	77 compl_grading	C — Prolognation Hospital Treatment D — Lasting major disability E — Death	2, 3, 4

Figure 2: Translation table from Fracture Registry complications into MDR Adverse Device Effects

7. RESULTS OF THE MDR FEASIBILITY IMPLEMENTATION

7.1. Results of activities of the MDR pilot

Specific activities were planned for the MDR pilot as described in chapter 5:

7.1.1. Develop a device-specific minimal data subset to fulfil the above requirements

Successfully a MDR device specific translation code for complications that are now clustered as AE, SAE, ADE and SADE have been generated.

The Common Minimal Dataset (CMD) of the BFCC Registry has been discussed with several stakeholders in the area of fracture treatment. The results showed, that the dataset applicable for the BFCC may also be sufficient for an MDR PMCF project. In July 2018, the BFCC MDR group met with the »German Society of Orthopedics and Traumatology (DGOU)« to discuss this outcome. The DGOU decided to implement the proposed CMD into their planned »Fraktur-Implantateregister« to make MDR relevant PMCF studies feasible.

7.1.2. Develop and test run a data input process, with focus on medical devices clinical data, e. g. via barcode scanner

Since the UKSH is required by law to collect data on the implants permanently implanted, document them and finally transfer them to the patient in the form of the so-called »Implantatpass«, every implant used at the UKSH has been documented manually patient-specific for several years. Now for this purpose, barcode scanners were implemented in the surgery areas of the UKSH. With these, the code of the implants can now be scanned from the wrapping and recorded, immediately prior to implantation into the patient, in the HIS.

The direct link with the material management ensures that on the one hand the necessary manufacturer and supplier information is recorded on a daily basis and on the other hand that necessary reorders of products are automatically initiated. Since the introduction of the scanner registration, implants are recorded for economic reasons. Within a specific form (see Figure 3), the physicians are asked to document the reasons, of not using the provided implant. However, the reasons for the non-implantation are only recorded with a not mandatory free-text field, so that the quantity and quality of this documentation is modest. In principle, however, it would be possible to implement the necessary documentation in the HIS. An essential component should then be a reference definition of the ADE, ideally in form of an international standard, supported by all manufacturers.

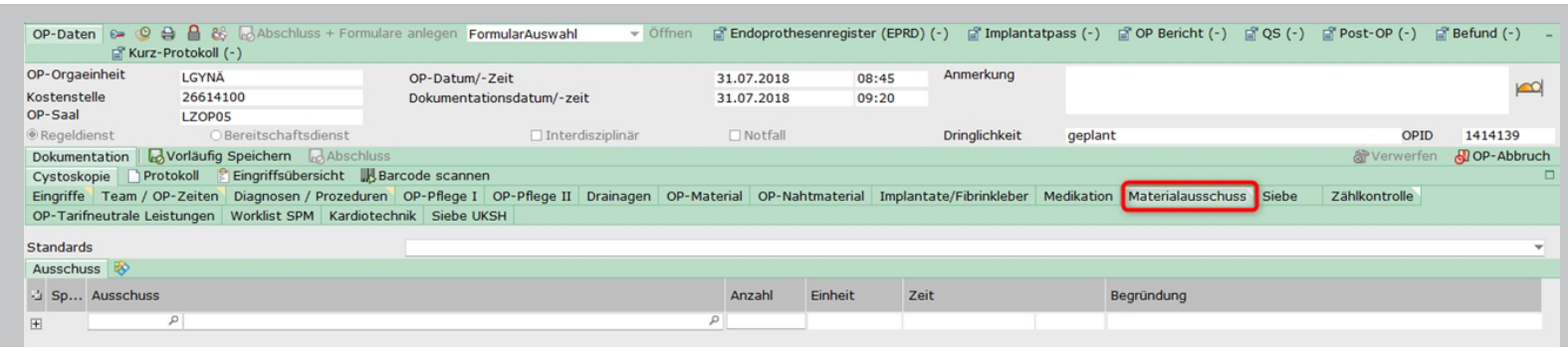


Figure 3: Documentation form for unused implants

7.1.3. Unique Device Identification

Today every manufacturer labels its products with different codes, representing individual information (i. e. type of implant, legal manufacturer, lot-number etc.). As part of the MDR an universal identification becomes mandatory: the Unique Device Identification (UDI). The traceability of devices by means of a UDI system based on international guidance should significantly enhance the effectiveness of the post-market safety-related activities for devices, which is owing to improved incident reporting, targeted field safety corrective actions and better monitoring by competent authorities. It should also help to reduce medical errors and to fight against falsified devices. Companies use global trade item numbers (GTIN) to fulfill the UDI requirements. At UKSH for all implants the GTIN is documented

a in the material management when received and
b in HIS when implanted or discarded

Associated with the GTIN many of the information provided by the manufacture are stored. This information can be linked with the associated information of the patient, who received the implant. To transfer this to the large scale of all manufacturers' codes of all available devices, a large workload would be required. Here the future will show if the database created by the EU authorities will have the required im-/export functions, otherwise the whole process will be challenging and has to be repeated for each hospital's HIS.

7.1.4. Develop IT infrastructure on the registry side (UMG) and hospitals side (UKSH, Orbis)

No additional development work is needed for the HIS at the moment. For the data export from the HIS, query routines have been developed which, in their basic design, can be used for future data exports — especially if the recording of ADE will be possible in standardized form.

7.2. Informed consent and the MDR pilot

During this study, it was necessary to identify and apply legal, ethical and data privacy requirements that have to be taken into account for the MDR pilot study.

To comply with ethical and legal regulations a modularised, uniform informed consent (IC) form and patient information is used within the BFCC project. Both documents are available in English, German and also in Estonian, Lithuanian and Polish as translations from the English version.

For IC version 1.2.0 (valid since 13.05.2018) specific MDR-adaptations were made to meet all requirements for this MDR pilot. For example, IC version 1.2.0 states clearly that »data will be used for medical, clinical and device related research« and that the patient consents to »upon request, to release such data in a pseudonymized form to third parties for scientific, clinical and/or device-related analyses«.

While those adaptions were made to meet the purpose of the MDR feasibility, no real patient data was used for the feasibility study. Only mock test data sets were used for the MDR pilot run.

7.3. Data entry at UKSH

If a surgery requiring an implant is planned, the necessary materials will be provided in advance in the operating room. During surgery, the materials to be implanted are presented to the surgeon by the operating room nursing staff. Before unpacking the material, it is assigned directly to the patient and the current stay via the barcode scanner in the operation room (OR) documentation (part of the HIS). Thus, the implant is part of the clinical documentation of the patient. To ensure the correct documentation, the information of the scanned material is displayed in a screen to the OR nursing staff.

The instruments, tools and small consumables are currently scanned as a whole packaging unit, sometimes containing more than 20 instruments or tools or more than 50 screws. If complications occur with these devices, tracking is only possible straight away after the procedure and in a lengthy process.

If the material is not implanted for whatever reason, the scanned information of the implant is recorded in a separate documentation form (»Discarded Materials«). In a free-text field of this documentation form a reason for the non-use can manually be entered.

After completion of the operation, the responsible surgeon is obliged to validate the documentation of the performed operation, including used materials, and to complete it by his electronic signature.

Basically, the current method is able to meet the requirements for MDR-compliant documentation of ADE — before and during an operation. However, purely free-text documentation of possible complications of the material results in unsatisfactory limitations: stringent recording cannot be ensured; without compulsory documentation, there are information gaps. In the future, standards for the definition of ADE, supported by the industry, should allow extended opportunities for implementation in HIS.

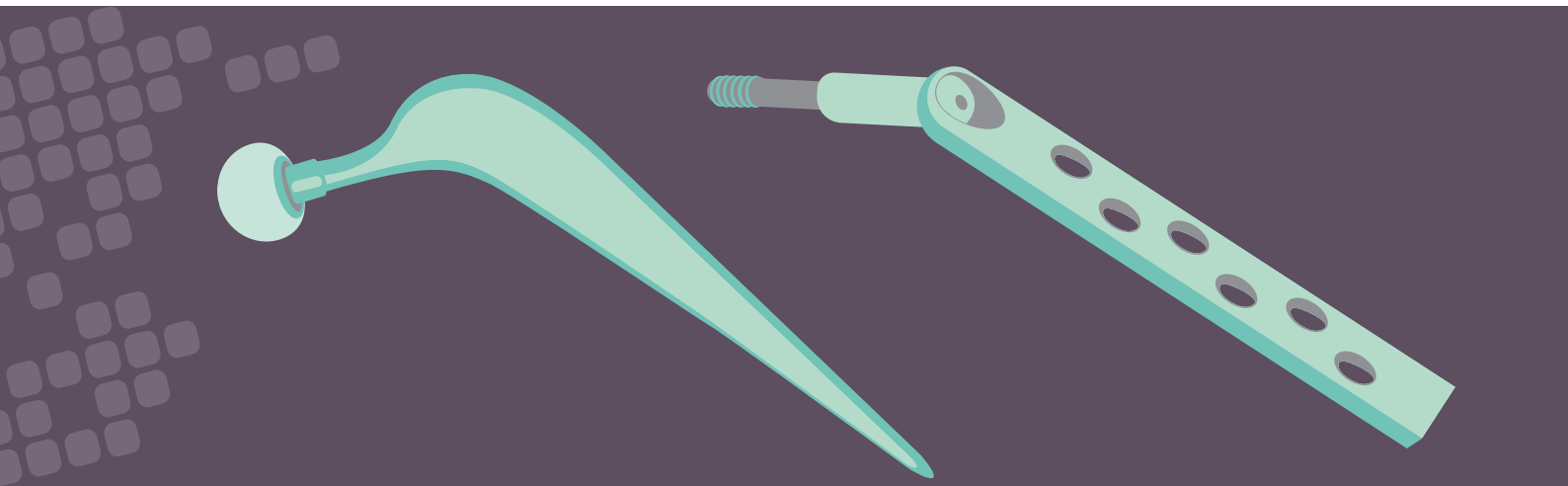
7.4. Connecting device data to the medical case

A core content of this pilot study was the connection of the device related data supplied by the manufacturers in form of excel charts and the digital identifying data (on the sterile packing of the devices in form of a barcode) with the medical data of the mock patients.

The general feasibility was shown swiftly in the beginning of 2018, shortly after connection of the barcode scanner system.

But it also became clear, that the huge HIS with sometimes > 3000 data items per patient in some cases makes it very difficult to find singular items in the database. The structure of this database is complex and is used on a daily routine. In order to not interfere with the running workflow and to test run in a safe environment, a mirrored system of the hospital system was build up and used for the MDR pilot.

By that method we were able to create test cases, and extract data related to specific implants.



7.5. Data transfer to BFCC registry

In order to pilot BFCC's fulfilment of the new EU MDR, an additional eCRF was implemented in TFRP's test system only. This eCRF is solely used by UKSH for this MDR pilot and is designed to receive implant information by UKSH (e. g. via data import or manual data entry). In a possible (major) scenario the implant information is recorded during surgery by scanning the implant's barcode, decoded by the HIS and sent to TFRP. The BFCC's MDR pilot tests the feasibility of this approach in a minor scenario: Within BFCC's MDR-pilot-eCRF (see Figure 4), the implant information (GTIN), production information, and implant description can be supplemented by eventual ADEs. If an ADE occurred, the time of occurrence (pre-/intra-/post-op as well as number of days before/after surgery, if applicable) and the type of ADE can be specified. This enables product-specific analyses for medical implants.

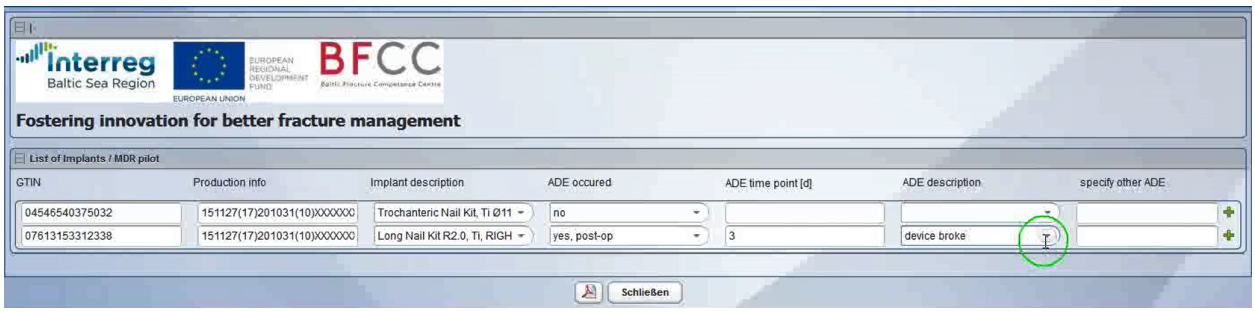


Figure 4: Draft for eCRF for MDR pilot in test system

However, the eCRF as of yet is not designed to automatically decode barcoded information, but allows to specify the used implants by selection from a predefined catalogue. In this pilot implementation the catalogue of implants is restricted to one product line. The complete dictionary of data items and allowed values added to BFCC's data set is listed in the file »MDR pilot, new data item«.

Consequently, in this (minor) scenario, the GTIN and production information from the implant's barcode must either be imported using the specific XML-scheme for this eCRF, or entered manually. The selection of ADEs in this minor scenario is limited to the following pre-defined ADEs:

- malfunction of the device
- device broken
- device damaged
- device bend or deformed
- packaging of device damaged
- part missing
- incorrect labelling of device
- misuse of the device
- other ADE

Thus, this approach also tests the ADE's categorisation.

PHOTO: Adobe Stock

7.6. Data analysis and output

The data sampled during the test of the MDR pilot was exported to csv-files and evaluated via the statistical programming software R (Version 3.5.1) in the R-Studio system (Version 1.1.456) with additional packages (reshape2, Version 1.4.3; dplyr, Version 0.76; tidyr, Version 0.8.1; gplot2, Version 3.0.0; PairedData, Version 1.1.1; readxl, Version 1.1.0; readr, Version 1.1.1; scales, Version 1.0.0; eeptools, Version 1.2.0; mondate, Version 0.10.01.02; operator.tools, Version 1.6.3) and their dependencies.

After importing the csv-files containing the data, filtering steps are conducted to remove identifying data and all data items irrelevant to the scope of the analysis. A unique pseudonym is created for the patients including the BFCC-pseudonym and the ID of the patient's visit ensuring to have all items regarding a possible ADE identifiable in the dataset and for correctly reporting the number of patients with and without ADE. Furthermore, all data items are removed that are not related to the implant manufacturer to prevent unwilling disclosure of data.

Additionally, a list with GTIN and full implant name that was provisioned is also imported to be able to display the correct product names in the report.

After processing the Markdown-document in the R-Studio system either locally for testing purposes or in a virtual computer in the BFCC computer centre, a report in form of a html-file is generated displaying the data related to the specific manufacturer and the supplied GTIN-list:

- The number as validated cases in the registry during the reporting period with implants from the manufacturer and matching the GTIN-list
- The number of patients with ADE
- The number of patients without ADE
- An interactive list of implants that were used (including the number of ADE related to the device)
- An interactive list of the implants (including the batch information) with ADEs

An interactive list of the Implants (including the batch information) with ADEs specifying the occurred ADEs (see Figure 6)

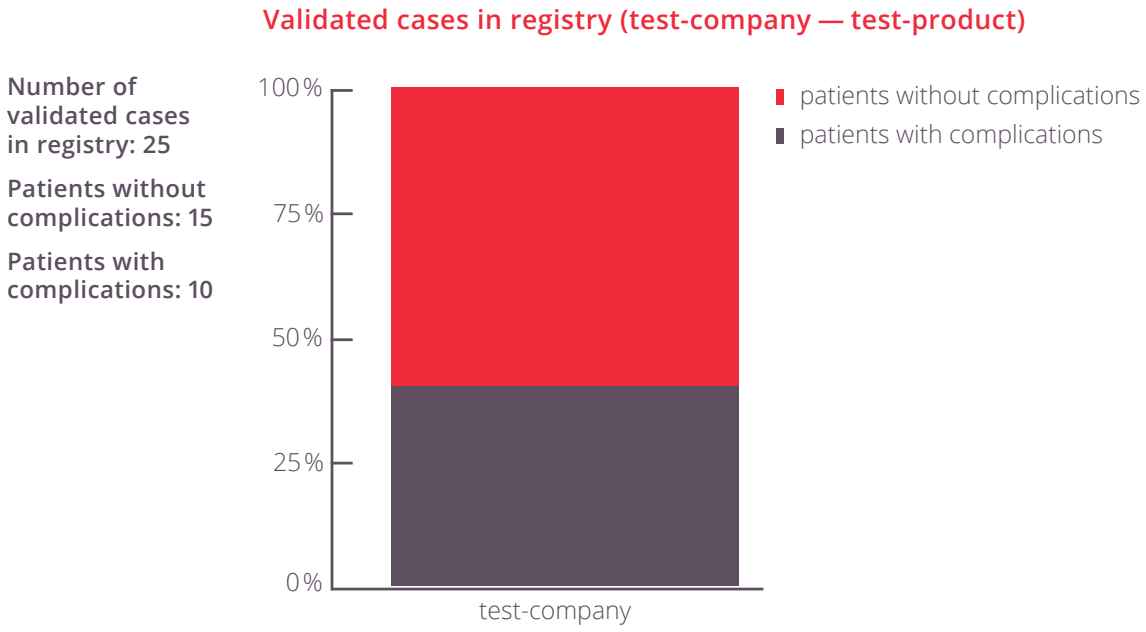


Figure 5: Sample figure showing the percentage of patients with and without complications

ADEs (Test-Company)

GTIN <chr>	Batch <chr>	Complication <chr>	Implants with ADE <int>
4546540374844	GH6737H64	malfunction of the device	1
4546540374844	GH6737H64	packaging of device damaged	1
4546540374844	GH6797T35	device bend or deformed	1
4546540374844	GH6797T35	packaging of device damaged	1
4546540374844	JK3489H89	device bend or deformed	1
4546540374929	K1634F89	device broken	1
4546540375001	K1234Z89	packaging of device damaged	1
4546540407719	JK8749J3	malfunction of the device	1
4546540407719	JK8749J3	packaging of device damaged	1
4546540409188	AX378H67	device broken	1

1-10 of 10 rows | 2-5 of 5 columns

Figure 6: Screenshot of the mock html-report with the download option for the result data

Additionally the result data is included in the html-file and can be accessed via a download link at the end of the report (see Figure 6).

The parameters of the report (i. e. reporting period, manufacturer, language of the report, GTIN-list) are defined as options for the R-markdown document. Thus, automation of the report generation can easily be facilitated.

The html-report can easily be distributed via email or encrypted email.

PHOTO: Adobe Stock

8. LESSONS LEARNED FROM THE MDR PILOT

8.1. Involved IT systems need to be capable and compatible

In this MDR pilot, three systems were involved: the HIS of UKSH, the software tools of the Trusted Third Party (TTP) of University Medicine Greifswald and web-based study and data management software (CentraXX), configured and provided by the Institute of Community Medicine Greifswald. The TTP tools are embedded via interfaces into the CentraXX software. Data exchange between the HIS and CentraXX regarding medical data requires mapping of divergent data structures — EHR-data in the HIS and the registry-specific data set in CentraXX, e. g. with different data items, types and allowed values. This mapping needs to be implemented by each HIS delivering data to the registry. CentraXX provides an XML scheme as interchange format for this purpose. When new data items are added or existing data items are changed, this mapping has to be adapted. Since different HIS have different or divergent medical data items and im-/export formats, a uniform format, exchange interface and data items for MDR specifications should be defined and implemented in the following projects to enable clinical partners to add data automatically and with less manual effort to the registry. This would also ensure the planned major scenario of the MDR usage within a fracture registry. In addition, it seems necessary to integrate the documentation of treatment complications and ADEs more tightly.

8.2. Re-usable instruments and non-sterile packed implants may be challenging

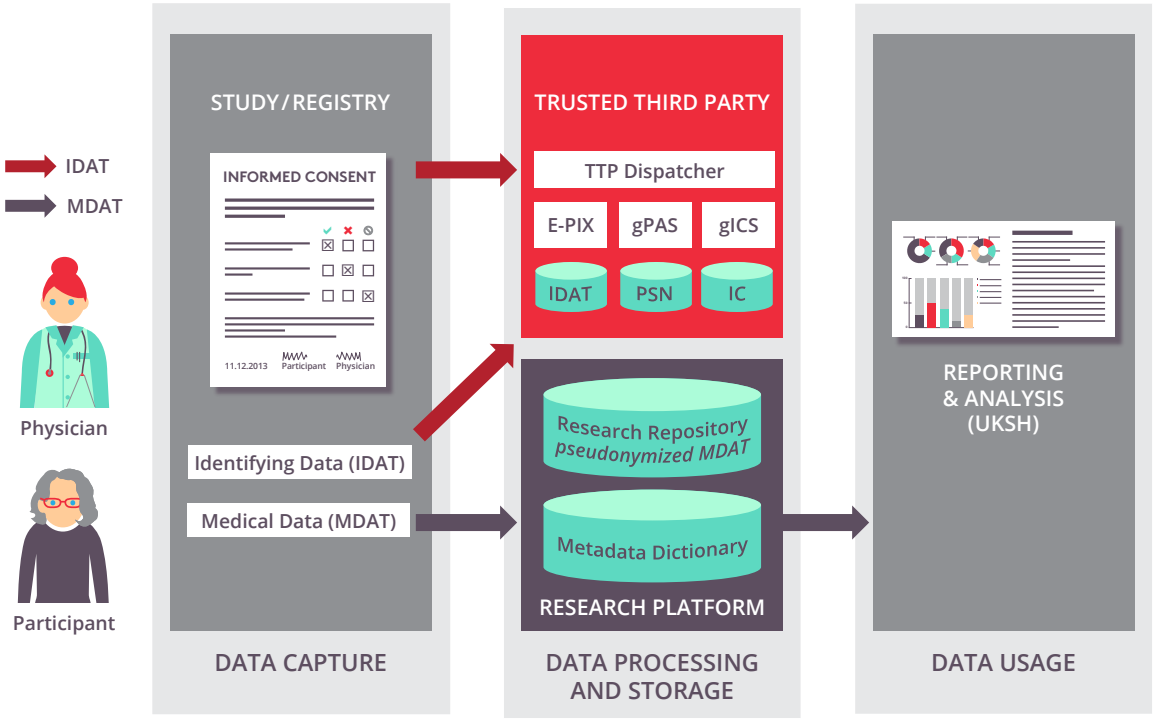
In this proof-of-concept we have focused on registering of uniquely identifiable implants. However, there are also implant sets whose individual components are no longer differentiated when performing an operation. Registering the ADE of such implants as part of a kit requires new concepts for identification and unambiguous assignment. Both, manufacturers and users are called upon.

PHOTO: Adobe Stock

8.3. Missing data

Basically, key data on implanted medical devices are already being documented in hospitals today. Focus thereby are the requirements of clinical documentation. In addition of recording the clinical condition of the patient in order to be able to optimally shape his further care — both inpatient and outpatient — also economic aspects play a role in the registration of implants. Often these are especially expensive products, which supposed to be considered as a cost factor, especially if they are discarded. While recording of problems or incidents with clinical relevance to the patient is mandatory, the registration of ADE is currently rarely required. Accordingly, the data situation is currently incomplete. This problem could be addressed by a standardized classification of ADE and mandatory documentation in case of occurrence.

Another problem that became clear in the context of the proof-of-concept is the risk that problems, that only arise outside the clinic, may not end up in the central registry. This will be the case when patients turn to other physicians for problems. This can be caused for example by loss of trust. This problem might be narrowed down by connecting all practitioners to the registry and by assigning a unique identifier to the patients, which is already implemented and managed by BFCC's TTP.



Based on: Bialke M, et al. A workflow-driven approach to integrate generic software modules in a Trusted Third Party. Journal of Translational Medicine 6. 2015;13(176).

Figure 7: Relationship between TTP, TFRP and external data sources

The conducted proof-of-concept has also shown that the manual input of the implant and the associated relevant clinical data into the registry as a downstream registration process is associated with a considerable effort (compare Figure 7). This method is not suitable for ensuring a comprehensive documentation of MDR-relevant information into the registry. However, most of the relevant data are recorded in the HIS during the clinical treatment and are already available in electronic form. UKSH's experiences showed that the standardized XML-based import-/export process needs to be further adapted for the BFCC as a standardized interface for the register. With such a software solution, it will be possible to automatically transfer the necessary MDR data, clinical data and the ADE (if they are already recorded in the HIS) to the registry (see Figure 8).

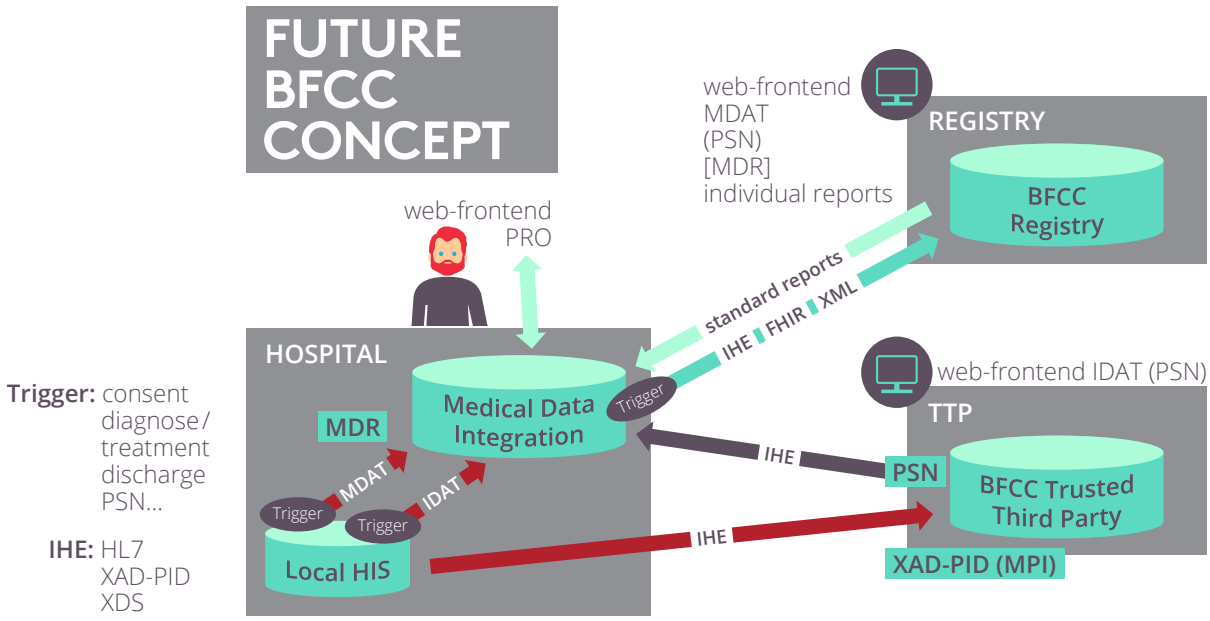


Figure 8: Future BFCC registry concept

8.4. Automated patient related data-extraction form hospital IT systems

We could establish, that >95% of all data required for the BFCC-registry and the MDR-Pilot study are already stored in the large hospital IT database.

Some data items have been found twice in different locations, some even three times. For data extraction feeding a registry, it became clear that our time frame for this pilot study was too small to identify all required items in the database. Also challenging are datasets that are double. Here it has to be decided if the HIS should be changed (which is not a very easy task) and if not, which of the available items to choose. It is the necessary to trace, on which occasion and by which specialty of employee the data are stored and what the purpose is. Only then, the decision can be made on a case to case basis.

9. OUTLOOK

We could clearly show that extraction of treatment data that is linked to certain implants from a hospital data system is possible in a meaningful fashion.

Also, it appears clear, that the data generated is significantly less cost intensive than clinical research projects are. Furthermore, the results indicate that some of the regulatory needs in the frame of a PMCF can potentially be met using a registry data source.

But there are still many aspects in such a project that need further insights. It appears clear, that a registry based PMCF can be a useful addendum to manufacturer's PMS systems. Currently, it cannot be used as a regulated reporting system of clinical complication and device related adverse events in the way that it could replace incident reporting systems to fulfil notified bodies expectations of a correct vigilance process. That will possibly change in the future.

The addendum of a PMCF procedure of a registry requires only a few extra data entries or specifications. Nevertheless, the question remains who will take the costs for this as the data entry adds effort and time on clinical staff — a question that health politics, health insurers and the medical product industry will have to answer.

PHOTO: Adobe Stock

MDR PILOT

10. USED ABBREVIATION

ABBREVIATION/TERM	DESCRIPTION
ADE	Adverse Device Event
BFCC	Baltic Fracture Competence Centre
BSR	Baltic Sea Region
CMD	Common Minimal Dataset
eCRF	Electronic Case Report Form
EU	European Union
GDPR	General Data Protection Regulation
GTIN	Global Trade Item Number
HIS	Hospital Information System
IC	Informed Consent
IDAT	Identifying Data
MDAT	Medical Data
MDR	Medical Device Regulation
OR	Operation Room
PMCF	Post-Market Clinical Follow-up
PMS	Post-Market Surveillance
PSN	pseudonym
PSUR	Periodic Safety Update Report
R & I	Research and Innovation
SADE	Severe Adverse Device Event

ABBREVIATION/TERM	DESCRIPTION
SSCP	Summary of Safety and Clinical Performance
TFRP	Transnational Fracture Registry Platform
TTP	Trusted Third Party
UDI	Device Identification
UKSH	University Medical Center Schleswig-Holstein
UMG	University Medicine Greifswald

11. LIST OF FIGURES

12. LIST OF TABLES

KEY FACTS

- Duration: 36 months (2016–2019)
- Total budget: about EUR 3.6 million
- Programme: Interreg Baltic Sea Region
- Fund: European Regional Development Fund
- Flagship project of the EU Baltic Sea Region strategy

PROJECT PARTNERS

- Life Science Nord Management GmbH (Germany; Lead Partner)
- Stryker Trauma GmbH (Germany)
- University Medical Center Schleswig-Holstein (Germany)
- University Medicine Greifswald (Germany)
- Sahlgrenska University Hospital (Sweden)
- ScanBalt fmba (Denmark)
- Lithuania University of Health Sciences (Lithuania)
- LifeScience Krakow Klaster (Poland)
- University Hospital in Krakow (Poland)
- University of Tartu (Estonia)
- Tartu Biotechnology Park (Estonia)
- Bone Index Finland Ltd. (Finland)
- BONESUPPORT AB (Sweden)

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