Use of an electronic Dropmeter for a phase 3 study, and compliance data integration into an EDC system

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aixial
AN ALTEN COMPANY
Théa
Driving innovation
Kali
CARE

ALTEN in Life Sciences

6.9%
of Revenue

>1000
Engineers/Scientists

Our Top Customers

Pharma. & Biotech
Actelion, BMS, GSK, Novagali, Merck, Novartis, Pfitzer, Sanofi, Servier, Shire…

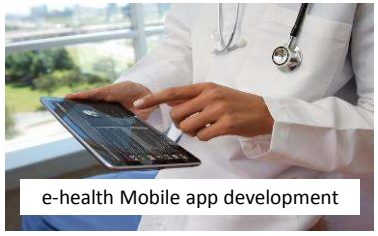
Medical technology
Baxter, Carmat, GE Healthcare, Philips Healthcare…

Food & Cosmectic
Danone Resarch, L'Oréal, Nestlé…

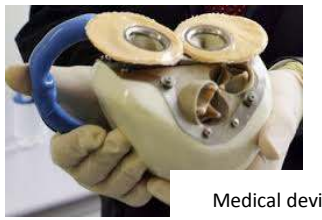
Our 2017 main projects

Production Automation
IT system validation

Mechanical design &
Embedded software



e-health Mobile app development



Medical devices

Production system
Qualification & Validation

Clinical Trials management

Théa Group

- Théa is an independent pharmaceutical company specialized in the research, development and commercialization of eye-care products (Turnover 2017: 465 M€).

- Based in Clermont-Ferrand, the laboratory has continued to expand by opening nearly 25 subsidiaries in Europe, Russia, North Africa and South America.

- Théa is an independent family group, developed from a Research and Development start-up

Strong internal and external growth

AIXIAL strategy is to be the European mid-Tier leader CRO as an alternative between the global CROs and the boutique CROs

Objective
1 000 Employees by 2019

2017:
480
Employees
40M€
Turnover

2013 :
ALTEN selects Life Sciences as a strategic diversification and growth vector

2013-2016
Acquisition and integration of complementary mid-sized CROs (APROVA, ADDS, AIXIAL, LINCOLN)

2017- 2018 :
Strong internal growth in line with Alten objectives

External growth through new acquisitions (Synergy, geographical coverage)

- A – THEA STUDY
- B – KALI – VENDOR SPECIALIZED IN DATA DIGITALISATION
- C – FROM DIGILITALISATION TO CLINICAL NUMERIC DATA
- D – COMPLIANCE DATA INTO AN COMPLEX EDC SYSTEM

Thea Study Context

Laboratoires Théa run a phase 3 study, focused on Dry Eye Disease:

- International, multicentre, randomised, 1-year study
a double-masked period with 2 parallel groups

- Carried out on approximately 100 sites in 20 countries

- Including 450 patients

Thea Study Context

- **Electonic Dropmeter use**:
  - Dropmeter is provided during the run-in period to the patient and use during all the study period
  - The Dropmeter aims at:
    - Measuring the number of Artificial Tears (AT) eye drops instillations,
    - Evaluating AT instillation compliance and possible impact on efficacy data.

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Who we are

Kali is based in Silicon Valley

The team
Is a blend of experts in AI, machine learning, cloud and smart sensors

World class investors: Aptar Group, Signatures Capital, Heuristic Capital, Amidi Group

Intellectual property: 29 patent applications

What we do

We collect millions of data points about how people take their medications

We apply analytics and extract valuable insights

Kali unique competitive advantage

Analytics are based on **real-time** data collected by Kali sensors

Providing robust **AI**

Kali smart and connected products

Eye drop

Smart pill box

Dermatology and cosmetics

Kali Dataflow

Personalized intervention

Kali device collects objective data

Interactive intervention

Data integration

Dosing regularity and adherence patterns

Kali Benefits

CLINICAL TRIALS

FASTER

SHORTER

MORE EFFICIENT

PATIENTS MARKET

MAKES EXISITNG MEDICATION MORE USEFUL

ENABLES BETTER TREATMENT DECISION

- A – THEA STUDY
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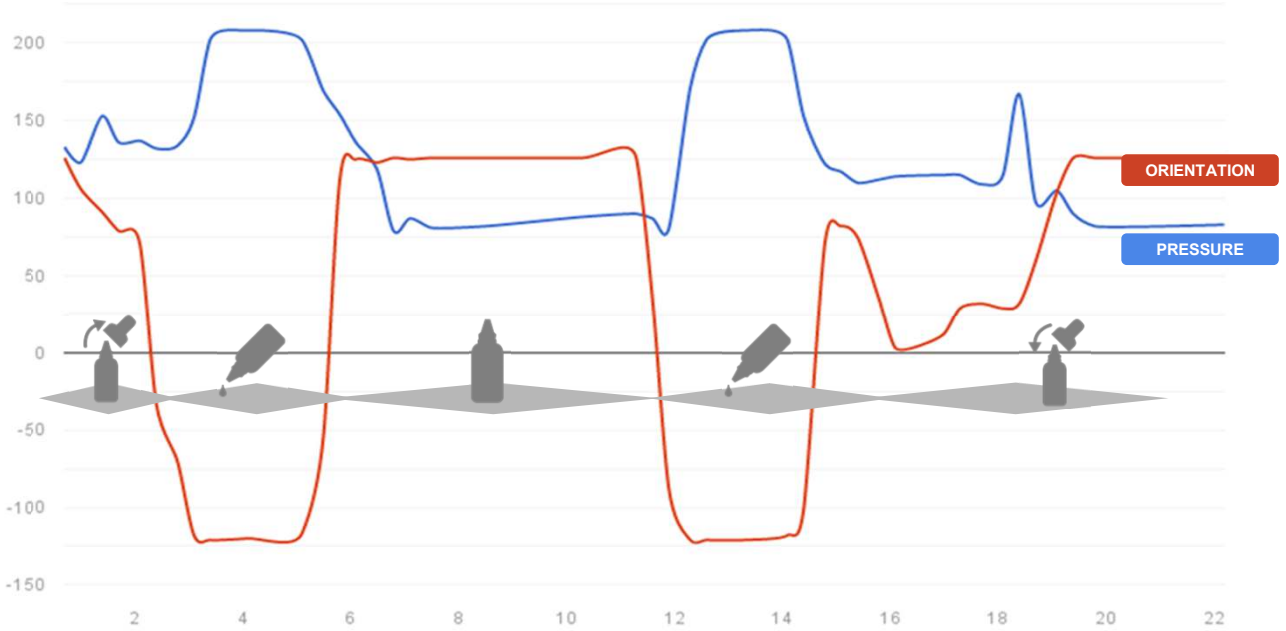
Definition

- Digitalization is the process of converting information into a digital (i.e. computer-readable) format.

- In the study the primary information relative to AT instillation is the electric signals that are recorded and transformed.

Kali sensor provides real-time and objective data



Dropmeter features

- The device (Dropmeter) will record each and every use of the AT eye drop container and store them locally.
- The device is synchronized with its base through Bluetooth connection.
- Data are transmitted to the KALI server from the device docking station via GSM transmitter.
- The internal memory embedded in the device can store around 3 weeks of collected data.

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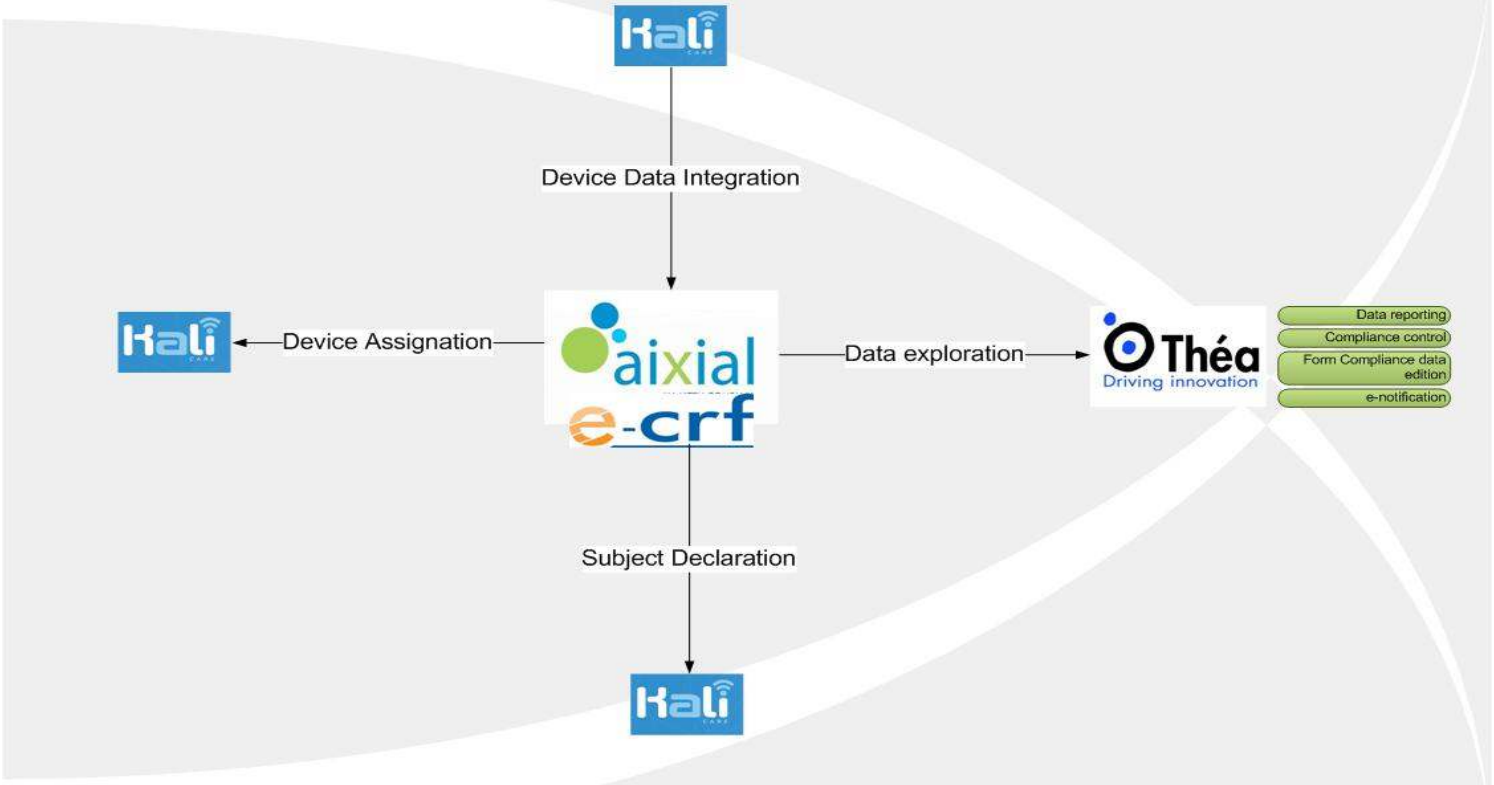
Data Exchanges

- The data exchanges performed through webservices, and especially using APIs (Application Programming Interface) developed by KALI.

Category of Data Exchanges



Patient Identification & Recording

- Acknowledgement of association of a device to a patient is performed through the e-CRF system.
- Identification data of the patient are to be created in the KALI database, whatever the status in the study (run-in, enrolled, or screen failure).
- “Timezone” is available as a dropdown list automatically filtered on the time zone’s values available in the country of the selected center.

Patient Identification & Recording

- In response to this data transfer, KALI will send back to Aixial the patient “RxMonitorId”.
- “RxMonitorId” is the patient identification in the KALI database.
- “RxMonitorId” is the common key indentifier

Device Assignation

- A device number is associated for each patient with “Run-in” or “Randomized” status,

- All other patients do not needed a device association:
  - Screen Failure,
  - Not Randomised patient,
  - Withdrawal patient,

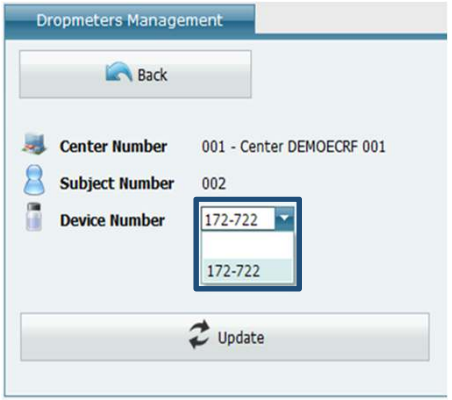
- e-notification are sent to remind to the site to associate a device to the patients .

Center Device Assignation

- Center-Dropmeter association:

Already associated to a patient

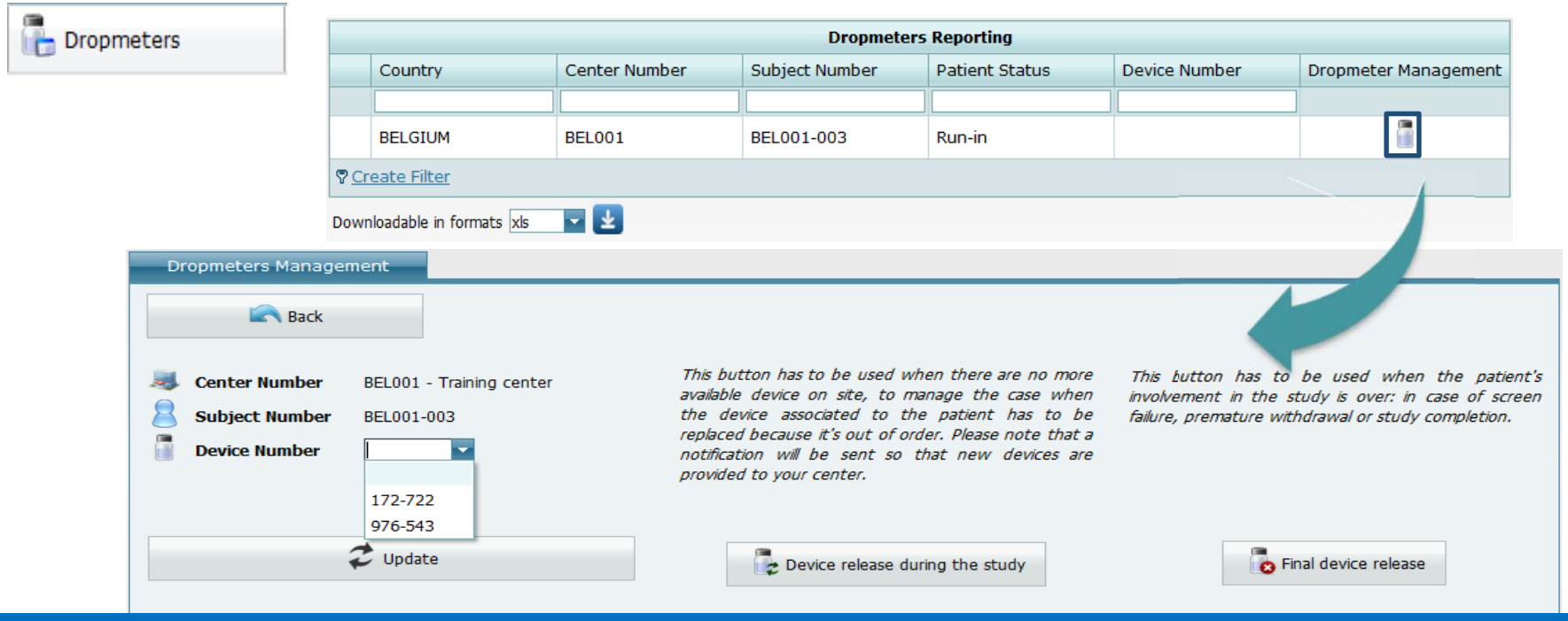
Available for patient association



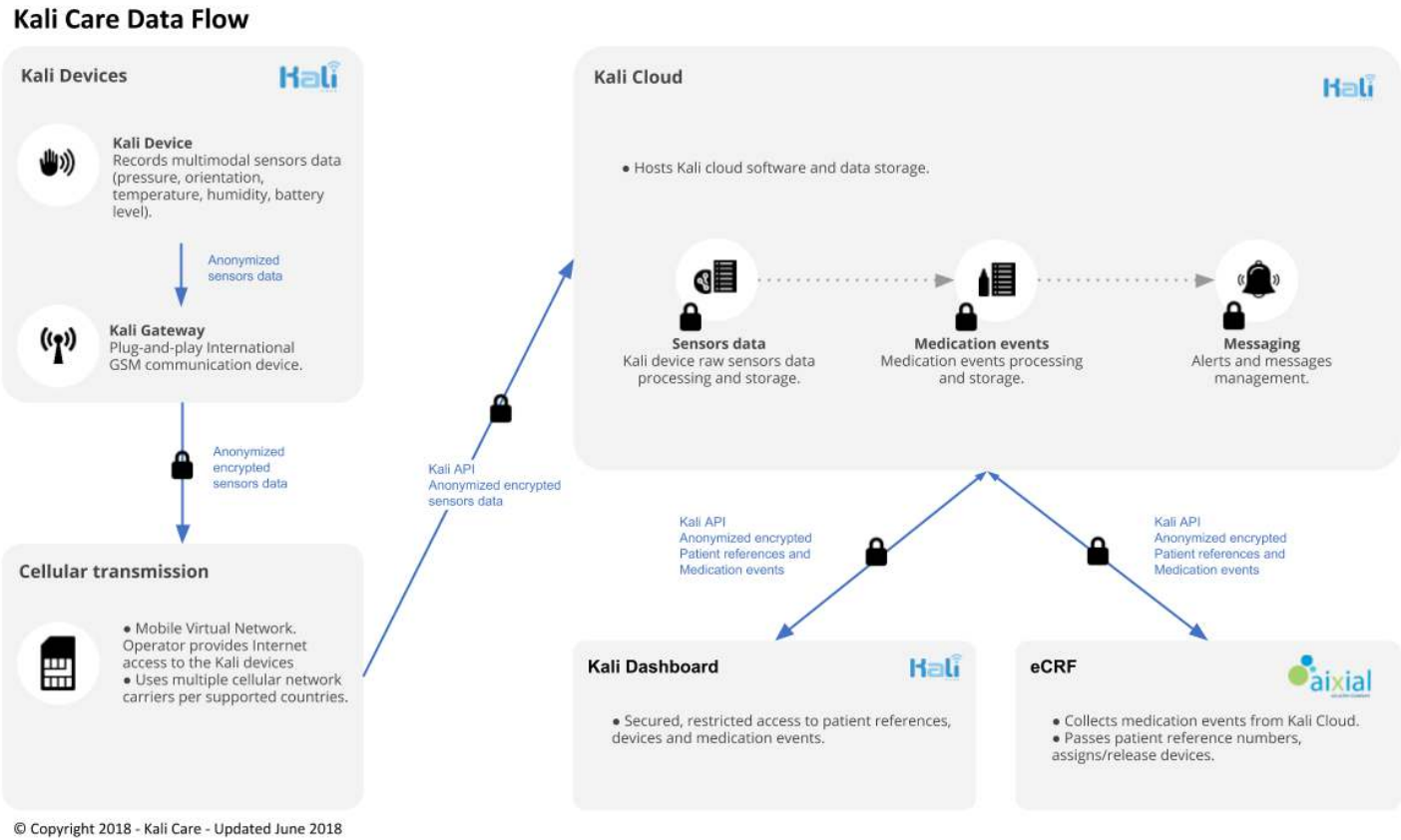
Center-Dropmeter association performed by CRAs
All other users have Read-Only access

Patient Device Association De-Assignation

- Patient dropmeter association-De-association performed by the investigator:



Data Integration: From raw data to daily instillation



Data Integration: From raw data to daily instillation

- A batch runs hourly and retrieves the events for each device using the API method.
- The data recorded by the sensors are transmitted from the device to Kali cloud where Kali proprietary machine data processing detect the drops.
- A confidence index is one indicator generated by the algorithms that indicate the probability of a drop based on historical contextual data such as device calibration and patient gesture.

Data Integration: From raw data to daily instillation

Drop data

Instillation data

Daily Instillation data

Kali CARE

First Mapping

e-crf

Second Mapping

e-crf


```
"LocalTime":"2016-06-13T22:30:00",
"TimezoneId":null,
"InsightId":111302,
"DeviceId":"DeviceNumber]",
"InsightTypeId":1,
"TimeStamp":"2016-06-14T05:30:00",
"Summary":"Took Medication",
"Confidence":0.9456445,
"RuleName":"Kali Drop basic
monitoring",
"RuleId":1,
"AccountID":"[AccountID]",
"DeviceUserId":"[DeviceUserID]",
"PatientNumber":"[SubjectNumber]",
"Activities":[],
"MonitorId":"[RxMonitorID]"
```


Distinct uses within a five-minute period will be considered as part of the same instillation

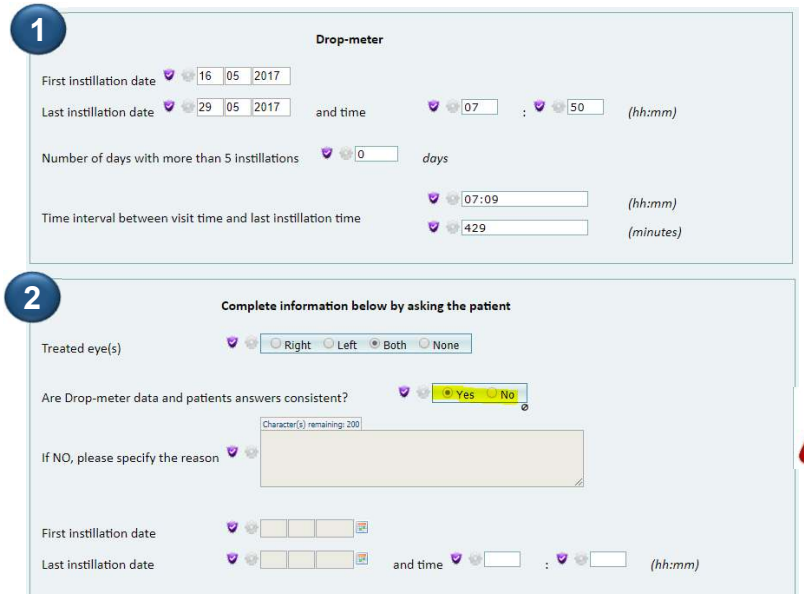
SubjectNumber	DeviceNumber	InstillationDate	InstillationTime
ARM001-079	449-733	2017-07-14	11:30:40
ARM001-079	449-733	2017-07-14	17:20:49
ARM001-079	449-733	2017-07-15	12:43:06

Calculation of number instillation per day

SubjectNumber	InstillationDate	NbInstillations
ARM001-079	2017-05-26	4
ARM001-079	2017-05-27	4
ARM001-079	2017-05-28	5

Data Integration in e-crf forms

- Dropmeter data are integrated in specific visit from.
- Form divided into two parts:



1 – Dropmeter integrated data

2 – Patient information if different from dropmeter data

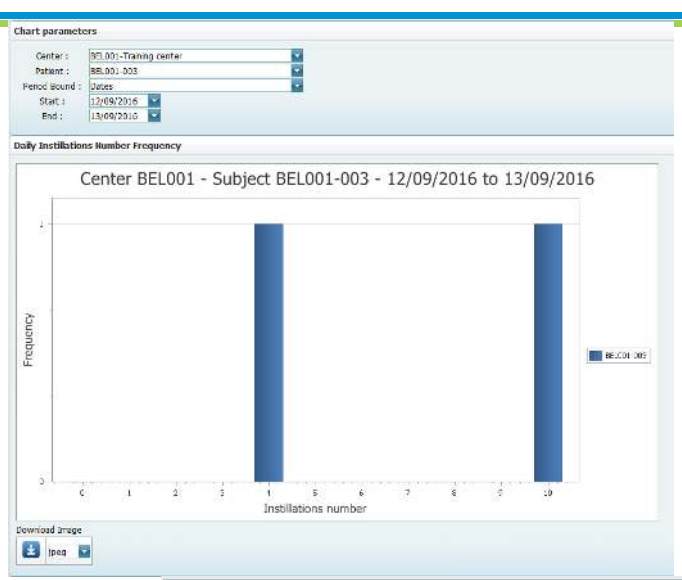
Patient information part has to be fully filled if at least one of the dropmeter integrated data is not consistent with patient's answers.

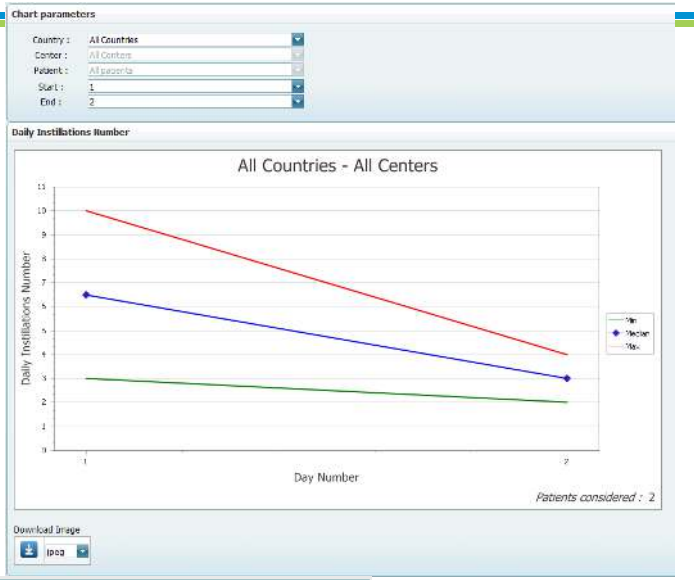
Data Integration in e-crf forms

- As soon as the form is saved, the "Drop-meter" part data will remain unchanged even if new dropmeter activities are applicable.

- The investigator will have the possibility to "Refresh drop-meter information“ in order to access to the must updated data.

Data reporting





Instillations listing

Country	Center Name	Center Number	Subject Number	Instillation Date	Instillation Time
BELGIUM	Training center	BEL001	BEL001-003	12/09/2016	09:37:08
BELGIUM	Training center	BEL001	BEL001-003	12/09/2016	09:49:25
BELGIUM	Training center	BEL001	BEL001-003	12/09/2016	10:09:26
BELGIUM	Training center	BEL001	BEL001-003	12/09/2016	10:29:29
BELGIUM	Training center	BEL001	BEL001-003	12/09/2016	10:46:05
BELGIUM	Training center	BEL001	BEL001-003	12/09/2016	11:08:22
BELGIUM	Training center	BEL001	BEL001-003	12/09/2016	11:16:33
BELGIUM	Training center	BEL001	BEL001-003	12/09/2016	11:27:27
BELGIUM	Training center	BEL001	BEL001-003	12/09/2016	11:34:20
BELGIUM	Training center	BEL001	BEL001-003	12/09/2016	11:51:06
BELGIUM	Training center	BEL001	BEL001-003	13/09/2016	13:28:25
BELGIUM	Training center	BEL001	BEL001-003	13/09/2016	13:37:22

e-notification

- Bases on the Kali API the following information can be returned in order to adress e-notification:
  - Low battery: The battery level is stored for each device.
  - No dropmeter connection attempt: When the device works correctly and is near its base, it contacts the server at least every two hours. Otherwise e-notifications are sent.
  - Depending of the study period: if the last transferred data dates back from 2 or 7 days, an e-notification is edited,

Conclusion

- Digitalisation of data is essential, but must be associated with strong associated services.
- Digitalisation is less critical than data handling into the EDC system.
- Data Managers are key players for implementation of innovative technologies

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