REAL WORLD DATA
LATE PHASE STUDIES

QUALITY CONTROL OF DATA COLLECTION IN OBSERVATIONNAL STUDIES

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Agenda

- Objectives
- Observational Studies
- Quality of Data Collection of Observational Trials- Quality Control process
- Conclusion

Goal of the presentation

- Key drivers of data collection in observational Trials
  - **Maintain the naturalistic setting of data collection by participating physicians which means to adhere to the real practice setting**
  - **Ensure adherence to patients/subjects' rights in observational studies**
  - **Ensure data quality**

- Describe the Quality control process during the course of the data collection

Observationnal studies

- Observational studies are programs dedicated to better understand:
  - **Characteristics and state of a disease, product prescription or patient management care in real life setting:**
    - Cross sectional or Longitudinal
    - Retrospective or Prospective
  - **Depict Disease to assess; its prevalence, its burden by defining co-morbidities, risk factors, and subpopulations, patient management care by the healthcare professionals,**
  - **Examine treatment prescription,**
  - **Assess safety of prescribed Product in everyday clinical practice.**

Quality control (QC) Process

- The Quality Control process must be establish in accordance with the design and objectives of the study and the potential associated risks of quality on data collection mechanism:

  - **Ensure a timely and effective quality control on site adapted to the data collection flow**
  - **Detect and prevent issues in data quality**
    - Ensure the existence of patients / subjects in adherence with patients/subjects 'right pertaining to data privacy
    - Adherence to the protocol with focus on adherence to safety data collection requirements when applicable (product registries) .
  - **Implement appropriate corrective actions during the course of the trial**
  - **Leverage quality in all participating sites.**

QC process

- TOOLs and operational strategy
  - **Design QC Questionnaire (QCQ)**
  - **Determine Site oversight through eCRF**
  - **Determine On site quality control visit (site sample and visit frequency are to be determined)**
  - **Determine remote Quality Control**
  - **Error rate (completed QC Questionnaire versus database) availability /timely manner**
  - **Enrollment cap**
  - **Criteria leading to leverage Quality control on site**

QC process

- The QC implementation performed by on site visits and remotly.
  - **Completed QC Questionnaire (QCQ) and error rate assessment**
  - **Protocol deviation and cases of scientific misconduct must be identified**
  - **QC visit reports escalation; root cause analysis of deviations and error(s) if any**
  - **Adapted corrective/preventive actions according to error rate and deviations.**
    - Site Level
    - Country Level
    - Study Level

QC Process

- The study manual should describe before the implementation of the study:
  - **Site initiation strategy (i.e large cross sectional trial)**
  - **The percentage of participating investigators to be quality controlled at country level (with a minimum of 5% to 10%), rules for incremental QC visits**
  - **% of additional QC to be performed remotely (eQuality Control questionnaire should be completed in a blind manner; eCRFs of the corresponding site are made not accessible during the course of the remote Quality control interview)**
  - **The percentage and modality of remote QC**
  - **The threshold of included patients/subjects leading to start the QC process**

Methods

- The study manual should describe before the implementation of the study:
  - **The QC process progression in line with the study conduct and completion**
  - **The methodology of site randomization**
  - **The key data to be quality controlled against source document**

Modalities of remote QC activities

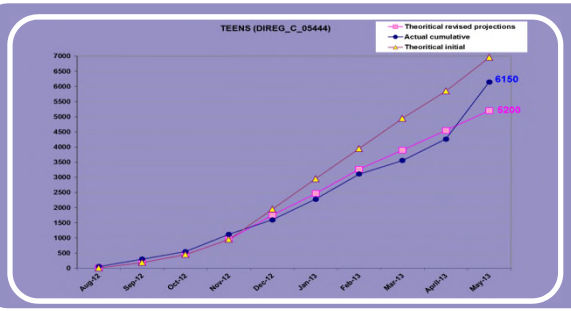
- The modalities of remote QC activities should also be described
  - **The tool used for this QC: eQC form and reports**
  - **Frequency of remote QC and rules for incremental QC**
  - **Site oversight and Criteria leading to QC i.e Missing data**
  - **Any issue raised must be appropriately documented**
  - **Study Core Team must be informed**
  - **Study core Team and Monitors Team are responsible to set up appropriate action plan to improve the quality at site, country and Study Level according as per need**

Example of one Cross sectional disease registry

- Argentina
- Algeria
- Denmark
- France
- Germany
- Egypt
- Hungary
- India
- Italy
- Jordan
- Lebanon
- Mexico
- Morocco
- Portugal
- Romania
- Russia
- Slovenia
- South-Africa
- Spain
- Sweden
- US

Patient population

- **Children,Teen & young adults from 8 to 25 year**
- **Over 21 countries, 230 active sites**



Recruitment period

- **FPI : August 14th 2012**
- **LPI : June 1st 2013**

- EUROPE
- INDIA
- LATIN AMERICA
- MIDDLE-EAST/NORTH-AFRICA
- SOUTH-AFRICA
- US

Enrolment status

- **6140 patients analyzed in**
- **8 regions/countries**

How the quality data check was performed?

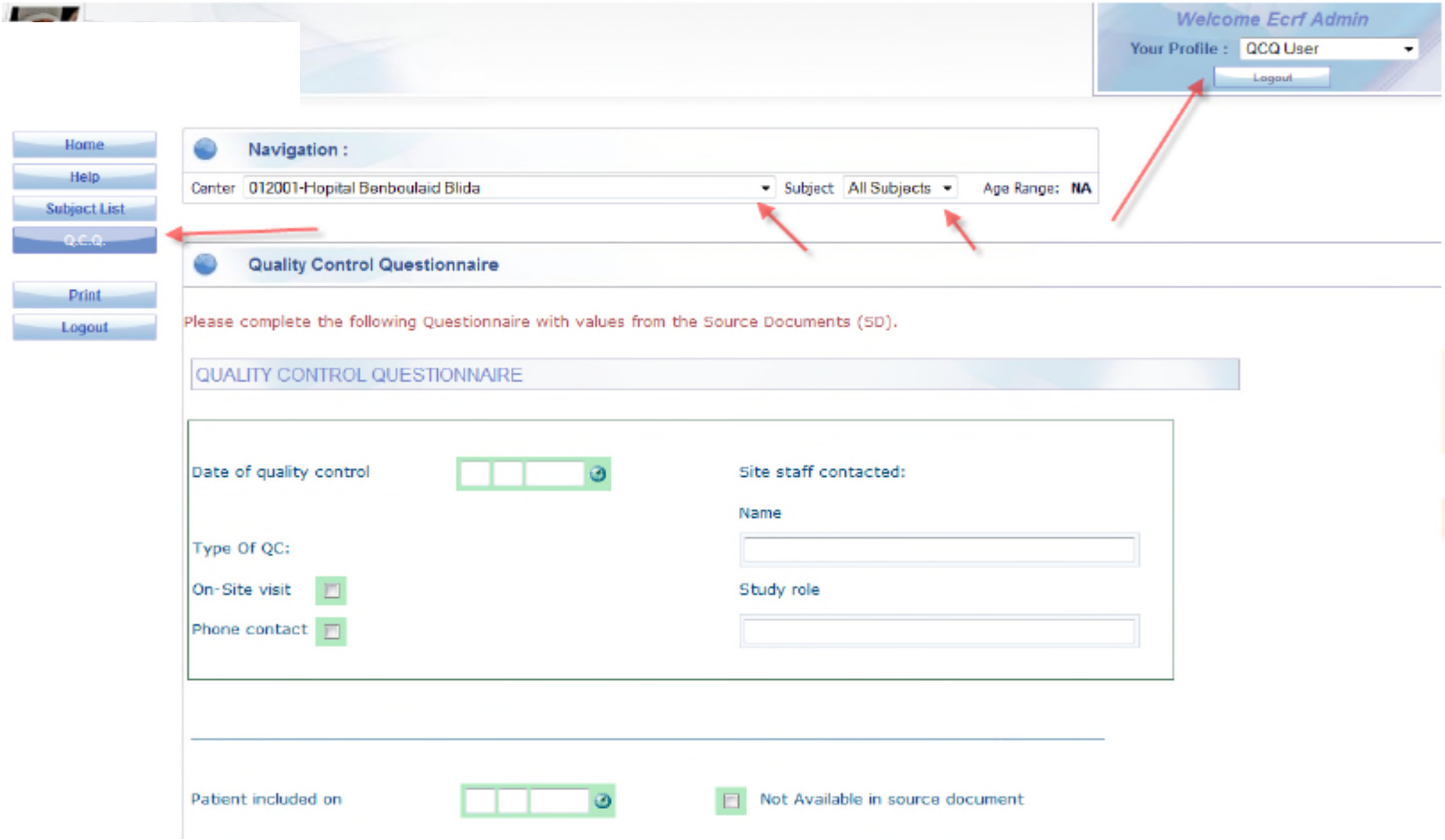
- **Site Oversight :**
  - **Specific surveillance on web portal done weekly by the monitors (CRA profile)**
  - **Monitors can generate queries, record deviation/ comment allowing corrective actions from the sites**
  - **All patients need to be reviewed on the following points at minimum to secure patients eligibility :**
    - **Adherence to class-age (25%-50%-25% in 8-12, 13-18 and 19-25 groups)**
    - **Potential outlier detection : Diagnosis date of T1D(at least one year prior to study entry and before 18 years)**
    - **Inclusion/exclusion criteria**
    - **Any deviation/missing data (i.e. speed of enrolment, missing key variable HbA1C, error in patient number allocation..)**
    - **QOL status e-crf module**

How the quality data check was performed?

- **Quality control (QC) process :**
  - On-site visit (10% of the sites visited at country level) performed when 20 to 70% of patients are included
  - Site randomly selected (QC rando list)
  - Documented by a QC questionnaire and QC visit report
  - e-QC : questionnaire available on-line in the e-crf system allows immediate information entry
  - Appropriate actions were implemented as per guidebook

QCQ form

QCQ form for QCQ user



Quality data measurement

Country	sites active	Patients enrolled	Selected sites for QC	Nb of pat QC'd	QC visit date	Consistency %	Remote Oversight
21	230	6140	31 (13%)	1825 (30%)	occurred between 20% and 80 % of enrolment rate*	78%- 99 %	All patients

- on-line system allows immediate reports availability and close surveillance of implementation since study set-up
- data extraction can be shared regularly with the monitors to discuss corrective actions (glucometer use issues, visit date..)

Experience feed-back

- Both systems were used to monitor the patient data quality and take corrective actions at site level when needed.

- Processes are **complementary** : whereas remote oversight helps to get a **global overview** on the site activity and detect specific trends (speed of enrolment, e-crf completion activity…), the QC process is **focused on consistency** between patient medical dossier and e-crf data.

Conclusion

- More than 100 observational Global or regional studies conducted by sanofi over 10 years
- The QC process conducted allowed control of data in Observational studies and ensured the quality and the respect of Data Privacy adherence within the naturalistic setting of Observational trials

  - **We observe:**
    - The importance of a regular training on the process
    - The benefice of using an e-CRF and on-line QC reports in e-CRF, especially for cross sectional studies with many countries when the set-up is done at the same time for all countries to be reactive enough
    - Most of correctives actions leads to perform queries, in some circumstances revise CRF completion guidelines and also re-train participating investigators

Questions or Comments