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Electronic transfer of sAE to Global Pharmocovigilance

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ABSTRACT

Serious Adverse Events (sAE) need to be forwarded to Pharmacovigilance (PV) by the investigators and this is usually done via paper, faxed to Pharmacovigilance. These days, however, more and more studies are set up in an EDC system for electronic data capture, which means that all needed subjects and related sAE data are available electronically as soon as they are entered in EDC. The original EDC data could be therefore transferred directly to Pharmacovigilance electronically and the investigator would not have to enter the data twice, which is also less error-prone.

INTRODUCTION

sAE data transfer and reconciliation is a time consuming and, if established as a manual approach, a resource intensive process. Therefore companies are looking into various options for automation or semi-automation of this process. The presentation will give an overview of different options for an sAE reconciliation process. In this context the first basic reconciliation approach is a manual listing comparison (one listing from PV data base and one from clinical data base) with no automation at all. Second option with also some business background from BSP is an integrated SAS based sAE report and tracking directly generated out of an extract from the Clinical database and the PV systems. The final, most desired option is an automated process from EDC to PV via E2B interfaces (either via direct interface or via SAS). In this paper, these options will be compared with each other and also an outlook of options and limitations for direct interfacing between an EDC and PV system will be discussed. Overall intention is to give the audience an impression of different options, hurdles and experience.

SERIOUS ADVERSE EVENT RECONCILIATION

Serious Adverse Events are reported to Pharmacovigilance by sending all sAE and further additional information to the responsible Pharmacavigilance unit of a sponsor. Usually the investigator fills in the paper page with sAE and complementary information and faxes this paper page to the local Pharmacovigilance unit. This has to be done for paper based CRF studies and also for studies which are set up in EDC, where no direct electronic interface to PV system is established. To ensure that Pharmacovigilance and clinical database contain the same sAE's, the two databases are reconciled in a two step approach.

RECONCILIATION BETWEEN GPV AND CLINICAL DATABASE

SEPARATE RECONCILIATION LISTINGS

For a complete manual and paper based approach all sAEs are forwarded to Pharmacovigilance, need to be entered and further processed in the according PV system. Afterwards listings from PV system and clinical data base need to be produced and manually compared. For bigger trials this processes should be done several times by PV and data management during the course of a study to avoid any delay of the clean data base, with respect to late query management, caused by the reconciliation process.

INTEGRATED RECONCILIATION LISTINGS (STEP1)

A much better approach, still with paper based sAE reporting, would be a combined comparison report as integration of PV and clinical data base. For this purpose BSP implemented a SAS macro to reconcile the two databases and create colored RTF reports. PVDB and clinical data base (CDB) are reconciled with a two step approach. First step is to match the subjects of both DBs. This means the subject identifiers between both databases must match. The second step is to match the sAE term for matching subjects. Serious AE's can be matched according the AE terms or

after coding via the MedDRA preferred Term (PT). At least close to the end of the trial all terms should have been coded, which also ensures a better match via MedDRA PT. An overview of match process is shown in Figure 1.

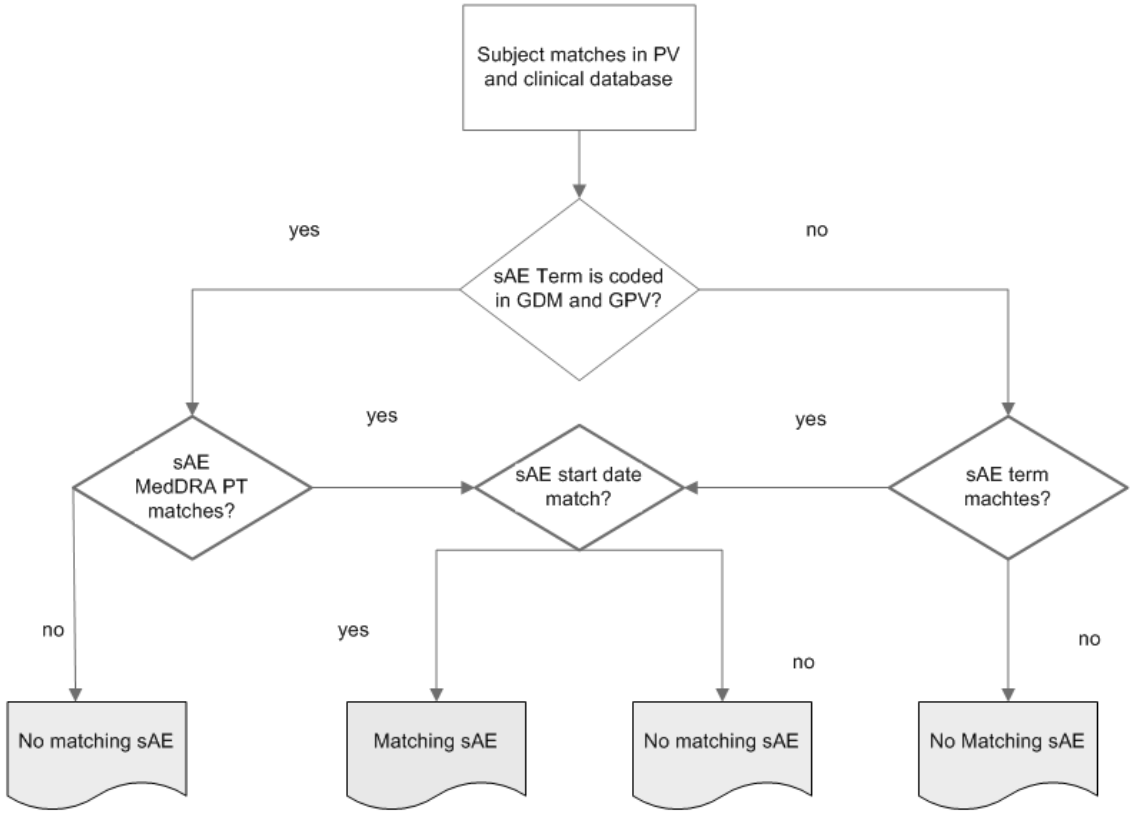


Figure 1

For each study sAE integrated reconciliation reports are produced. The reports are created in RTF format and all discrepancies are marked in red. These reports have to be produced on an ongoing basis until clean database and contain the following three outputs.

This first report compares information only on a subject level and lists only subject information.

Country	Trial unit	Clinical DB Random number	Safety DB Random number	Clinical DB Patient number	Safety DB Patient number	Birth Date	Death Date	Gender
C1	1	100	100	100	100	01FEB1940	-	Female [Male]
C1	1	200	200	200	200	23MAY1942	-	Female
C2	2	300	300	300	300	01DEC1931 [26DEC1931]	-	Female
C2	2	400	400	400	400	01NOV1967	-	Female
C2	2	500	501	501	501	01JAN1935	-	Female
C3	3	600	600	600	600	01AUG1934 [13AUG1934]	-	Female
C4	1	700	700	700	700	14DEC1942	12JAN2010	Female

The second report lists all sAEs from PV and clinical data base. Matching information is marked in yellow as well as discrepancies are marked in red. Key information that records matches is going down to MedDRA PT level and start date. All non-matching records will be not processed in the third report anymore.

Country	Trial unit	Patient/ random number	SOURCE	MedDRA preferred term	Adverse event	Start date of adverse event	
C1	1	301	GDM	Headache unspecified	Headache	07JAN2009	2: 1
C1	1	301	GPV	Headache unspecified	Headache, nos	07JAN2009	: ..
C2	6	600	GDM	Atrial flutter	ATRIAL FLUTTER, LEFT	22MAY2008	
C2	6	600	GPV	Atrial flutter	ATRIAL FLUTTER	20APR2008	?
C3	5	200	GDM	Humerus fracture	FRACTURE OF THE LEFT ARM BONE	20JAN2007	??
C3	5	200	GPV	Upper limb fracture	FRACTURE OF THE LEFT ARM BONE	20JAN2007	??

This third report compares all the other important sAE information, which was only listed in the second report, but no further differences highlighted. This last report is only created for sAE information, which is matching on the former report.

Country	Trial unit	Patient/ random number	Start date of adverse event	MedDRA preferred term	Adverse event	VARIABLE NAME	Safety database	Clinical database
C1	1	200	19JANV2007	Pneumonia	ACUTE PNEUMONIA	Action taken	93=Unknown	1=None
C1	1	200	10NOV2007	Syncope	SYNCOPE	Action taken	93=Unknown	1=None

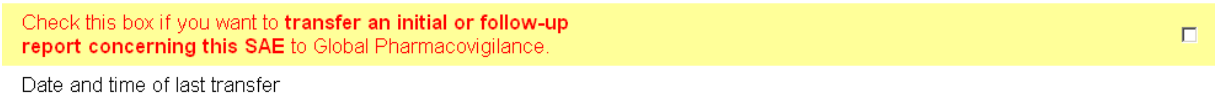
ELECTRONIC SERIOUS ADVERSE EVENT TRANSFER

Over the last years the majority of studies are set up in EDC. Almost all data needed in Pharmacovigilance are available electronically. Any additional data required by PV have to be included into the eCRF (electronic case form). There are two options to transfer the data electronically to Pharmacovigilance. One option is any kind of direct interface from EDC to PV. The other option is a SAS based solution, where the data are constantly extracted from EDC, transformed into E2B and transferred to Pharmacovigilance

SAS BASED SOLUTION TO TRANSFER SAES TO GPV

In EDC all needed additional items are included in the eCRF. The investigator has still to decide, whether the AE is a serious one and has to be reported to GPV or not. For that reason a tick box is added on the Adverse Event page for the investigator to choose when the AE should be reported. This mimics faxing the paper based sAEs to Pharmacovigilance . After the investigator ticked the box a date is stored on the page, which is important to know whether it is an initial or a follow-up sAE report.

Example of a tick box in an EDC



The original EDC data are transferred on a daily basis to the data management system. The SAS macro is based on the original EDC source data and PV receives the electronic data files once per day. The file format of the electronic sAE reports is XML based.
All items which are transferred to PV have to be E2B conformant in an extended format (E2B is a group within ICH and describes how Pharmacovigilance has to deliver their data to Health Authorities).

In a study CRF there might be information which does not need to be delivered to authorities, but GPV needs this information. These items get a special tag name but the name is close to the E2B tag name.

The picture below shows an example XML file with E2B tags. The last tag name (baypatientrace) is a tag which does not exist in the E2B.

```
<patient>
  <patientinvestigationnumb>1001</patientinvestigationnumb>
  <baypatientrandomnumb>12345</baypatientrandomnumb>
  <patientbirthdateformat>102</patientbirthdateformat>
  <patientbirthdate>19500101</patientbirthdate>
  <patientweight>88</patientweight>
  <patientheight>190</patientheight>
  <patientsex>1</patientsex>
  <baypatientrace>CAUCASIAN</baypatientrace>
```

Every day the SAS macro creates XML files and stores these files in an exchange area. PV can upload these XML files into their system. The investigator and the responsible site monitor receive an email with a PDF file of the sAE which was reported to PV. This PDF file is also stored in the study directory in the central data management system.

CONCLUSION (HEADER 1)

sAE's which are sent via paper to PV have to be entered and reconciled much more often than only close to clean data base. This is a very time consuming task for Pharmacovigilance and data management, especially as all information from paper AE complementary page has to enter manually into PV data base.
An electronic sAE transfer would reduce the reconciliation cycles and time. The investigator does not need to enter all sAE information twice. Nevertheless, a paper based reconciliation between PV and data management is still needed to ensure both databases contain the same information. As nearly all information should be exactly the same and data entry is only needed as exception the reconciliation effort should be minimal.

CONTACT INFORMATION (HEADER 1)

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