association for **clinical data management**

Machine Readable Study Schedule of Activities Definition

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December 2021

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Introduction

The June 2021 ACDM Hot Topic was dedicated to a presentation and discussion focused on some of the issues involved in developing and using machine readable study schedule of activities (SoA) that can be consumed and integrated into study definitions and operational processes. The subtitle 'Why are they still Visits?' highlighted one of the major issues in this area – that the protocol SoA presents a limited view of all the details required to automatically drive operational processes, such as EDC configuration. Presented by Andy Richardson from Zenetar; the talk and discussion focused on highlighting current SoA strengths and weaknesses and how these might be addressed to implement and exploit machine readable SoA into daily data management practice.

Key SoA Objectives

The principal objective of the SoA as presented in protocols is to define an over ideal sequence of contacts and activities in order to meet the objectives of the study. The level of detail is various, varying from extremely detailed descriptions of required tests, tasks, contact with study sites and personnel – explicitly stated, to almost no detail at all other than the general understanding that the data are to be collected – i.e. implied. Data specified by implication then need expanding and confirming, whilst those explicitly specified can be so complex as to challenge what exactly should occur. Neither are ideal for automating operational implementation.

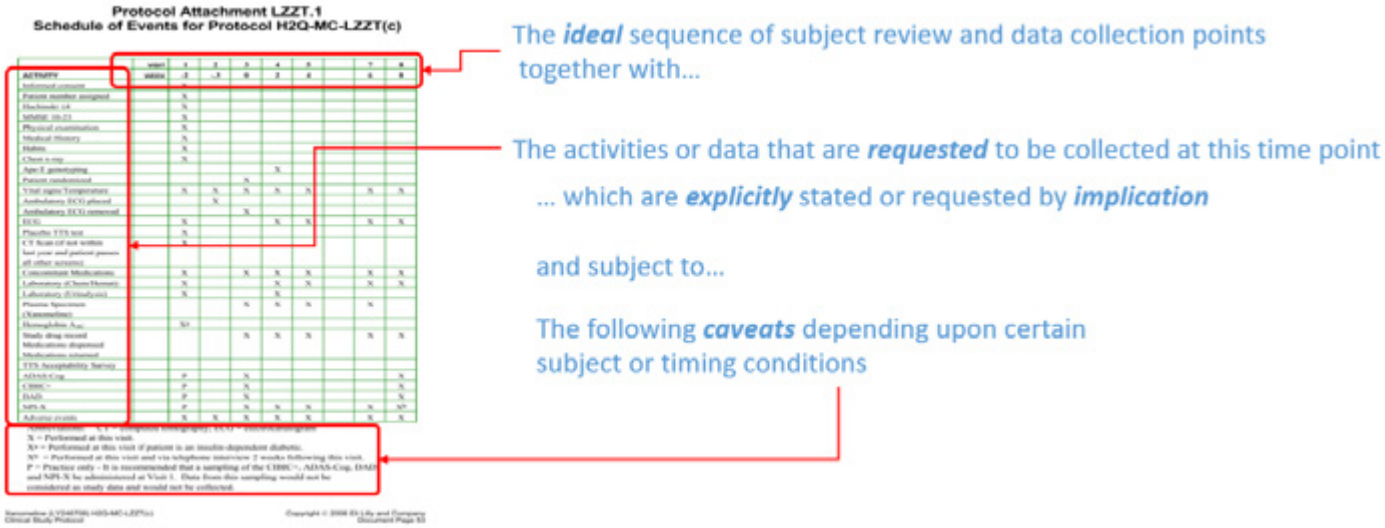

Figure 1: Typical presentation of a study's schedule of activities annotated to illustrate the key components and their contribution to the required/requested operations defined by the study.

Why are they still Visits?

What is a 'Visit' actually defining? Using the contention that "In order for protocol SoAs to improve operational efficiency their component parts need clearer definition", are visits a "planned <something> between a study team/sponsor/site staff/investigator and the patient/participant research subject where planned activities/tasks/jobs are to occur?

Where the <something> might be 'contact', 'event', 'dialogue', 'interaction', 'encounter' … reflecting the actual protocol intent and recognising that some of the <somethings> are to be undertaken by study subjects turning up at clinic appointments, whist others are completed using other methods (e.g. by telephone).

Who is the SoA talking too?

Operationally, the visit schedule and related activities in a SoA impacts many actors during the setup, conduct and close of a clinical trial. The figure below illustrates some of the direct (in pale yellow) and indirect groups that are impacted by the SoA during a study. If the purpose of the SoA is to communicate study objectives clearly and this is to be achieved automatically then the machine readable SoA needs to be able to incorporate these objectives. Currently the main study team objective for the SoA is 'internal' (the centre and left of the diagram). The potential for supporting directly the 'external' elements in the diagram (centre and right) is already recognised (e.g. supporting site operations via electronic health record systems). Machine-readable SoAs need to be able to recognise and accommodate these objectives.

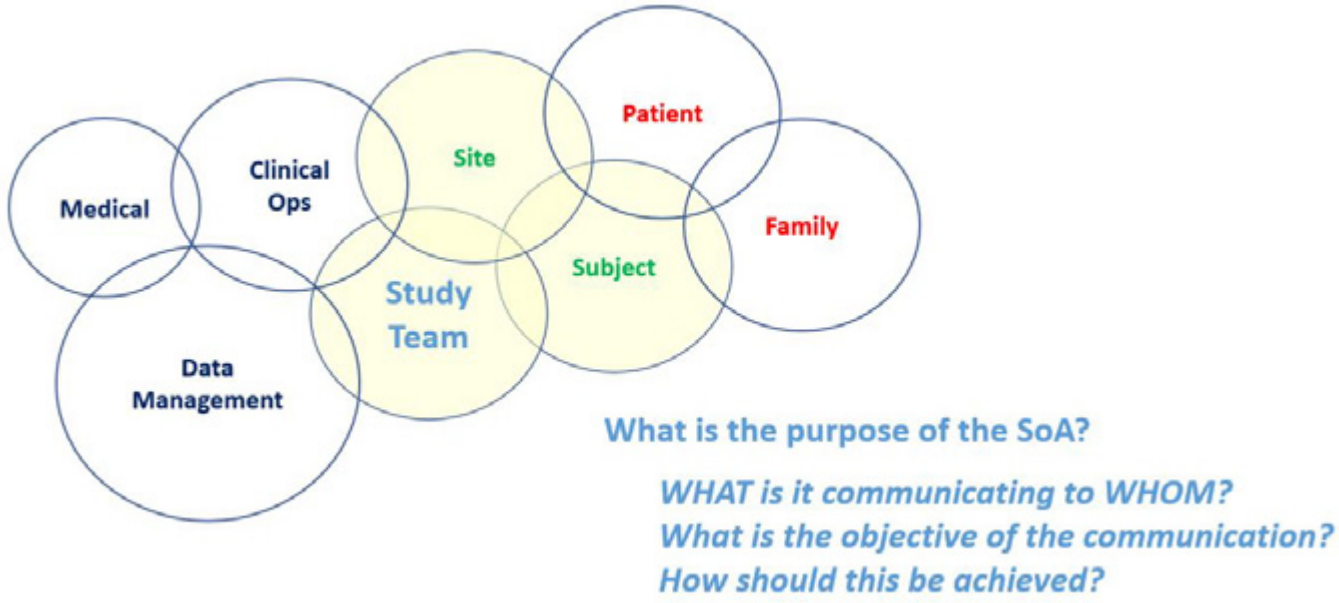

Figure 2: Schematic showing some of the relationships between key users of the schedule of activities.

For example, the order of SoA as defined in the protocol is highly study-team-centric. The figure (Fig 3) below shows how the order of activities in the protocol is not an optimal order for the study site. A simple re-ordering of the activities to reflect the type of activity, the site staff involved and the practical recognition that ECG, X-Ray and CT-Scan are conducted in a separate part of the building should be possible if SoA are to automatically support site operations.

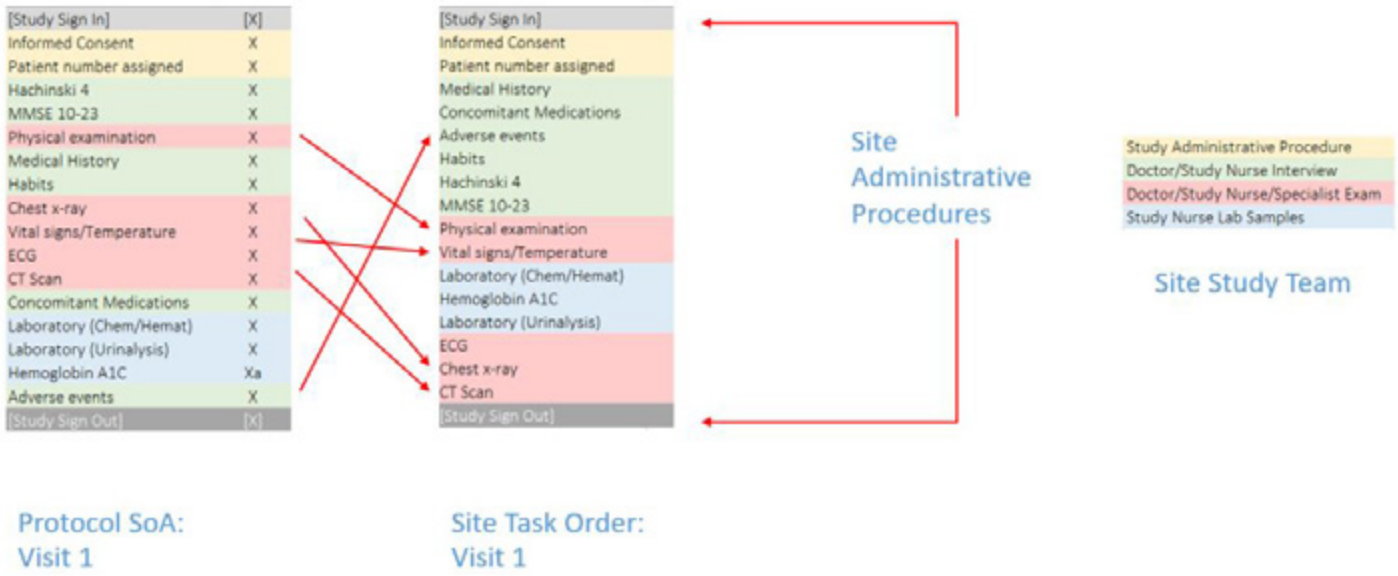

Figure 3: Studies requested activities as presented in the protocol (left) and re-ordered (right) as they might be scheduled by a study site to optimise tasks and assign the correct qualified resource to the tasks.

To be successful and add real value the machine-readable SoA needs;

- Unambiguous definitions of activities, supported by;
- Unambiguous and complete scheduling specifications

With the machine being able to;

- Exchange SoA details seamlessly with other systems (syntactic interoperability)
- 'Understand' the SoA meaning with additional explanation (semantic interoperability)
- Generate consistent views on the SoA, whatever view is required
- Add operational value, recognised as improvements in data or procedural accuracy and efficiency

An Example

The diagram below (Figure 4) shows the SoA in figure 1 re-represented and revised to incorporate early-dropouts from the study. In this form it is easy to see where and what data will be collected under various study subject situations with no ambiguity surrounding when a subject may drop-out nor the activities required thereafter. Using the same machine-readable definition, the associated table (Figure 5) shows the unique set of activity-visit identifiers from the graph that can now be used by, for example, an EDC system, to tag each form with a direct reference to the SoA.

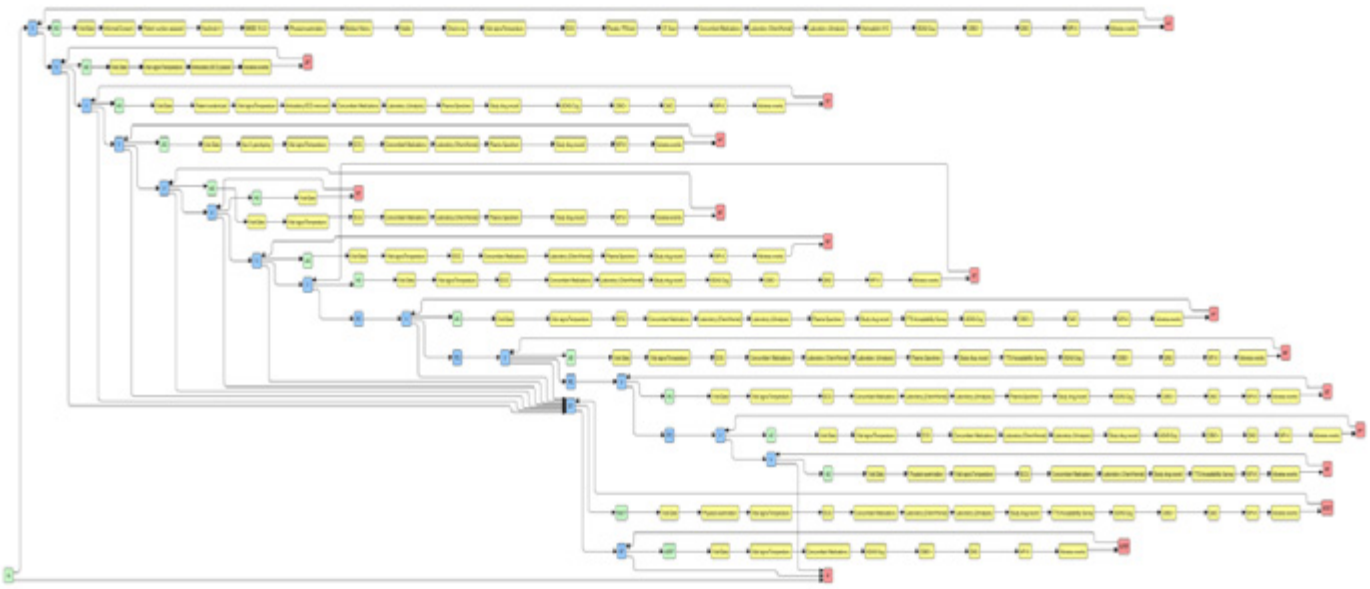

Figure 4: Re-presentation of the schedule of activities shown in figure 1 as a connected graph including the paths through the study if the study participant leaves the study early (drop-outs, blue boxes). In this form the procedures and expected data can be un-ambiguously determined for any route thought the schedule of activities.

Activity	IS	V_1	V_2	V_3	V_4	V_5	V_6	V_7	V_8	PC_9	V_10	PC_11	V_12	PC_13	V_14	PC_15	V_16	V_17	IF	ET	RT
Activity [omID]	IS	V	V	V	V	V	V	V	V	PC	V	PC	V	PC	V	PC	V	V	IF	ET	RT
A5		A5_1	A5_2	A5_3	A5_4	A5_5	A5_6	A5_7	A5_8		A5_10		A5_12		A5_14		A5_16	A5_17			
Visit-Date		A1_1	A1_2	A1_3	A1_4	A1_5	A1_6	A1_7	A1_8		A1_10		A1_12		A1_14		A1_16	A1_17		A1_ET	A1_RT
Informed Consent		A2_1																			
Patient number assigned		A3_1																			
Hachinski 4		A4_1																			
MMSE 10-23		A5_1																			
Physical examination		A6_1																A6_17		A6_ET	
Medical History		A7_1																			
Habits		A8_1																			
Chest x-ray		A9_1																			
Vital signs/Temperature		A12_1	A12_2	A12_3	A12_4	A12_5		A12_7	A12_8		A12_10		A12_12		A12_14		A12_16	A12_17		A12_ET	A12_RT
ECG		A15_1			A15_4	A15_5		A15_7	A15_8		A15_10		A15_12		A15_14		A15_16	A15_17		A15_ET	
Placebo TTS test		A16_1																			
CT Scan		A17_1																			
Concomitant Medications		A18_1		A18_3	A18_4	A18_5		A18_7	A18_8		A18_10		A18_12		A18_14		A18_16	A18_17		A18_ET	A18_RT
Laboratory (Chem/Hemat)		A19_1			A19_4	A19_5		A19_7	A19_8		A19_10		A19_12		A19_14		A19_16	A19_17		A19_ET	
Laboratory (Urinalysis)		A20_1		A20_3							A20_10		A20_12		A20_14		A20_16			A20_ET	
Hemoglobin A1C		A22_1																			
ADAS-Cog		A27_1		A27_3					A27_8		A27_10		A27_12		A27_14		A27_16			A27_ET	A27_RT
CIBIC+		A28_1		A28_3					A28_8		A28_10		A28_12		A28_14		A28_16			A28_ET	A28_RT
DAD		A29_1		A29_3					A29_8		A29_10		A29_12		A29_14		A29_16			A29_ET	A29_RT
NPI-X		A30_1		A30_3	A30_4	A30_5		A30_7	A30_8		A30_10		A30_12		A30_14		A30_16	A30_17		A30_ET	A30_RT
Adverse events		A31_1	A31_2	A31_3	A31_4	A31_5		A31_7	A31_8		A31_10		A31_12		A31_14		A31_16	A31_17		A31_ET	A31_RT
AF		AF_1	AF_2	AF_3	AF_4	AF_5	AF_6	AF_7	AF_8		AF_10		AF_12		AF_14		AF_16	AF_17			
Ambulatory ECG placed			A13_2																		
Patient randomized				A11_3																	
Ambulatory ECG removed				A14_3																	
Plasma Specimen				A21_3	A21_4	A21_5		A21_7			A21_10		A21_12		A21_14						
Study drug record				A23_3	A23_4	A23_5		A23_7	A23_8		A23_10		A23_12		A23_14		A23_16	A23_17		A23_ET	
Apo E genotyping					A10_4																
TTS Acceptability Survey											A26_10		A26_12					A26_17		A26_ET	
ASET																				ASET_ET	
AFET																				AFET_ET	
ASRT																					ASRT_RT
AFRT																					AFRT_RT

Figure 5: Human readable presentation of the schedule of activities schematic shown in Figure 4 annotated with a unique identifier associated with each visit-activity combination. These could be used, for example, as an EDC form ID.

Acknowledgement

The examples used here are from the Lilly Xanomeline Clinical Study Protocol which is publicly available as an example study resource to support operational proof-of-concept and similar investigations (https://wiki.ihe.net/images/4/47/Lzzt_protocol_redacted.pdf)

If you have any questions, please contact the author by email: andy.richardson@zenetar.com