D3.5 Written Report on Quality Evaluation - I

777363– DRIVE

Development of Robust and Innovative Vaccine Effectiveness

WP3 – Evaluation of studies' quality and feasibility

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V.1	27/08/2019	Final version for submission, incorporating feedback from reviewers

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Glossary

Operational model	In this context, this refers to how countries make the DRIVE VE study protocol locally operational.
Organization	Administration where the (coordinating) study team is located.
Quality management	A continuum of activities to prevent, detect, correct or control common types of errors. which may include use of written procedures, systems, governance, audits, etc. Quality management in this survey is used as a general term encompassing both quality control and assurance activities: Quality control: activities focused on identifying defects in the actual products produced. Quality assurance: activities aimed to prevent defects with a focus on the applied process.
Study sites	All individuals/organization actively involved in performing the study at the local level.
Written procedures	A collective term used in this survey to refer to written standard procedural related documents such as standard operating procedures (SOPs), work instructions, forms or templates.

Abbreviations

FISABIO - Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana
GCP - Good Clinical Practice
GEP - Good Epidemiological Practice
GEP-UCMA - Good Epidemiological Practice of the U.S. Chemical Manufacturer's Association
GEP –IEA - Good Epidemiological Guidelines International Epidemiological Association
QCAC - Quality Control & Audit Committee
SOP – Standard Operating Procedure
SWOT - Strengths, weaknesses, opportunities, and threats
THL - The National Institute for Health and Welfare Finland
WP – Work Package

Publishable Summary

Beyond applying scientific robust design and methodology, quality in research also involves activities to prevent, detect, correct or control errors and may involve the use of written procedures, standardized systems and governance to ensure that quality of the output is robust. Specifically for the pharmaceutical industry, such quality practices are highly regulated, directed primarily by the Good Clinical Practice (GCP) standards. However, for public health and other relevant stakeholders different quality management standards, guidances and regulations apply.

This deliverable describes the first implementation of the Quality Management Questionnaire within the DRIVE project to understand such "quality management" activities at the local study sites conducting vaccine effectiveness surveillance. The Questionnaire contained 59 questions organized by themes: General Procedures, Protocol development, Personnel and training. Data management Document management and Security and confidentiality.

Response rates to the Questionnaire were relatively good, overall (83%, 10 out of 12 sites) and to the individual questions (70-100% response rate per question).

Sites appear to conduct a range of activities beyond vaccine effectiveness surveillance to which different standards apply. The information provided suggest that quality management is applied mostly at the study level than that is embedded in the overall organization. For example, 40% of responding sites indicated to have dedicated quality functions, processes to manage SOPs or regular inspections and 60% of sites create study specific documents to describe the operational details of a study as opposed to having generic procedures. Protocol development and issue escalation were generally dealt with at the study team level or by the Principal Investigator. Better insights into the process around maintaining data integrity during collection and processing of data would be important in a next survey. Processes to warrant confidentially and security were common across sites. The DRIVE Code Book was applied by all but one site. However, based on the responses familiarity and gaps in the application of the DRIVE Standard Operating Procedures (SOPs) should be further examined. Some inconsistencies were found between the responses which suggest that the questions may be differently interpreted. A better understanding of the study organization at the site level is needed to support process development and improvement.

The information collected herein supported the initial evaluation by the Quality Control & Audit Committee (QCAC) of the quality of the study conduct for compliance with regulatory standards, site protocols and local SOPs for the 2018-19 season. In addition, it will support the further development of the process for study and tender site selection, DRIVE SOP and tool development (WP2) and the further development of the generic study protocols (WP7).

Note on Scope of Deliverable

WP3, Task 3.3 aims to support the evaluation of Quality and feasibility of the operational model originally by:

- providing data on the quality management at the site level
- development and execution of a SWOT plan to assess strengths, weaknesses, opportunities, and threats to support the feasibility assessment at the site level

However, an amendment of the Description of Action concerning WP3 and WP7 is pending in which

the execution of and reporting on the SWOT analysis will be transferred from WP3 to WP7. The rationale for this change is that the execution of the SWOT analysis requires in-depth dialogue with the study sites. In order to maintain the firewall principle as per the DRIVE Study Governance model, it was considered that the execution and reporting of the SWOT analysis would therefore fit better in WP7.

The current deliverable (D3.5) related to this Task 3.3 thus only reports on quality management at the site level and not the SWOT analysis.

Background

Beyond applying scientific robust design and methodology, quality in research also involves activities to prevent, detect, correct or control errors. These "quality management" activities may involve the use of written procedures, standardized systems and governance to ensure that quality of the output is robust. Because the data generated in DRIVE is used in the regulatory and public health framework and in line with the aim of DRIVE to establish a robust and high quality framework, quality management is of key interest to the evaluation in DRIVE.

Specifically for the pharmaceutical industry, such quality practices are highly regulated and well defined for most activities and applied fairly consistent across countries, directed primarily by the Good Clinical Practice (GCP) standards. However, for public health and other relevant stakeholders different quality management standards, guidances and regulations apply, depending on the activities performed and locations. Although within DRIVE the operations at the individual site level should preferably use the DRIVE study tools and follow the DRIVE standard operating procedures (SOPs) to cover key generic aspects of the study operations, these tools and procedures are not exhaustive and tailored to the individual sites. Study sites may require or desire additional or different tools and SOPs to manage quality of study conduct, either based on local regulations, compliance with procedures existing within their own organization, and may depend on available resources.

The work from WP3 on Quality and Feasibility (specifically Task 3.3 on Operational Quality and feasibility evaluation of pilot studies) will help to understand how quality is managed across the different participating sites, understand gaps in relation to the quality of the study operations. It will inform recommendations and decisions on mitigating the risks which may arise from such gaps (on the quality of the data or compliance) and ultimately guide the appropriate level of resources needed to manage quality to support the feasibility of the future DRIVE framework.

For the current deliverable in relation to Task 3.3, we aimed to understand how quality is managed at the individual study sites participating in DRIVE for the 2018-19 Northern Hemisphere influenza season. It describes the development of "DRIVE Quality Management Questionnaire" which was designed to collect information on how quality is managed at the site level. In addition it provides a summary of the responses to the survey. The information collected herein supported the initial evaluation by the Quality Control & Audit Committee (QCAC) of the quality of the study conduct for compliance with regulatory standards, site protocols and local SOPs. Hence, this deliverable needs to be viewed and read in conjunction with the *2018-19 QCAC Report* in which the assessment of the collected data has been reflected. In addition, it will support the further development of the process for study and tender site selection, DRIVE SOP and tool development (WP2) and inform the further development of the generic protocols (WP7).

Methods

Questionnaire Development

The Quality Management Questionnaire was based on the elements of quality management developed by the IMI ADVANCE project (Accelerated Development of VAccine beNefit-risk Collaboration in Europe) [1].
The questionnaire was developed by Task owners of Task 3.3, reviewed by WP3 members and the QCAC. In addition the content of the questionnaire was piloted with two DRIVE study sites.

Adaptations to the previous work of ADVANCE were made during the development of the questionnaire in order to:

- **Fit to the DRIVE project implementation context;**
    - Incorporating questions regarding the use of the DRIVE Tools and Procedures and rationale for non-use.
    - Removal of Ethics related aspects, since this addressed in a separate WP3 survey (Task 3.2, Deliverable 3.4). Integration into the current deliverable was considered but due to the expected length of the questionnaire decided to keep separate at this stage.
    - Since the Resource assessment is done as part of the study site tender, the questionnaire did not consider this element of quality management.
    - Elements of QM around Analysis and Reporting were removed since analysis and reporting at the local level is not in scope of DRIVE
    - Adaptations for elements which were inherent to the DRIVE study platform, such as the quality and consistency checks devised by the "DRIVE Electronic Study Support Application".

- **To incorporate additional elements of quality management from the Good Epidemiological Practice (GEP) by the U.S. Chemical Manufacturer's Association (1991) [2].**
    - The EMA guideline [3] states that annual vaccine effectiveness data requires that vaccine manufacturers follow Good Epidemiological Practice (GEP), but without any specific reference whereas multiple exist. For the ADVANCE Quality Module – the International Epidemiological Association - Good Epidemiological guidelines (GEP-IEA) [4] was used. In the process of developing the current questionnaire, the GEP of the U.S. Chemical Manufacturer's Association (GEP-UCMA) was identified [2]. The GEP-UCMA was found to be more exhaustive in relation to aspects of quality management in the context of non-interventional research than the GEP of the IEA. A comparison was made to the ADVANCE quality elements and key missing elements were reflected in the questionnaire.

- **Pilot of the questionnaire by two DRIVE study sites**
    - A pilot of the questionnaire with the study sites was originally not planned, but considered useful following the WP3 review.
    - The questionnaire was piloted among two partnering DRIVE study sites (THL, FISABIO) who participated in both the 2017-18 and 2018-19 season. Outside suggestions for textual improvements, the following main feedback was obtained from the two sites:

- Next to the online questionnaire provide the sites with the full set of questions so that questions can be read in relation to other questions. Also it would facilitate the situation where multiple persons would need to contribute to completing the questionnaire.
    - A Word version of the questionnaire was created. Completion of the word document versus the online questionnaire was permitted.
- Concern with the length of the survey
    - Following consultation with the QCAC several questions were removed – particularly those of more administrative nature, such as details on password configurations.
    - A distinction was made between mandatory and optional questions. Optional questions could be skipped.
- Request for additional clarification of the applied terminology
    - Descriptions were added, for example:
        - ***Does the organisation have any written procedures which describe how quality is managed?*** *(i.e. procedure which may describe which role or function is responsible for quality management, which quality standards are applied, which governance exists around managing quality, etc)*
- Provide the possibility to add additional comments to all questions
    - Given the various constructs of how the local vaccine surveillances are set up and the differences in organization among the partners involved, it was anticipated by the pilot sites that the response options provided in the questionnaire may not adequately fit all the possible different situations. Hence most questions had the option of a free text comment.
    - Due to the technical limitation of the online survey software (SurveyMonkey Platform) which assigned counts to all questions include sub-fields this did increase the total question count to 109
- Add a "Helpdesk service"
    - To keep within the governance principle of the firewall, the Helpdesk service was provided by UNIFI.

- **Test of the online version of the questionnaire**
    - Several modifications were made to improve the technical performance of the questionnaire.
    - Many questions were structured as multiple choice to facilitate the response as well as processing of the responses

The final Questionnaire contained 59 questions[1], organized by themes in Quality Management applicable to the DRIVE context, namely:

- Procedures – general (15 questions)
- Protocol development (8 questions)
- Personnel and training (8 questions)
- Data management (10 questions)
- Document management (7 questions)
- Security and confidentiality (11 questions)

[1] The question count in the online survey is 109, due to the inclusion of free-text fields for the majority of questions to permit the option of providing additional comments.

Where applicable sites were requested to share existing local written procedures with the DRIVE consortium.

Planning

Considerations for the timelines for issuing the survey included:

- **Experience of the sites with the DRIVE platform**
  - Most sites which participated in the 2018-19 season were new to DRIVE, hence it was considered that the questionnaire should be issued towards the end of the season such that the sites had gained experience with the DRIVE study platform and consortium.
    - Post-hoc note: because of the competing activities of the sites at the end of the season, this criterion was considered less critical. For the next season an earlier planning of the survey is anticipated.
- **QCAC Workplan**
  - The responses of the Quality Management Questionnaire needed to be available to the QCAC to permit their evaluation in line with the timelines of the Annual report – *by end of April but at the latest end of May*
- **Other planned activities of the study sites.**
  - Competing priorities in relation to DRIVE activities and known on other priorities included:
    - Interim data upload for the 2018-19 season – 1 March 2019
    - Final data upload for the 20119 season – 15 May 2019
    - Site tender application for the 2019-20 season – 15 April 2019
    - Completion of the Ethics survey – 9 April 2019
    - Influenza seasonal surveillance activities - ~ end of April to June
- **Ad-hoc decision to pilot the survey among 2 study sites**
  - The addition of the pilot to the development phase of the questionnaire resulted in a delay of response availability by approximately 2 weeks. As a result the original review timelines of the QCAC were condensed. Also the updated timelines did not permit to create an initial draft of the current deliverable prior to the QCAC review as originally planned. Since QCAC evaluation is based mainly on the individual site responses and the survey output provides the QCAC with summary frequency of the responses, the lack of a draft version of the current deliverable prior to the QCAC review was not considered to significantly impact the QCAC review. Hence, the value of the survey pilot was considered to outweigh the availability of the draft of the current deliverable prior to the QCAC evaluation.

Based on these considerations, the Questionnaire was issued on 17 April 2019 with a requested response due date by 7 May 2019.

Software

The online questionnaire was created using the online survey software SurveyMonkey. The online survey can be found here and in Annex 1.

Results

Overall response rates

At the time of the response due date (7 May 2019), 3 sites had responded to the questionnaire. An extension was issued to 13 May 2019 at which time 7 sites in total had responded to the survey. Responses of the remaining sites followed after - to ultimately reach a response rate of 83% (10 out of 12 sites; one site ultimately did not participate in DRIVE and one site did not respond). The last site submitted their response on 30 May 2019.

Only one site extensively used the helpdesk support for guidance to complete the questionnaire.

Summary

A full (aggregated) report of the survey responses across sites is provided in Annex 2. Individual responses of the sites are not shown in line with the agreed disclosure principles for this survey.

A summary of the responses is provided below. The basis for the response rates for the individual questions is the 10 responding sites. Percentages given per response options reflect the proportion of responding sites who had selected that specific response.

Please note that the interpretation and evaluation of the responses is left to the DRIVE QCAC and is not in scope of the current report, but included as Annex with the seasonal annual report of 2018-19.

Procedures – general

This section consisted of 15 questions. Response rates to the individual questions in this section was 100%.

Five sites (50%) responded to the question if it was permitted to share written procedures with the DRIVE consortium and of those two sites also uploaded a written procedure (related) document in response to the questionnaire. One document concerned a form, the other a study specific operations guidance.

Functions or roles responsible for quality management varied across sites. Specific functions or roles dedicated to Quality management applied to only three sites. For other sites, responsibilities for quality management generally appeared to be embedded in overall managerial functions, central research offices or as part of the principle investigator/research team responsibilities. Also Ethics and Data Privacy functions were mentioned as responsible groups for quality management.

Four sites (40%) indicated to have a written procedure on Process Management within the organization of which one site indicated that this only applied to patient care and not research activities. Other sites (60%) confirmed not have such procedures available.

Procedures for Risk Management exist at the organizational, study specific level or both, or indicated to be part of the contract between research parties. Again for one site this applied only at

the patient care level and not for research activities. This applied similarly to Issue Escalation, Governance and Non-Compliance matters.

Electronic Document Management Systems (EMDS) for maintaining written procedures were used by 4 (40%) sites, whereas others used a centrally accessible electronic repository. Version control of written procedures was performed manually (70% of sites).

Internal inspections were conducted at least every 5 years for 3 (30%) sites or at the study specific level (1 site, 10%), generally by external organizations. For other sites inspections were not conducted or the activities with respect to vaccine effectiveness were not in scope of the inspection.

Overall the responses in relation to the existing procedures at the site level suggested that the sites conduct a range of activities beyond vaccine effectiveness surveillance and that the vaccine effectiveness surveillance was not always in scope of the organization's quality management system. Some inconsistencies were found between the responses which suggests that the questions may be differently interpreted.

Familiarity and application of the DRIVE Standard Operating Procedures (SOPs) varied across the sites (see Table 1). The use and application of the DRIVE SOPs versus alternative procedures was about 50/50. Two sites indicated not to be familiar with the DRIVE SOPs or where these could be found.

Table 1: Implementation of the DRIVE Study SOPs.

DRIVE SOP	**Implemented in its original form (n_{total})**	**Implemented as locally modified version (n_{total})**	**Familiar with the DRIVE SOP, but a different relevant procedure was applied (n_{total})**	**Not familiar with the DRIVE process – an relevant alternative procedure was applied (n_{total})**	**Not familiar with the DRIVE process – no alternative procedure was applied (n_{total})**	**Other – N/A**
Study Process	1	3	3	2	0	N/A due to different design
Integrity and transparency	3	1	3	2	0	N/A due to different design
Data management	4	1	2	2	0	Not possible to change current practices
Data quality assessment	5	0	2	2	1	0

Protocol development

This section consisted of 8 questions. Response rates to the individual questions in this section was mostly 100% with two exceptions of lower response rates (70-80%).

Availability of written procedures for Protocol Development were uncommon across sites (30%). Four sites (40%) used the DRIVE template for Protocol Development, whereas other sites indicated not to have standard protocol templates available for the vaccine effectiveness surveillance. Similarly the protocol underwent expert review (beyond the study team and ethics committee review) at 40% of the sites - which was also documented. Sign-off of the protocol was generally by the protocol authors and study team members or their respective management.

Three sites had an EDMS to store the Study Protocol, whereas others used a centrally accessible electronic repository.

Principal Investigators are generally informed and tasked with the handling of protocol deviations and the assessment of their impact (minor or major). In many sites, additional approvals are required beyond the Principal Investigator for major deviations. Where specified, protocol deviations are documented.
In addition to the Study Protocol, 60% of sites create other study specific documents to describe the specific operational aspects of a study. One site indicated the need for such detailed instructions and intention to apply these in subsequent research.

Personnel and training

This section consisted of 8 questions. Response rates to the individual questions was nearly complete (90-100%) though the level of detail and informativeness to the open questions varied substantially.

Professional qualifications of the personnel are generally verified at the commencement of employment. Substantive insights on personnel training were not provided for most sites.
Job Descriptions are available in 70% of the sites for the majority or all positions. Where roles and responsibilities of study team members are documented (60%) this is described primarily in the study protocol. Similarly if the annual vaccine effectiveness studies involve a collaboration across multiple partnering entities (66% of sites), this is also documented in the Study Protocol. At two sites Commercial parties are involved in the study conduct, more specifically for data management and transfer.

Data management

This section consisted of 10 questions. Response rates to the individual questions was nearly complete (90-100%).

Three sites (30%) indicated not to apply any specific written procedures for Data management and did not have a Data Management Plan available specific to the study and one site exclusively applied the DRIVE procedure for Data Management, whereas the other sites also had their own procedures for Data Management (40%). Where written procedures for Data management were available processes commonly covered in these written procedures (>50%) included Database Validation, Data

Collection, Transfer and Processing. Less frequently these written procedures included processes around Databased Programming (20%), Data revisions (50%), Database lock and unlock (17%) and Data Management reporting (30%).

Both paper (30% of sites) and Electronic (or Web-based) Data Collection Forms (40%) were used at the study sites. 30% of sites indicated not to use any standard forms, but this appeared to pertain to the regiter based cohort and a site where both paper and electronic based data collection forms were used.

Documentation of the Database Design was maintained by 70% of sites (including 1 site response under "Other"), primarily for documenting Study database design and related programming (100%) and to less extent for Study specific database validation and testing (40%).

All but one site used the DRIVE Code Book for data entry, either as stand-alone (40%) or in addition to local Code books (50%).
All sites performed quality and consistency checks in addition to those devised by the "DRIVE Electronic Study Support Application, except in the context of the register based cohort setting.

Sites maintained either a manual (30%) or system audit trail (20%) of historical revisions of the data points in the database, or a combination of both (20%). For two sites (20%) no audit trail was maintained, whereas in the register based cohort study audit trials are not available for changes made by the data provider. 60% of Sites create a Data Management Report during the study conduct or indicate to document the rationale for data revisions as part of the audit trail. Better insights into the process around maintaining data integrity during collection and processing of data would be important in a next survey.

Document management

This section consisted of 7 questions. Response rates to the individual questions was nearly complete (90-100%).

Procedures for Document management exist at the organizational (40%, including appropriate response under "Other"), study specific level (20%) or both (20%). Where available, these procedures cover mainly Approval (75%), Security (75%) and Archival (75%) of Study Documents. A study specific Documentation Plan is available for 33% of the sites.

Most sites (70%) have defined which documents should at minimum be retained in the study archive which is indexed. Three sites uploaded their document list.

Security and confidentiality

This section consisted of 11 questions. Response rates to 9 of 11 questions were complete (i.e. 100%).

All but two sites (80%) maintain a back-up of the electronic data at a different location from the primary storage, alternatively at the same location (10%). No back-up (local or remote) is made of the study data at one site.

Written procedures covering Security were available for 80% of the sites, of which the majority

covered all key access of personnel to physical areas, systems, servers, study data and documentation. Where applicable, access to physical storage areas for paper study documents and laboratory samples as well as server locations at all sites was controlled. Access logs were maintained by all but one site.

Individual work stations were password protected as well as access to electronic systems/ applications relevant for study conduct either separately or via the invidual works stations.

Sites obtained confidentiality agreements of the study team members (90%) or collaborating partners or commercial suppliers (100% where applicable).

Discussion

This was the first implementation of the Quality Management Questionnaire. Response rates to the Questionnaire were relatively good, overall and to the individual questions. The responses of the Questionnaire were made available for the QCAC evaluation for the 2018-19 seasonal report.

Sites appear to conduct a range of activities beyond vaccine effectiveness surveillance to which different standards apply. The information provided suggest that quality management is applied mostly at the study level than that is embedded in the overall organizational level. For example, few sites indicated to have dedicated quality functions, processes to manage SOPs or regular inspections and 60% of sites create study specific documents to describe the operational details of a study as opposed to having generic procedures. Protocol development and issue escalation were generally dealt with at the study team level or by the Principal Investigator. Processes to warrant confidentially and security were common across sites. Better insights into the process around maintaining data integrity during collection and processing of data would be important in a next survey. The DRIVE Code Book was applied by all but one site. However except for the DRIVE SOP related to Data quality assessment, a minority of the sites implemented the other DRIVE SOPs in their orginal form and two sites indicated not to be familiar with the DRIVE SOPs or where they could be found. Additional awareness needs to be raised around the DRIVE SOPs. In addition, a better understanding of the hurdles at the site level to the DRIVE SOP implementation or application of quality management activities in general would be interest to the project to support the future framework development

Several limitations to the Questionnaire apply. First, although most sites responded to almost all questions, based on inconsistencies between the site responses and the additional free-text information provided it seemed that the questions may have been interpreted differently by the various sites and not always in the way they were intended. Only one site extensively used the helpdesk support for guidance to complete the questionnaire.

One key limitation is that the survey confirmed only if written procedures were in place, but not the content of the SOPs. Though access to written procedures at the site level was requested, this was not permitted for some sites and only two of the sites uploaded a single procedures limiting a more in-depth assessment of the appropriateness of the local procedures. Site visits may provide an opportunity to review written procedures locally but needs to be balanced with the available resources.

Some complaints were received about the length of the survey. Further prioritization of the more critical questions will be discuss with the QCAC. The questions were not always appropriate for the specific local site situations and the appropriateness of the questions in relation to a register based

cohort study was challenged. A better understanding of the study organization at the site level is needed to support process development and improvement, if applicable. The study site visits may provide a good opportunity to obtain information on the study organization at the site level.

While the responses to the survey were available to support the QCAC in their evaluation, timelines were tight and some sites well exceeded the due date for the responses. Also the current timelines limits the wider use of the survey output in the immediate subsequent influenza season. One specific important purpose is to inform the site tender and selection process. An earlier timeframe would also allow to inform changes to the generic protocol, study tool applications and SOP development for the immediate subsequent season. Permitting the use of the survey for such purposes implies that the results from the survey would need to be available around January of each year. Although this may coincide with the peak of the influenza period, an earlier planning of the survey will be proposed. Alternatively, information on essential elements of quality management could be collected at time of the site tender and be considered as site selection criteria. In addition, making the final site payment conditional on timely response to the survey is under consideration.

As per the QCAC conclusions, the Quality Management Questionnaire responses from the study sites provided an indicative assessment of each responding site's quality management systems. Issues were not identified to trigger a recommendation for a site visit or a formal audit. All study sites that returned the completed questionnaires will receive at least one recommendation for improvement from the QCAC (see QCAC report 2018-19 for further details). Non-response will be investigated.

Next steps

The results from the quality survey and the QCAC assessments will be discussed in relation to the further development of the generic protocols (WP7), tools of WP2 (electronic study support application, SOPs, site selection criteria and study tender process). The scope of the sites visits may be expanded to include the topic of quality management. Further prioritization of the more critical questions will be discuss with the QCAC.

Timelines and content of the Quality Management Questionnaire will be reviewed to increase its use for these purposes and adjusted accordingly where possible.

An additional survey will be considered for the following season to specifically assess the quality management of the laboratory testing.

References

1. ADVANCE project Accelerated Development of VAccine beNefit-risk Collaboration in Europe D5.9 White paper WP5 – Proof-of-concept studies of a framework to perform vaccine benefit-risk monitoring. V1.0 Draft, January 2018
2. Guidelines for Good Epidemiology Practices for Occupational and Environmental Epidemiologic Research. The Chemical Manufacturers Association's Epidemiology Task Group. J Occup Med. 1991 Dec;33(12):1221-9.
3. Guideline on Influenza Vaccines, Non-clinical and Clinical Module, EMA/CHMP/VWP/457259/2014, Committee for Medicinal Products for Human Use, European Medicines Agency, 21 July 2016

4. Good Epidemiological guidelines, IEA guidelines for proper conduct in epidemiologic Research, November, 2007

Annex 1 - Quality Management Questionnaire

Background

Beyond applying scientific robust design and methodology, quality in research also involves activities to prevent, detect, correct or control errors. These "quality management" (QM) activities may involve the use of written procedures, standardized systems and governance to ensure that quality of the output is robust. Different quality management standards, guidances and regulations generally apply to different stakeholders and also depending on the activities which they perform. Specifically, for the pharmaceutical industry, quality practices are highly regulated and well defined for most activities. Because the data generated in DRIVE is used in the regulatory and public health framework and in line with the aim of DRIVE to establish a robust and high quality framework, quality management is of key interest to the evaluation in DRIVE.

Objective of the Survey and Use of the Information

This Quality Management Survey will be used to understand how quality is managed at individual study sites participating in DRIVE. This information will be provided to the project's Quality Control and Audit Committee (QCAC) and Steering Committee/Partners for DRIVE. The QCAC will evaluate whether there are any limitations from a quality perspective which may have an impact on the study results or compliance to applicable requirements. The QCAC may suggest improvements to or additional quality related activities. The QCAC may advise for a site visit to be conducted.
The site-specific results of the quality assessment will be shared with the site in question. A general (i.e. non-site-specific) summary on the quality assessment will be described in the seasonal report. The knowledge gained from this survey will support future protocols, analysis plans, procedures and tool development, as well as a DRIVE deliverable (report on quality and feasibility).

Scope

The scope of this survey is the QM of the locally conducted vaccine effectiveness studies from which the results - used in DRIVE for the pooled analysis - originate. Some of the aspects of QM may extend to your broader organisation's operations. The elements of Quality Management covered in this survey include:

- Procedures general
- Protocol development
- Personnel and training
- Data management
- Document management
- Security and confidentiality

Please note that the topic of the ethics – issued by Miriam Levi (Azienda USL Toscana Centro) - and the quality of the laboratory testing – issued by Bruno Lina (UCBL, France) - will be addressed in a separate survey.

Instructions - please read carefully

We are issuing this survey to organisations listed as DRIVE study participant. We understand however that locally the study conduct may involve (collaboration across) multiple local parties. We leave it at your discretion to involve those parties to support the response to this survey.

Where different QM related activities may be performed for various activities in your organization, please reflect in your response how they apply in the context of the influenza vaccine effectiveness studies. For example, if your institution also

conducts clinical trials or vaccine safety monitoring, please do not reflect QM for those activities in your responses (unless these also apply to the influenza vaccine effectiveness studies).

Most questions are multiple choice. Please choose the option which is most relevant. For the majority of questions it offers a follow-up question where additional information can be provided in free text. We invite you to provide further explanation to help our understanding of the situation. Where descriptions are requested, please describe the key elements in 5 to 10 sentences. **All questions marked with * require a response.**

Responses can be provided via the online survey (preferred) or using this word document. Some questions are mandatory. We anticipate that the completion of this survey will take approx. 2 hours if most knowledge is available with the primary responder. More time may be needed in case other persons need to be consulted.

We kindly request you to complete the survey by at the latest by 7 May 2019. By adhering to this timeline the QCAC can perform their assessment within the specified timelines for the annual report. A timely response is therefore highly appreciated.

If you need clarifications on the questions (or if you are experiencing technical issues), please do not hesitate to contact Roberto Bonaiuti by email roberto.bonaiuti@unifi.it.

Documentation requests

As part of this survey we request to share several written standard operating procedures (SOPs), work instructions or templates, i.e. referred to collectively as “written procedures” in this survey. This documentation will be used for the purpose of the quality assessment and may support the development of the DRIVE procedures.

Written procedures which are shared by your organisation are made available to the partners in DRIVE, its Independent Scientific Committee (ISC) and any external vendor(s) which may potentially be contracted by DRIVE on the advice of the QCAC to perform the site visits. In case of an interest or need to share your written procedures beyond these aforementioned parties we will obtain your organisation’s permission.

In case your organization has a general administrative requirement to be able to share procedures (for example completion of a form), please contact Mónica Vázquez-Moreno, email: vazquez_monmor@gva.es.

1. In case of a general restriction to share written procedures outside your organisation, please indicate this below:

Written procedures can be shared under the following condition(s) - Please specify:

Other comments:

Terminology as applied in this Survey

Quality management - a continuum of activities to prevent, detect, correct or control common types of errors. which may include use of written procedures, systems, governance, audits, etc. Quality management in this survey is used as a general term encompassing both quality control and assurance activities:

Quality control: activities focused on identifying defects in the actual products produced.
Quality assurance: activities aimed to prevent defects with a focus on the applied process.

Written procedures - a collective term used in this survey to refer to written standard procedural related documents such as standard operating procedures (SOPs), work instructions, forms or templates.

2. Responder information

- Name of the contact person for this questionnaire
- Title
- Organisation:

- Email Address:

Processes – general part 1

The following questions relate to how quality is managed in your organization. Written procedures is a collective term used in this survey to refer to written procedural related documents and include standard operating procedures (SOPs), work instructions, forms or templates.

3. Department/roles info

Which department and/or roles in the organization are responsible for quality management?
Answer:

Which department and/or roles in the organization are responsible for the development of the organization's written procedure?
Answer:

*4. Does the organisation have any written procedures which describe **how quality is managed**?

(i.e. procedure which may describe which role or function is responsible for quality management, which quality standards are applied, which governance exists around managing quality, etc)

- ☐ Yes, written procedure(s) exist at the organizational level AND study-specific level which address such aspects
- ☐ Yes, written procedure(s) exist at the ORGANIZATIONAL Level which address such aspects
- ☐ Yes, written procedure(s) exist at the STUDY-specific level which address such aspects
- ☐ No
- ☐ Other (please specify):

5. If needed, please add any additional comment to the previous question: _____

6. Does the organisation have a written procedure which describes **how written processes are managed**?

(i.e. in essence "a written procedure on written procedures" which may describe how new written processes (incl templates/forms) are created, or existing processes are updated, how they are approved and where they are stored, etc)

- ☐ Yes, written procedure(s) exist at the organizational level AND study-specific level which address such aspects
- ☐ Yes, written procedure(s) exist at the ORGANIZATIONAL Level which address such aspects
- ☐ Yes, written procedure(s) exist at the STUDY-specific level which address such aspects
- ☐ No
- ☐ Other (please specify):

7. If needed, please add any additional comment to the previous question: _____

8. Does the organisation have a written procedure which describes **how risks are managed**?

(i.e. a procedure which may describe how risks (i.e. risks to resources, timelines, safety) are identified, documented reviewed and how actions are decided, etc.)

- ☐ Yes, written procedure(s) exist at the organizational level AND study-specific level which address such aspects
- ☐ Yes, written procedure(s) exist at the ORGANIZATIONAL Level which address such aspects
- ☐ Yes, written procedure(s) exist at the STUDY-specific level which address such aspects
- ☐ No
- ☐ Other (please specify):

9. If needed, please add any additional comment to the previous question: _____

10. Does the organisation have a procedure which describes how the organization is **informed of issues**?

(i.e. a procedure which may describe how issues (i.e. noncompliance, violation of privacy etc) are documented, who within the organization is informed of issues (i.e. escalation path), on which issues they are informed and within what timeframe, etc)

- ☐ Yes, written procedure(s) exist at the organizational level AND study-specific level which address such aspects
- ☐ Yes, written procedure(s) exist at the ORGANIZATIONAL Level which address such aspects
- ☐ Yes, written procedure(s) exist at the STUDY-specific level which address such aspects
- ☐ No
- ☐ Other (please specify):

11. If needed, please add any additional comment to the previous question: _____

12. Does the organisation have a procedure which describes **governance**?

(i.e. a procedure which may describe how different functions or decision bodies relate to each other and where decisions are taken and by whom, etc)

- ☐ Yes, written procedure(s) exist at the organizational level AND study-specific level which address such aspects
- ☐ Yes, written procedure(s) exist at the ORGANIZATIONAL Level which address such aspects
- ☐ Yes, written procedure(s) exist at the STUDY-specific level which address such aspects
- ☐ No
- ☐ Other (please specify):

13. If needed, please add any additional comment to the previous question: _____

*14. Does the organisation have a procedure which describes how **non-compliance with a procedure** is handled?

(i.e. a procedure which may describe how non-compliance is documented, if actions are taken to correct and/or in the future to prevent non-compliance, and how completion of those actions is monitored etc.)

- ☐ Yes, written procedure(s) exist at the organizational level AND study-specific level which address such aspects
- ☐ Yes, written procedure(s) exist at the ORGANIZATIONAL Level which address such aspects
- ☐ Yes, written procedure(s) exist at the STUDY-specific level which address such aspects
- ☐ No
- ☐ Other (please specify):

15. If needed, please add any additional comment to the previous question: _____

*16. How are written procedures stored within the organisation?

☐ In an Electronic Document Management System
☐ In a centrally accessible electronic repository, E.g., Network Drive, SharePoint, Dropbox) (not using a specific electronic document management system)
☐ Other (please specify)

17. If needed, please add any additional comment to the previous question: _____

* 18. Is there version control applied for written procedures?

(i.e. version control is the means by which different versions and drafts of a document/file/dataset are managed. It provides an audit trail for the revision and update of draft and final versions. Specifically, it allows for the latest approved and effective version of a written procedure (including templates, forms etc) to be identified, such that outdated procedures are no longer used)

☐ Version control for written procedures is managed as part of an Electronic Document Management System
☐ Version control for written procedures is management manually
☐ No version control for written procedures is applied
☐ Other (please specify)

19. If needed, please add any additional comment to the previous question: _____

20. Do you conduct regular *internal* inspections to check the activities being performed by your organization, including the activities related to the vaccine effectiveness studies?

☐ Yes, internal inspections are regularly conducted (at least every 5 years)
☐ Only study-specific inspections are internally conducted, including for the vaccine effectiveness studies.
☐ Internal inspections are performed, but activities related to the vaccine effectiveness studies are never in scope of such inspections
☐ No: no internal inspections are conducted OR inspections are conducted less than every 5 years
☐ Other (please specify)

22. Is your organization regularly inspected or audited by an *external* organization(s)?

☐ Yes, external inspections are regularly conducted (at least every 5 years)
☐ Only study-specific external inspections are conducted, including for the vaccine effectiveness studies.
☐ External inspections/audits are performed but activities related to the vaccine effectiveness studies are never in scope of such inspections
☐ No: no external inspections/audits are conducted OR inspections/audits are conducted less than every 5 years
Other (please specify)

23. If needed, please add any additional comment to the previous question _____

(survey continued on the next page)

Processes – general part 2

*24. Has the organization used the DRIVE written procedure on “Study process”?

☐ Yes, the “DRIVE Study Process” procedure has been implemented in its original form
☐ A local modified version of the “DRIVE Study Process” has been implemented
☐ We are familiar with the “DRIVE Study Process” procedure, but the organization used its own procedure for study process
☐ We are not familiar with the “DRIVE Study Process” procedure, but an alternative similar procedure was used.
☐ We are not familiar with the “DRIVE Study Process” procedure and NO alternative similar procedure was used.
☐ Other (please specify)

25. If needed, please add any additional comment to the previous question _____

*26. Has the organization used the DRIVE written procedure on “Integrity and transparency”?

☐ Yes, the “DRIVE Study Process” procedure has been implemented in its original form
☐ A local modified version of the “DRIVE Study Process” has been implemented
☐ We are familiar with the “DRIVE Study Process” procedure, but the organization used its own procedure for study process
☐ We are not familiar with the “DRIVE Study Process” procedure, but an alternative similar procedure was used.
☐ We are not familiar with the “DRIVE Study Process” procedure and NO alternative similar procedure was used.
☐ Other (please specify)

27. If needed, please add any additional comment to the previous question _____

*28. Has the organization used the DRIVE written procedure on “Data management”?

☐ Yes, the “DRIVE Study Process” procedure has been implemented in its original form
☐ A local modified version of the “DRIVE Study Process” has been implemented
☐ We are familiar with the “DRIVE Study Process” procedure, but the organization used its own procedure for study process
☐ We are not familiar with the “DRIVE Study Process” procedure, but an alternative similar procedure was used.
☐ We are not familiar with the “DRIVE Study Process” procedure and NO alternative similar procedure was used.
☐ Other (please specify)

29. If needed, please add any additional comment to the previous question _____

* 30. Has the organization used the DRIVE written procedure on “Data quality assessment”?

☐ Yes, the “DRIVE Study Process” procedure has been implemented in its original form
☐ A local modified version of the “DRIVE Study Process” has been implemented
☐ We are familiar with the “DRIVE Study Process” procedure, but the organization used its own procedure for study process
☐ We are not familiar with the “DRIVE Study Process” procedure, but an alternative similar procedure was used.
☐ We are not familiar with the “DRIVE Study Process” procedure and NO alternative similar procedure was used.
☐ Other (please specify)

31. If needed, please add any additional comment to the previous question _____

Protocol development

The following questions are intended to understand the process around the protocols development, review and approval as well as questions on how deviations to a study protocol are handled.
Please note that the specifics of the ethics review are covered in a separate survey issued earlier by Miriam Levi.

32. Does the organisation have a written procedure which describes how a study protocol is developed?

(i.e. a procedure which may describe which template should be used to write the protocol, which role/function is responsible for the writing of the protocol, how and which stakeholders should be consulted to provide input, who reviews the protocol, how the protocol is approved etc.)

☐Yes
☐No
☐Other (please specify):

33. If needed, please add any additional comment to the previous question _____

34. If possible, please upload your written procedure (or other relevant documentation) which describes the study protocol development process, or alternatively send by email to Roberto Bonaiuti at roberto.bonaiuti@unifi.it.

35. If you did NOT use the DRIVE generic protocol template, does the organisation use a standard template for the protocol development?

☐Not applicable, the generic DRIVE generic protocol template was applied
☐The organization has its own standard protocol template which was applied for the vaccine effectiveness studies.
☐Another external standard protocol template was applied
☐The organisation does not apply any standard protocol template for the vaccine effectiveness studies; this can be determined by the author/study team/management
☐Other (please specify)

36. If needed, please add any additional comment to the previous question _____

*37. Does a protocol undergo review by an expert review committee - separate from the review by the study team members or ethics committee review?

☐Yes
☐No
☐Other (please specify)

38. If needed, please add any additional comment to the previous question _____

*39. Is the review of a protocol by the expert committee documented?

☐Yes
☐No
☐Other (please specify)

40. If needed, please add any additional comment to the previous question _____

*41. Is formal sign-off (i.e. wet-ink, signature) of the study protocol required? Check all that apply:

☐ Author(s)
☐ Study team member(s)
☐ Manager(s) of the author or other study team members
☐ Expert committee member(s)
☐ No - the expert committee review is documented and constitutes approval of the protocol
☐ Other (please specify) or additional comments

*42. Where are the study protocols maintained?

☐ In an Electronic Document Management System
☐ In a centrally accessible electronic repository (E.g., Network Drive, SharePoint, Dropbox) (not using a specific document management system)
☐ Other (please specify)

43. If needed, please add any additional comment to the previous question _____

*44. Please describe briefly how deviations from the protocol are handled, i.e. how these are documented, who is informed, how are actions decided (5-10 sentences) _____

45. Beyond the protocol, are study specific documents created to describe the specific operational aspects of a study?

(i.e. documents processes/instructions/plans with contain more detailed instructions for the study staff how to perform the study in real-life)

☐Yes
☐No
☐Other (please specify)

46. If needed, please add any additional comment to the previous question _____

Personnel and Training

This following questions aim to provide insight into how personnel is qualified and trained so that they can competently perform the activities which are assigned to them.

*47. Please describe in briefly how **professional qualifications** of study team members (i.e. for example GLP, GEP) are verified, records maintained and updated.

Please consider aspects of educational degree, work and skills certifications, professional certifications, maintaining and updating CVs etc. (5-10 sentences)

_____

*48. Please describe briefly how **training requirements for study personnel** are organized

(i.e. how it is determined on which written procedures the personnel should be trained, how training is assigned to the associate, how completion is documented, systems which may be used for this purpose etc.) (5-10 sentences)

_____

49. Are institutional Job Descriptions of personnel available?

(i.e. a job description describes the general (not-study specific) tasks, or other related duties, and responsibilities of a specific position/role)

☐ Yes - for the majority/all positions
☐ No
☐ Other (please specify)

50. If needed, please add any additional comment to the previous question _____

*51. Does the organisation document the study-specific roles and responsibilities of study team members?

☐ Yes, - for the majority/all/key roles
☐ No
☐ Other (please specify)

52. If needed, please add any additional comment to the previous question _____

53. If your organisation documents the study-specific roles and responsibilities of study team members, please detail where the specific roles and responsibilities are documented

☐ Protocol
☐ Other study specific document: Please specify:

54. If the annual vaccine effectiveness studies involve a collaboration across multiple partnering entities outside your organization (i.e. coordinating center, hospital/GP, laboratory), is the role of each of the partners clearly described in writing?

☐ Yes, the role of each collaborating partner is described in writing (for example in an agreement and/or protocol and/or written procedure, etc)
☐ No
☐ N/A – no other partnering entities are involved
☐ Other (please specify)

55. If needed, please add any additional comment to the previous question _____

56. Do any commercial parties (i.e. suppliers) have a critical role in the vaccine effectiveness study conduct (for example for the testing of the swab samples, or conduct of the data management)?

☐ Yes
☐ No
☐ Other (please specify)

57. If needed, please add any additional comment to the previous question _____

58. If any commercial parties (i.e. suppliers) have a critical role in the vaccine effectiveness study conduct, please describe which critical activities such commercial suppliers perform (5-10 sentences)

_____

Data management

The following questions address quality management activities in relation to data management. Data management is a term that describes the organization, storage, preservation, and sharing of data collected and used in a research project.

*59. Does the organisation have written procedure(s) for data management which were applied for the vaccine effectiveness studies?

(i.e. a procedure which describes the flow of the research data from acquiring, validating, storing, and processing of data to ensure the accessibility, reliability, and timeliness for its users)
This can be in addition to the DRIVE Data Management procedure.

☐ Yes, written procedure(s) at the organizational level AND at the study-specific level which address such aspects are applied
☐ Yes, written procedure(s) at the organizational level which address such aspects are applied
☐ Yes, written procedure(s) at the study specific level which address such aspects are applied
☐ Only the DRIVE procedure for Data Management was applied
☐ No procedures for Data management are applied
☐ Other (please specify)

60. If needed, please add any additional comment to the previous question _____

61. If your organisation has written procedure(s) for data management, please detail which processes are covered by your written procedure(s) for data management of vaccine effectiveness studies (tick all that apply)

☐ Database validation
☐ Programming of the electronic database
☐ Data collection
☐ Data transfer and processing
☐ Data revisions
☐ Database lock and unlock
☐ Data Management report
☐ Other (please specify) or additional comments

*62. Does the organisation have study-specific Data Management Plan(s) which describes the study-specific considerations for the data management?

☐ Yes
☐ No
☐ Other (please specify)

63. If needed, please add any additional comment to the previous question _____

*64. Are standard forms used for the original data collection?

☐ Yes, mostly in electronic format
☐ Yes, mostly in paper format
☐ No
☐ Other (please specify)

65. If needed, please add any additional comment to the previous question _____

*66. Does the organisation maintain documentation of the study-specific database design, programming and validation?

☐ Yes
☐ No
☐ Other (please specify)

67. If needed, please add any additional comment to the previous question _____

68. If you maintain a technical specification of the study-specific database design, please detail for which aspects documentation is maintained (please tick which apply)

☐ Study database design and related programming
☐ Study specific database validation and testing

*69. Did the organisation use the DRIVE Code Book to guide the data entry in relation to the vaccine effectiveness studies from which the data was used in DRIVE?

☐ Yes, the DRIVE Code Book was used exclusively
☐ Yes, the DRIVE Code Book was used in addition to local code books to guide the data entry
☐ No, other guidance(s) for data entry was used
☐ Other (please specify)

70. If needed, please add any additional comment to the previous question _____

71. In addition to the quality and consistency checks devised by the “DRIVE Electronic Study Support Application”, does the organisation perform any additional local quality and consistency checks of the data?

☐ Yes
☐ No
☐ Other (please specify)

72. If needed, please add any additional comment to the previous question _____

*73. Does the organisation maintain a historical list of any revisions of the data points in the database?

☐ Yes, a manual list of changes is maintained
☐ Yes, an audit trail of changes is maintained by a system
☐ Yes, a combination of a manual and system generated audit trail is used
☐ No audit trail is maintained
☐ Other (please specify)

74. If needed, please add any additional comment to the previous question _____

75. Does the organisation maintain a Data Management Report during the study conducts (i.e. a report which describes the events (i.e. identified inconsistencies, applied changes etc) which occurred in relation to the database?

☐ Yes
☐ No
☐ Other (please specify)

76. If needed, please add any additional comment to the previous question _____

Document management

* 77. Does the organisation have any written procedures covering document management?

(i.e. a procedure which describes how electronic or paper documents are stored, retrieved, processed, distributed, secured etc), how documents are made accessible to authorized personnel etc.)

☐ Yes, written procedure(s) exist at the organizational level AND at the study-specific level which address such aspects
☐ Yes, written procedure(s) exist at the organizational level which address such aspects
☐ Yes, written procedure(s) exist at the study-specific level which address such aspects
☐ No - such written procedures are not available
☐ Other (please specify)

78. If needed, please add any additional comment to the previous question _____

79. If your organisation has any written procedures covering document management, please detail the processes covered by the written procedures (tick all that apply)

- ☐ Template for a Document Management Plan
- ☐ Approval process for study documents
- ☐ System used for document management
- ☐ Security of study documents
- ☐ Archival of study documents
- ☐ Other key processes covered in these procedures include, please specify

80. Does the organisation use a study-specific Document Management plan?

- ☐ Yes
- ☐ No
- ☐ Other (please specify)

81. If needed, please add any additional comment to the previous question _____

*82. Has the organisation defined which documents should at minimum be retained in the study archive?

- ☐ Yes
- ☐ No
- ☐ Other (please specify)

83. If needed, please add any additional comment to the previous question _____

84. If available, please upload the standard list of documents to be archived for a typical study (only the list of document types/titles – not the actual documents) or send by email to Roberto Bonaiuti roberto.bonaiuti@unifi.it.

*85. Does the organisation maintain an index/list of archived study materials, documents and data?

- ☐ Yes
- ☐ No
- ☐ Other (please specify)

86. If needed, please add any additional comment to the previous question _____

*87. Does the organisation maintain a regular back-up during the study conduct of the electronic data (i.e. server) and is this back-up in a different location than the location of the primary data server?

☐ Yes, the organisation maintains a back-up and the location of the back-up is different location from the primary storage
☐ Yes, the organisation maintains a back-up, but the location of the back-up is the same location as the primary storage
☐ No, the organisation does not maintain back-up of the data
☐ Other (please specify)

88. If needed, please add any additional comment to the previous question _____

Security and confidentiality

Securing study data and maintaining confidentiality are an important aspect of ensuring data integrity and privacy of subject data.

*89. Does the organisation have any written procedure(s) covering security? (i.e. a processes which describes protection of data, physical storage areas etc)

☐ Yes
☐ No
☐ Other (please specify)

90. If needed, please add any additional comment to the previous question _____

91. If your organization has any written procedure(s) covering security, please detail the processes covered by written procedures for security (tick all that apply)

☐ Access of personnel to physical areas
☐ Access of personnel to systems
☐ Access of personnel to the server
☐ Access of personnel to study data
☐ Access of personnel to study documentation
☐ Other (please specify)

92. Is access to physical storage locations of paper study documents “controlled”?

(i.e. controlled meaning that it is possible to restrict access to authorized personnel to a place or other resource, that previous access is logged (manually or by a system) etc)

☐ Yes – this applies to most physical storage locations
☐ Yes - this applies to some physical storage locations
☐ No
☐ Other (please specify)

93. If needed, please add any additional comment to the previous question _____

94. Is access to laboratory sample storage “controlled”?

(i.e. controlled meaning that it is possible to restrict access to authorized personnel to a place or other resource, that previous access is logged (manually or by a system) etc)

- ☐ Yes – this applies to most laboratory sample storage
- ☐ Yes - this applies to some laboratory sample storage
- ☐ No
- ☐ Other (please specify)

93. If needed, please add any additional comment to the previous question _____

*96. Is access to the main server locations “controlled”?

(i.e. controlled meaning that it is possible to restrict access to authorized personnel to a place or other resource, that previous access is logged (manually or by a system) etc.)

- ☐ Yes – this applies to the main server location(s)
- ☐ Yes - this applies to some server location(s) – if multiple server
- ☐ No
- ☐ Other (please specify)

97. If needed, please add any additional comment to the previous question _____

* 98. Does the organisation maintain access logs for systems where study data is processed (excluding applications provided by DRIVE)?

- ☐ Yes – this applies to all systems where study data is processed
- ☐ Yes - this applies to some systems where study data is processed
- ☐ No
- ☐ Other (please specify)

99. If needed, please add any additional comment to the previous question _____

* 100. Does the organisation apply password access for individual work stations (i.e. laptops, desktops)?

- ☐ Yes, passwords are individual for all individual work stations - i.e. each person has their own a username or password for workstations
- ☐ No, no passwords are required for individual workstations
- ☐ Other (please specify)

101. If needed, please add any additional comment to the previous question _____

* 102. Does the organisation require password access to electronic systems/ applications relevant for study conduct (not considering the applications provided by DRIVE)?

☐ Yes – separate personal passwords are used for key systems/applications (i.e. in addition to password access for individual work stations)
☐ Shared/common passwords are used for key systems/applications (i.e. in addition to password access for individual work stations)
☐ N/A - password log on to individual workstations also grants access to key electronic systems/applications for named users only
☐ No passwords are sued for key electronic systems/applications
☐ Other (please specify)

103. If needed, please add any additional comment to the previous question _____

*104. Does the organisation obtain confidentiality agreements of the study team members (as part of their contract or as separate agreements)?

☐ Yes
☐ No
☐ Other (please specify)

105. If needed, please add any additional comment to the previous question _____

106. Does the organisation obtain confidentiality agreements of collaborating partners if they have access to study data?

☐ Yes
☐ NA - there are no collaborating partners OR these partners do not have access to study data
☐ No
☐ Other (please specify)

107. If needed, please add any additional comment to the previous question _____

108. Does the organisation obtain confidentiality agreements of commercial suppliers if they have access to study data?

☐ Yes
☐ NA - commercial suppliers are not used or do not have access to study data
☐ No

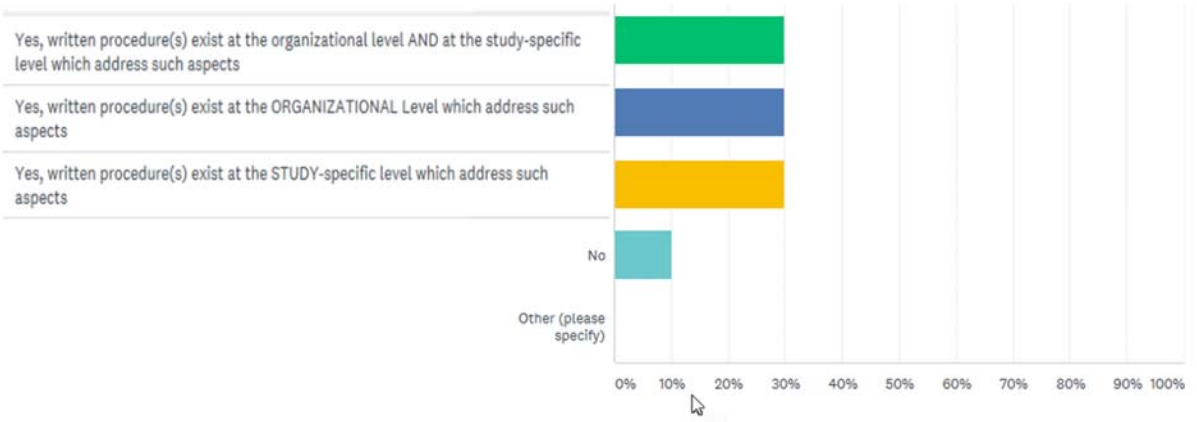
109. Please indicate any remaining input you wish to share:

We wish to thank you for completing this extensive, but important questionnaire! Your input is highly valued!

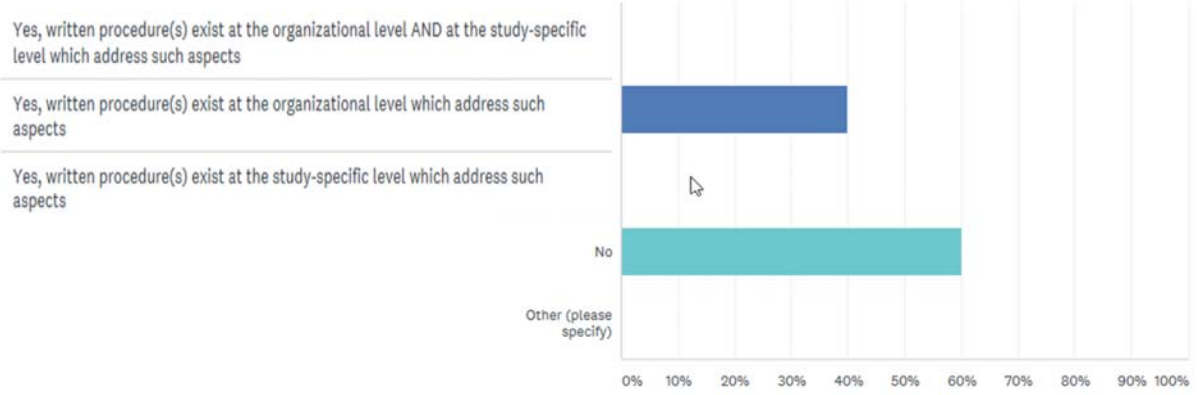
Annex 2- Aggregated summary of the survey responses

Questions of administrative nature are not shown. In line with the agreed confidentiality, only multiple choice responses are shown.

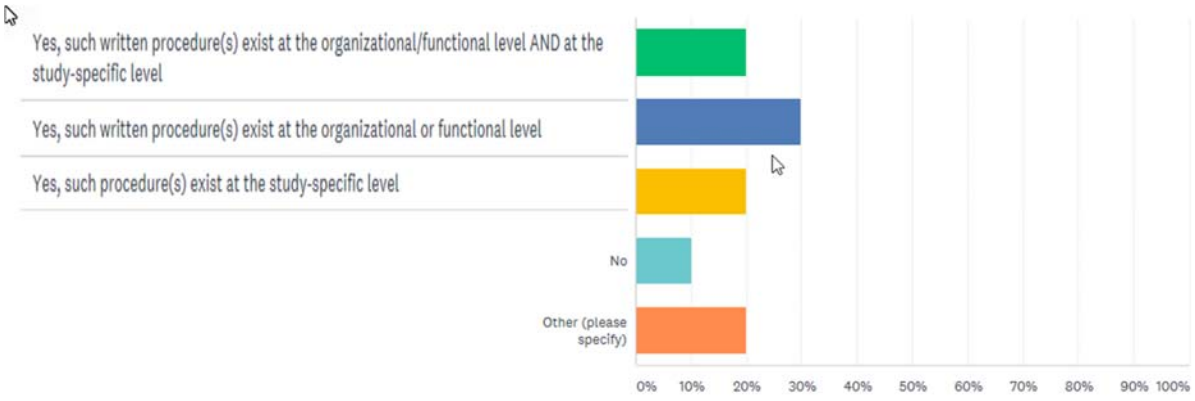
4. Does the organisation have any written procedures which describe **how quality is managed**? (i.e. procedure which may describe which role or function is responsible for quality management, which quality standards are applied, which governance exists around managing quality, etc)



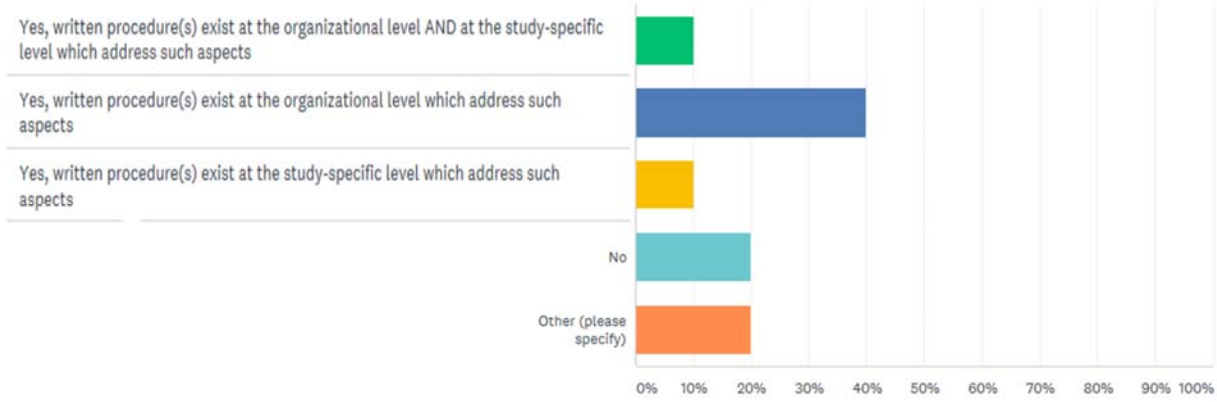
6. Does the organisation have a written procedure which describes **how written processes are managed**? (i.e. in essence "a written procedure on written procedures" which may describe how new written processes (incl templates/forms) are created, or existing processes are updated, how they are approved and where they are stored, etc)



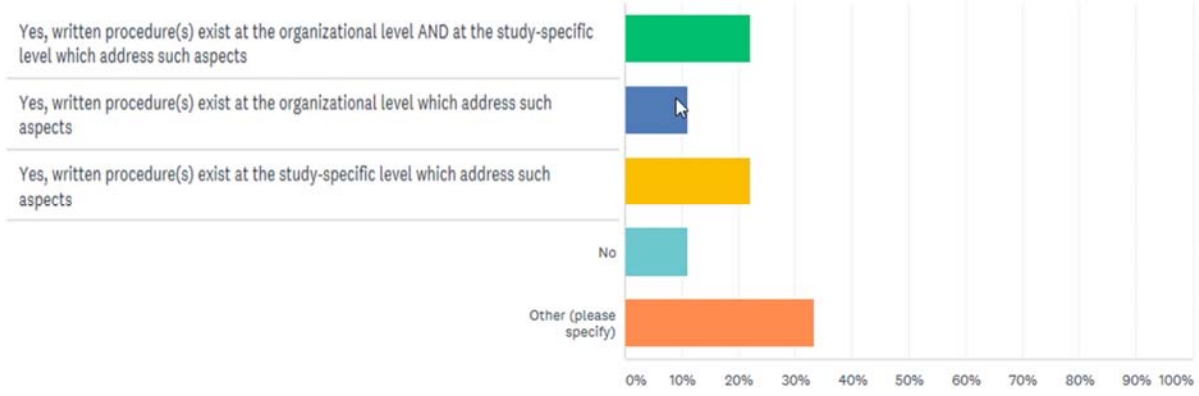
8. Does the organisation have a written procedure which describes **how risks are managed**? (i.e. a procedure which may describe how risks (i.e. risks to resources, timelines, safety) are identified, documented reviewed and how actions are decided, etc.)



10. Does the organisation have a procedure which describes how the organization is **informed of issues**? (i.e. a procedure which may describe how issues (i.e. noncompliance, violation of privacy etc) are documented, who within the organization is informed of issues (i.e. escalation path), on which issues they are informed and within what timeframe, etc)

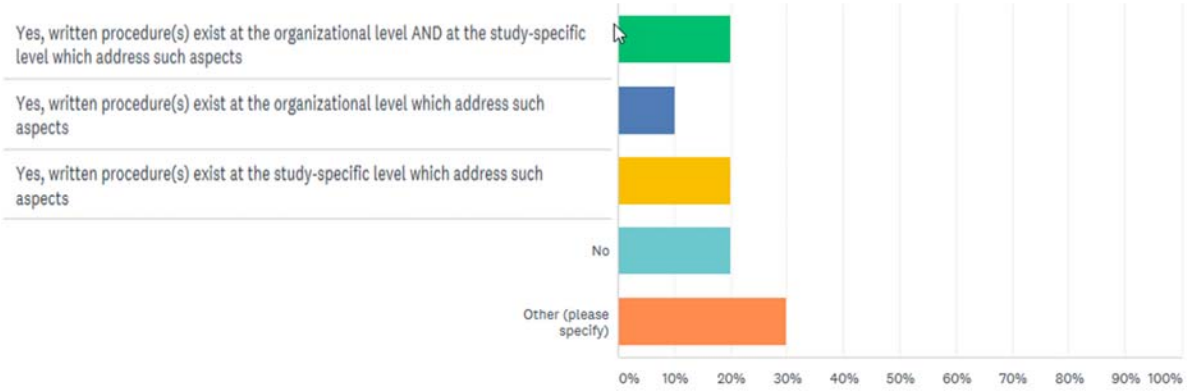


12. Does the organisation have a procedure which describes **governance**? (i.e. a procedure which may describe how different functions or decision bodies relate to each other and where decisions are taken and by whom, etc)

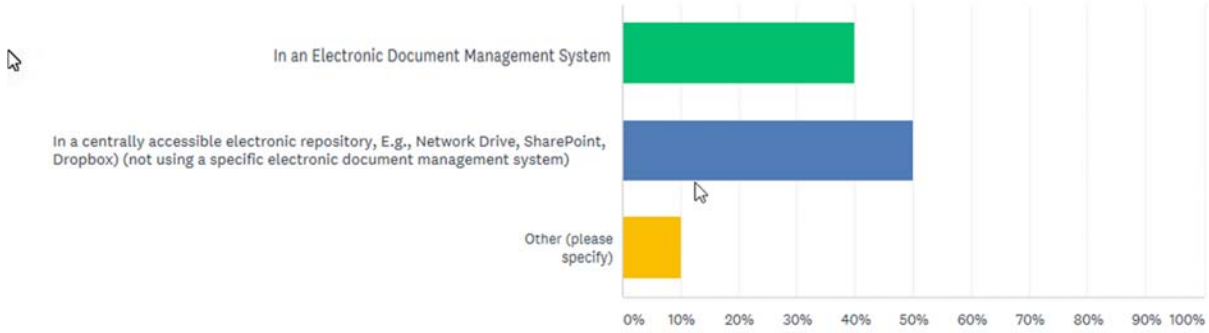


*14. Does the organisation have a procedure which describes how **non-compliance with a procedure** is handled?

(i.e. a procedure which may describe how non-compliance is documented, if actions are taken to correct and/or in the future to prevent non-compliance, and how completion of those actions is monitored etc.)

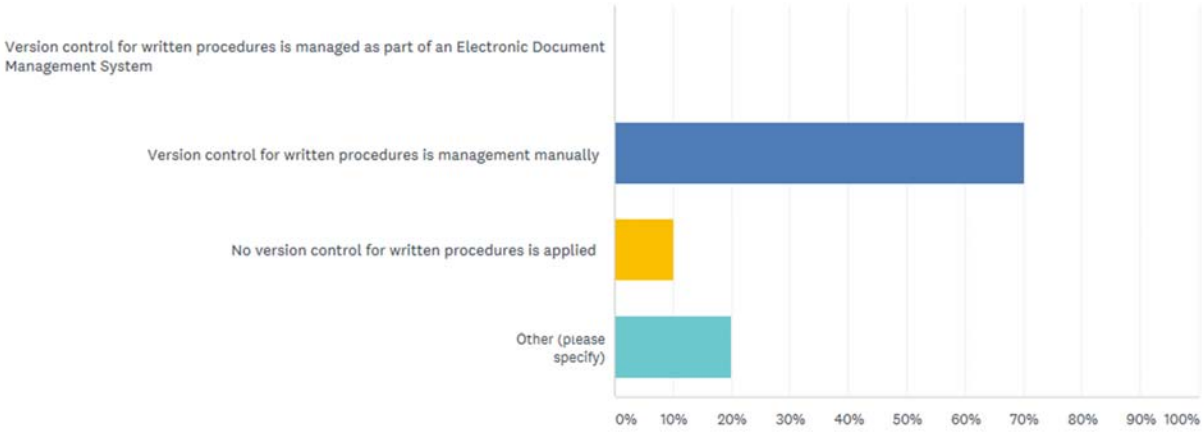


*16. How are written procedures stored within the organisation?

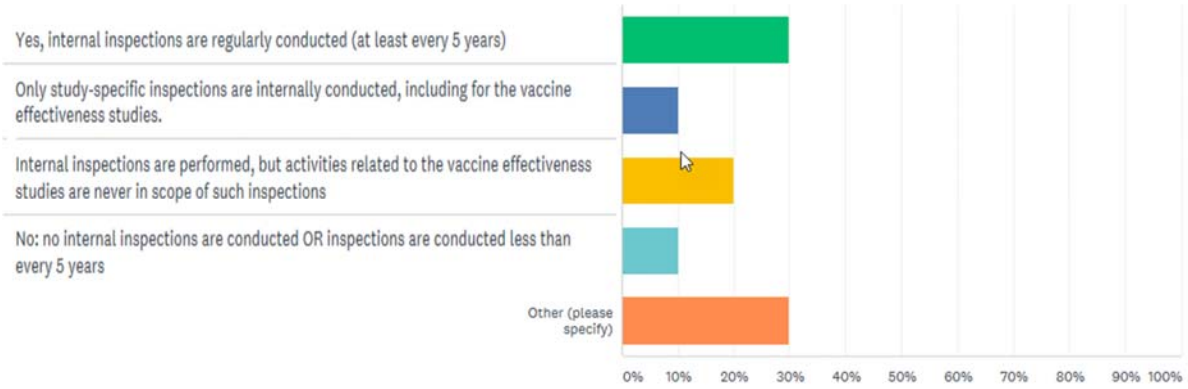


* 18. Is there version control applied for written procedures?

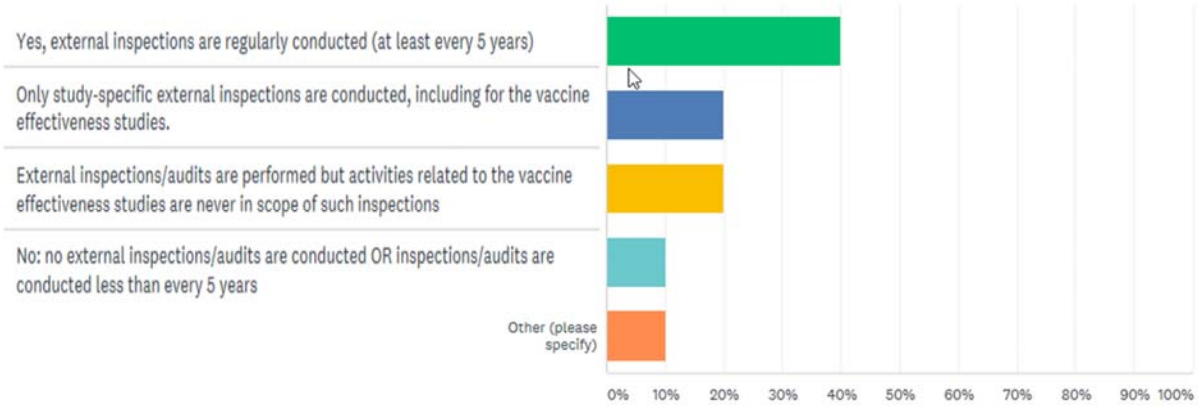
(i.e. version control is the means by which different versions and drafts of a document/file/dataset are managed. It provides an audit trail for the revision and update of draft and final versions. Specifically, it allows for the latest approved and effective version of a written procedure (including templates, forms etc) to be identified, such that outdated procedures are no longer used)



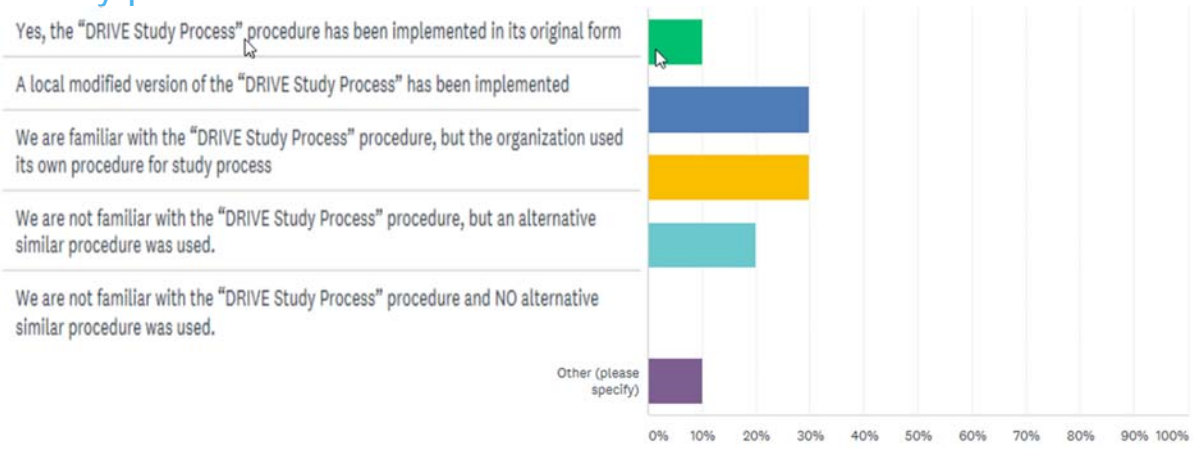
20. Do you conduct regular *internal* inspections to check the activities being performed by your organization, including the activities related to the vaccine effectiveness studies?



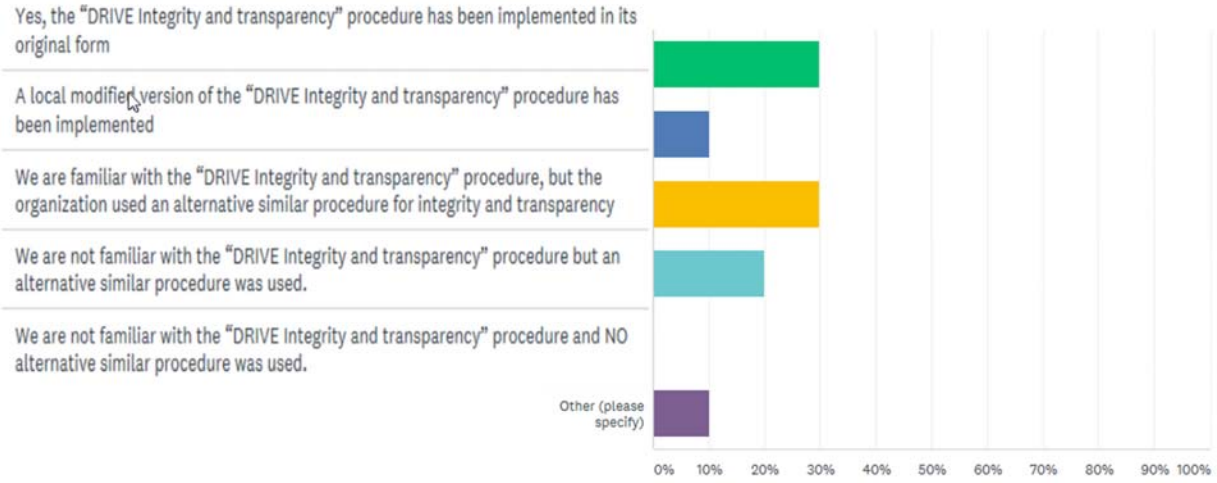
22. Is your organization regularly inspected or audited by an *external* organization(s)?



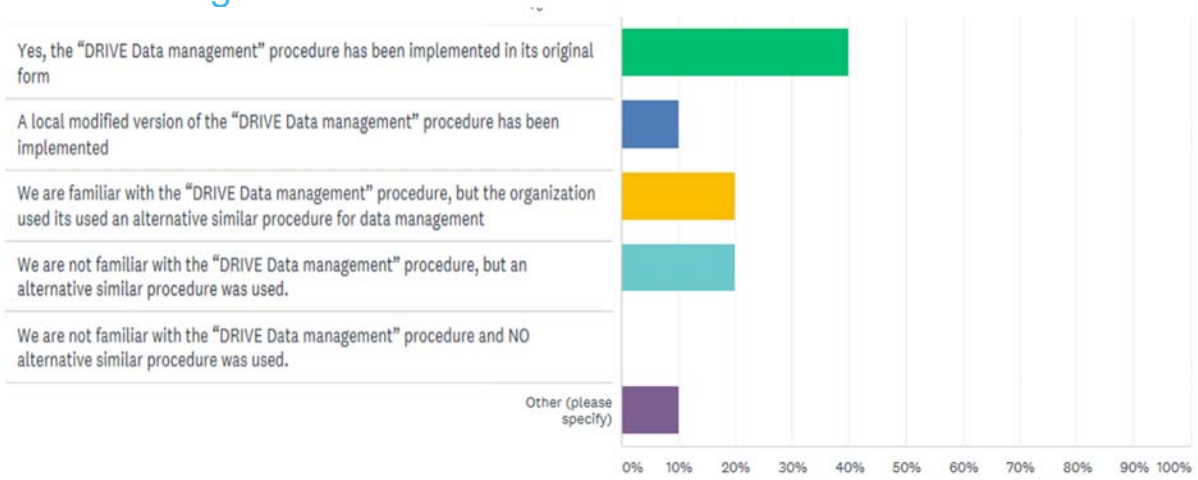
*24. Has the organization used the DRIVE written procedure on "Study process"?



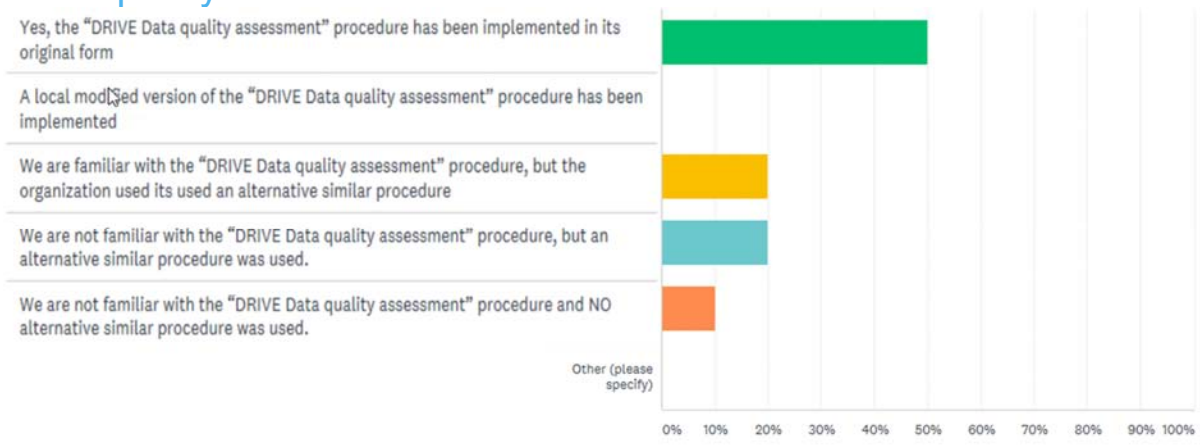
*26. Has the organization used the DRIVE written procedure on “Integrity and transparency”?



*28. Has the organization used the DRIVE written procedure on “Data management”?



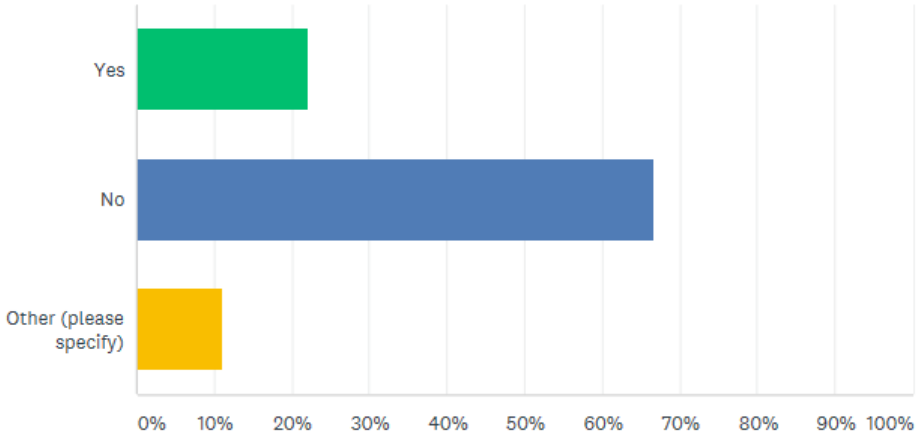
* 30. Has the organization used the DRIVE written procedure on “Data quality assessment”?



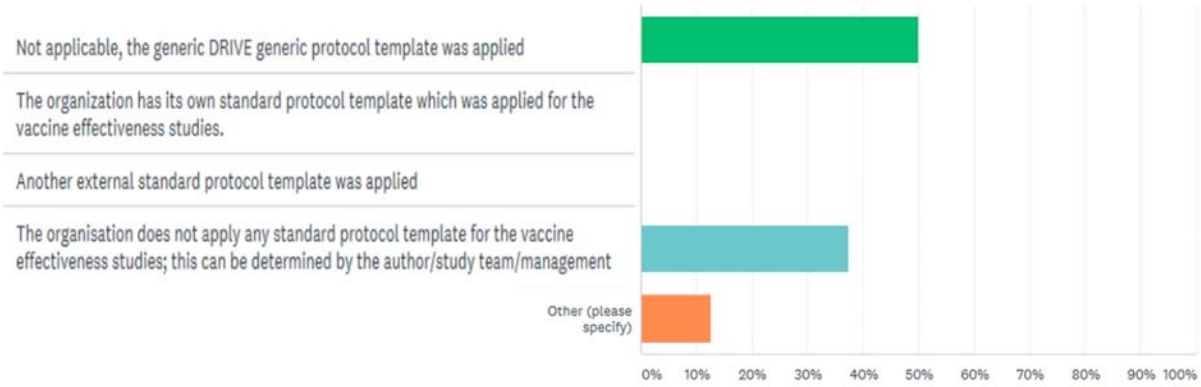
Protocol development

32. Does the organisation have a written procedure which describes how a study protocol is developed?

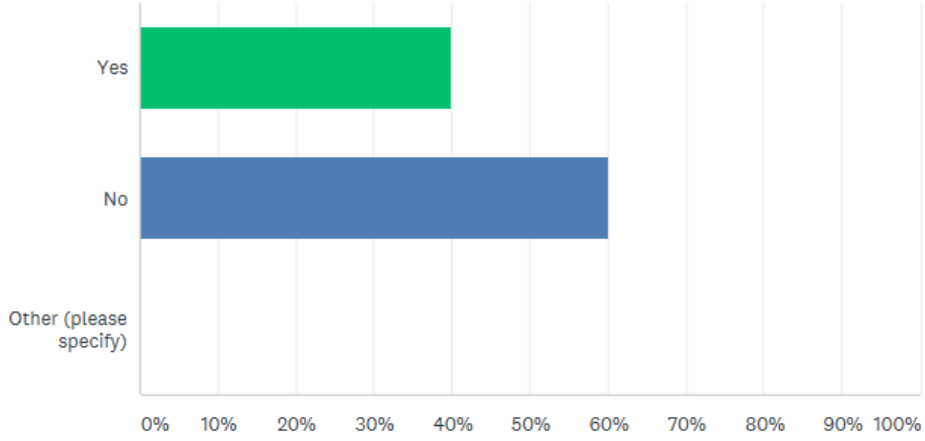
(i.e. a procedure which may describe which template should be used to write the protocol, which role/function is responsible for the writing of the protocol, how and which stakeholders should be consulted to provide input, who reviews the protocol, how the protocol is approved etc.)



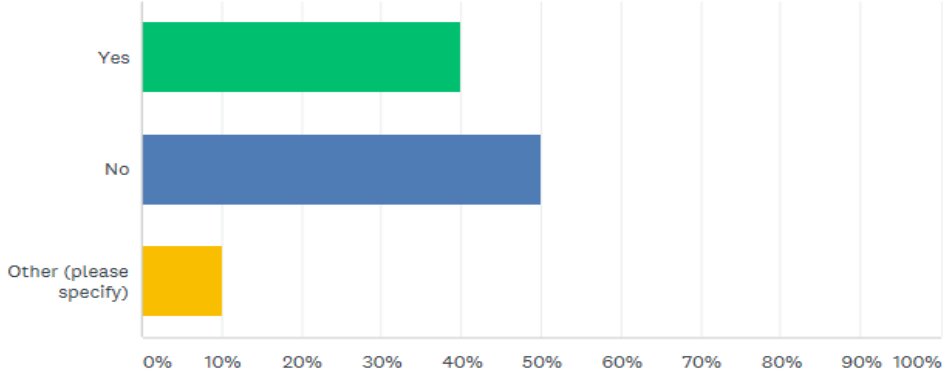
35. If you did NOT use the DRIVE generic protocol template, does the organisation use a standard template for the protocol development?



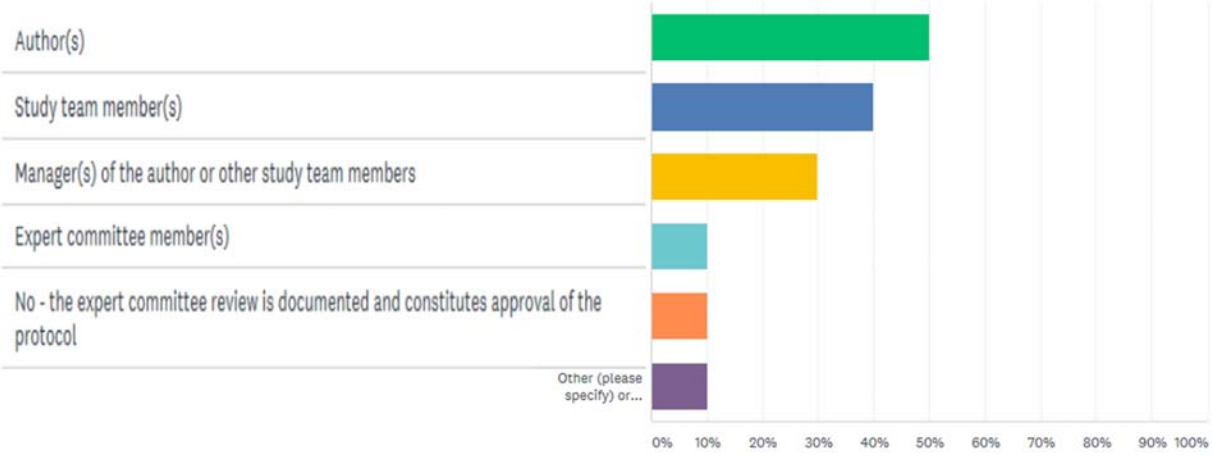
*37. Does a protocol undergo review by an expert review committee - separate from the review by the study team members or ethics committee review?



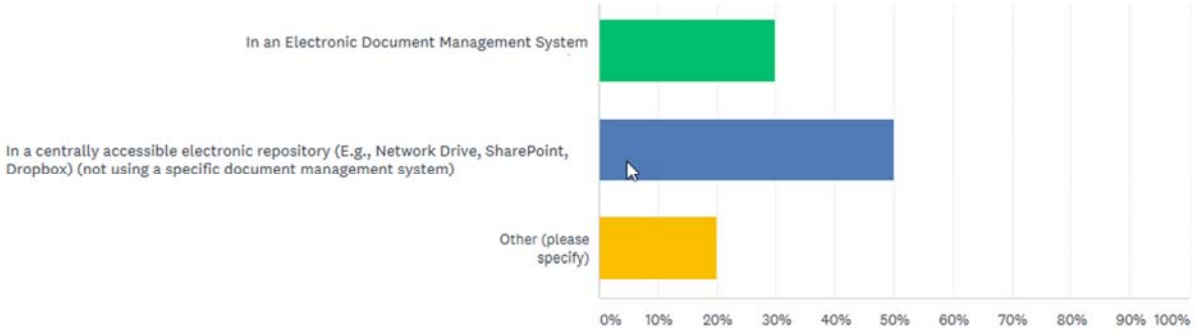
*39. Is the review of a protocol by the expert committee documented?



*41. Is formal sign-off (i.e. wet-ink, signature) of the study protocol required? Check all that apply:

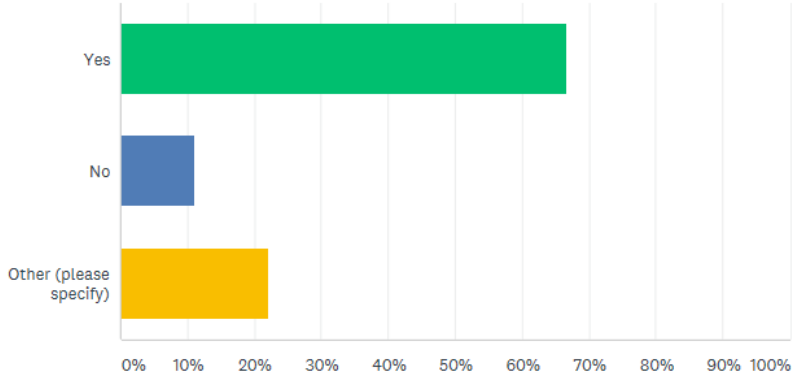


*42. Where are the study protocols maintained?



45. Beyond the protocol, are study specific documents created to describe the specific operational aspects of a study?

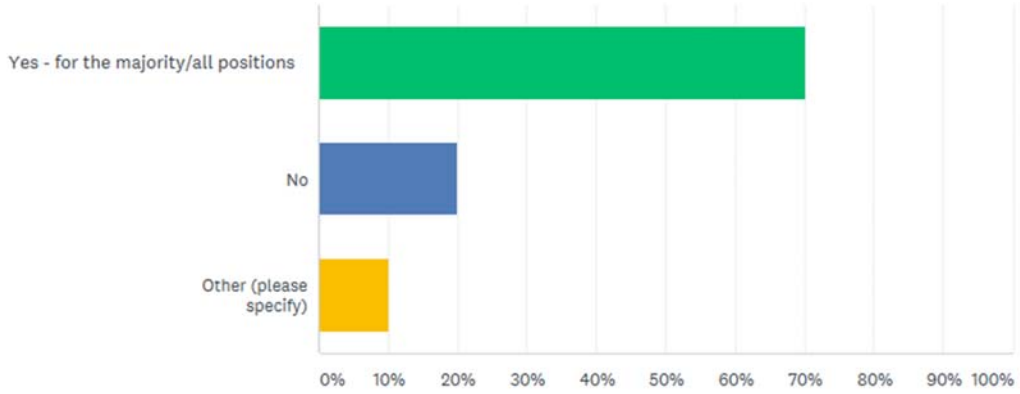
(i.e. documents processes/instructions/plans with contain more detailed instructions for the study staff how to perform the study in real-life)



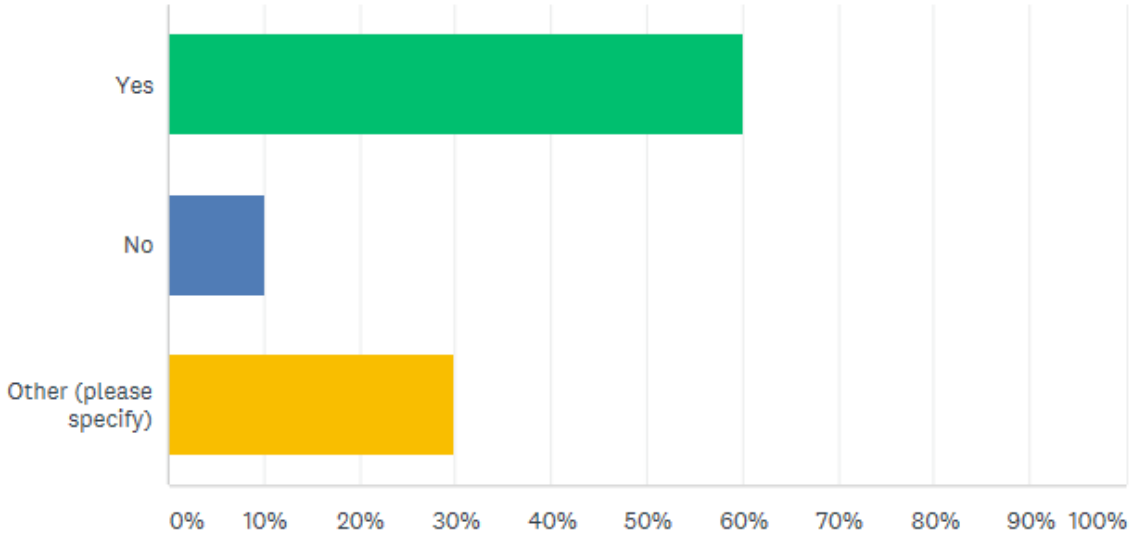
Personnel and Training

49. Are institutional Job Descriptions of personnel available?

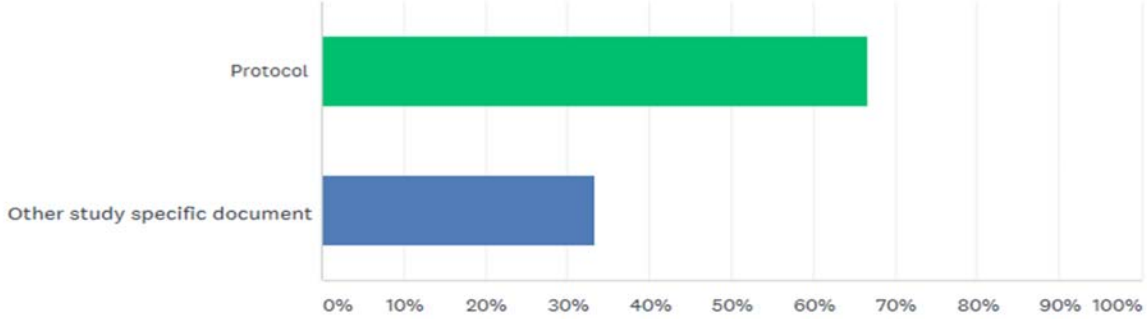
(i.e. a job description describes the general (not-study specific) tasks, or other related duties, and responsibilities of a specific position/role)



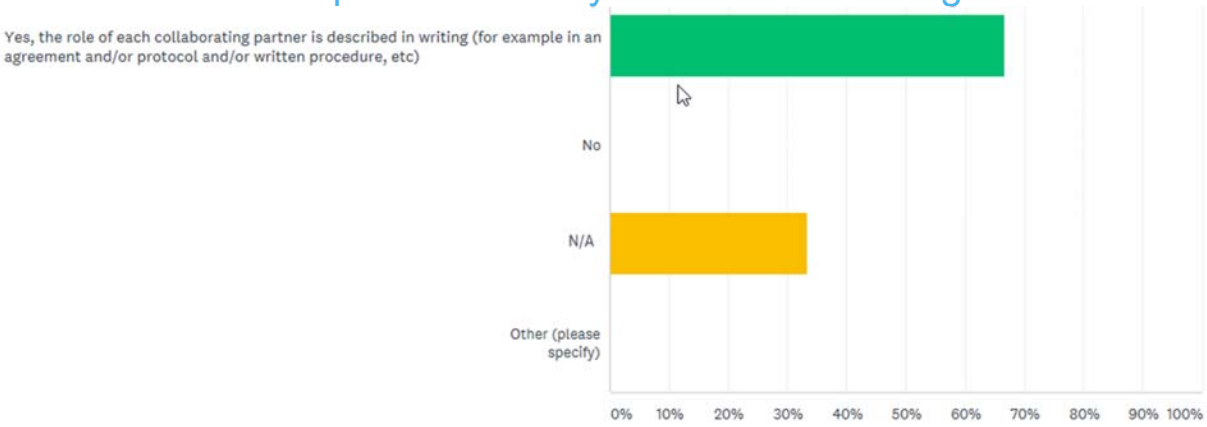
*51. Does the organisation document the study-specific roles and responsibilities of study team members?



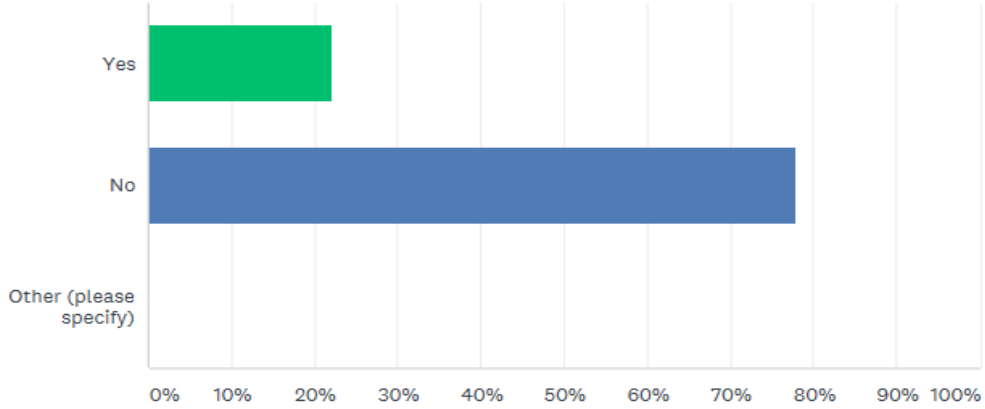
53. If your organisation documents the study-specific roles and responsibilities of study team members, please detail where the specific roles and responsibilities are documented



54. If the annual vaccine effectiveness studies involve a collaboration across multiple partnering entities outside your organization (i.e. coordinating center, hospital/GP, laboratory), is the role of each of the partners clearly described in writing?

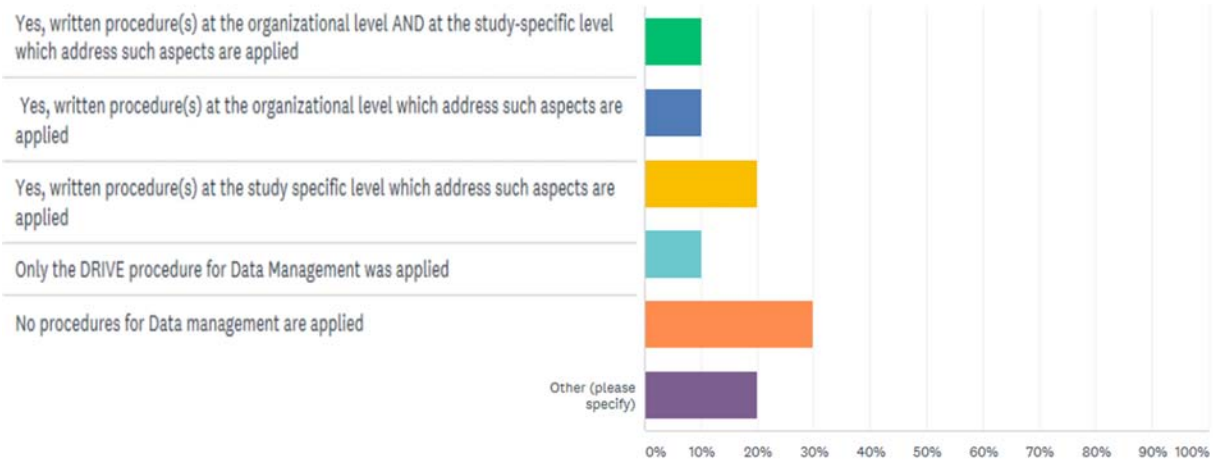


56. Do any commercial parties (i.e. suppliers) have a critical role in the vaccine effectiveness study conduct (for example for the testing of the swab samples, or conduct of the data management)?

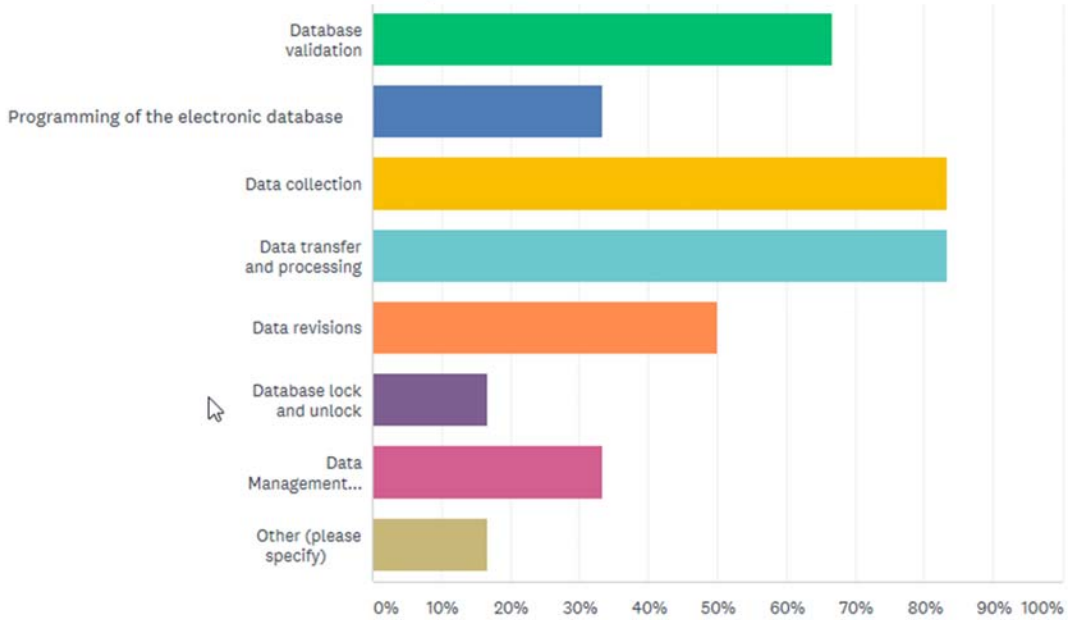


Data management

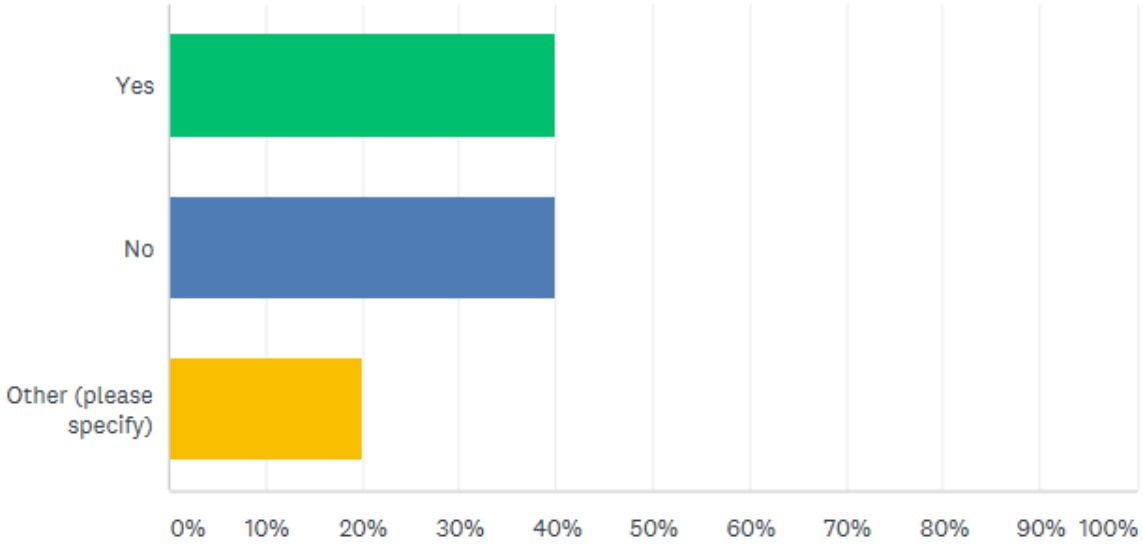
*59. Does the organisation have written procedure(s) for data management which were applied for the vaccine effectiveness studies? (i.e. a procedure which describes the flow of the research data from acquiring, validating, storing, and processing of data to ensure the accessibility, reliability, and timeliness for its users)
This can be in addition to the DRIVE Data Management procedure.



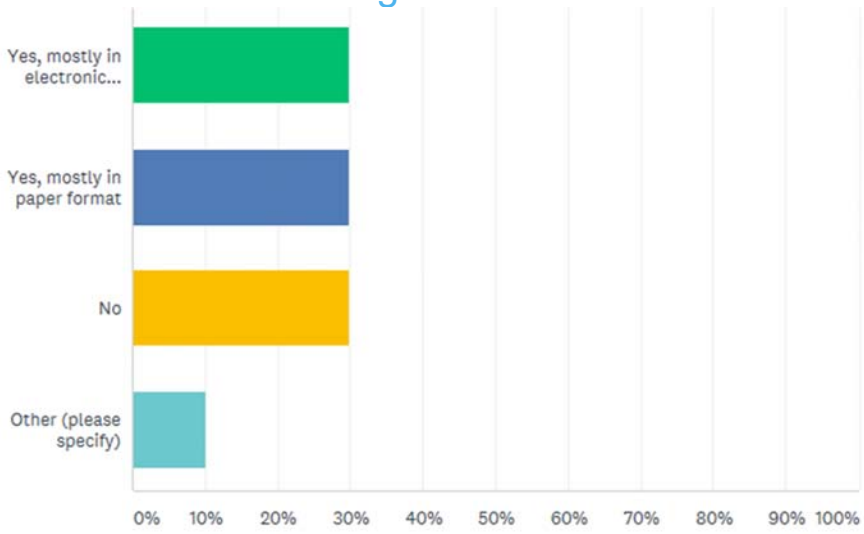
61. If your organisation has written procedure(s) for data management, please detail which processes are covered by your written procedure(s) for data management of vaccine effectiveness studies (tick all that apply



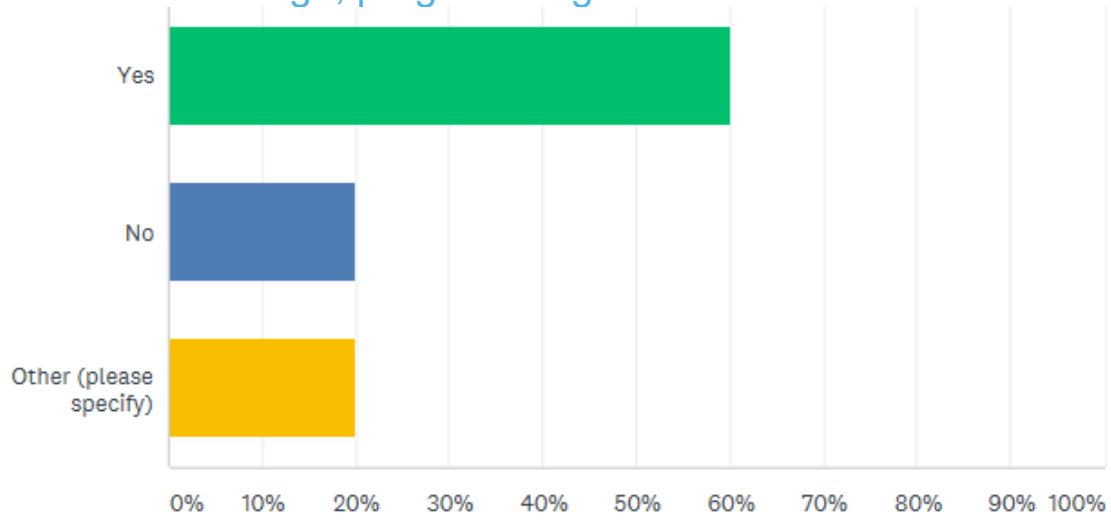
*62. Does the organisation have study-specific Data Management Plan(s) which describes the study-specific considerations for the data management?



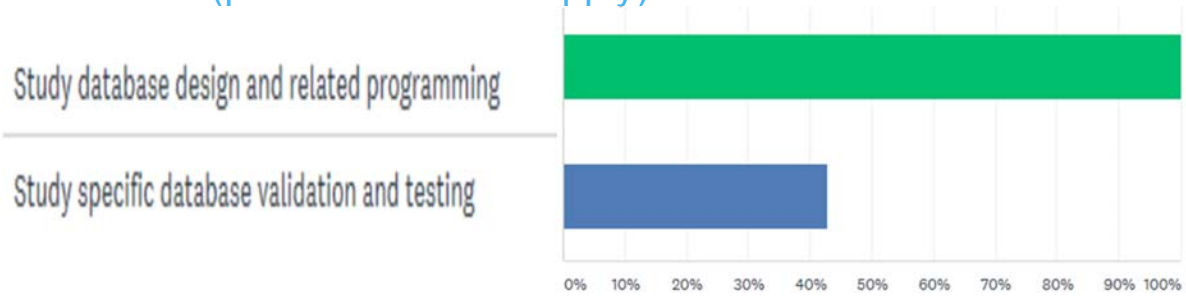
*64. Are standard forms used for the original data collection?



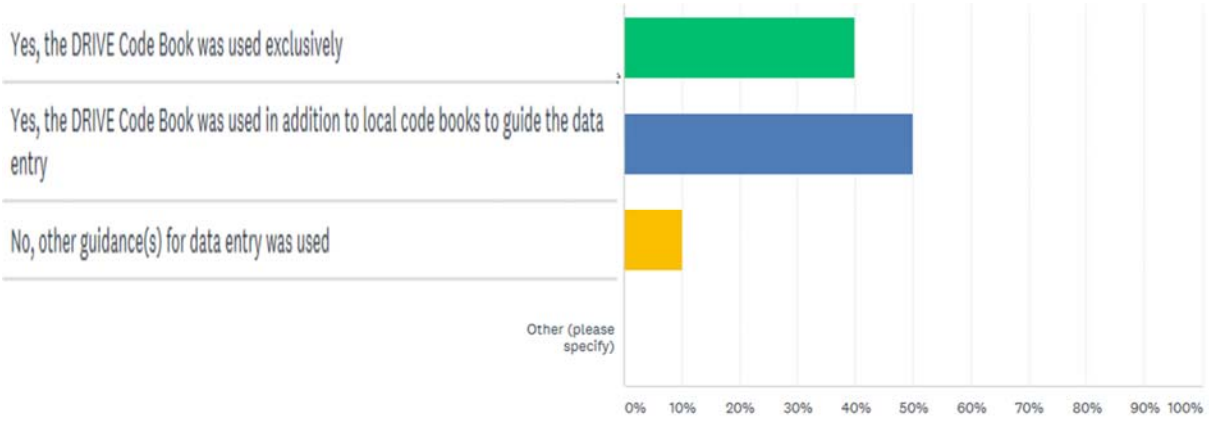
*66. Does the organisation maintain documentation of the study-specific database design, programming and validation?



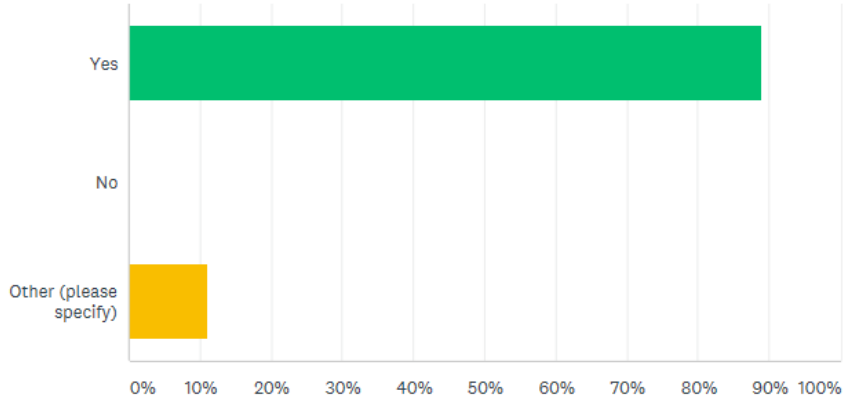
68. If you maintain a technical specification of the study-specific database design, please detail for which aspects documentation is maintained (please tick which apply)



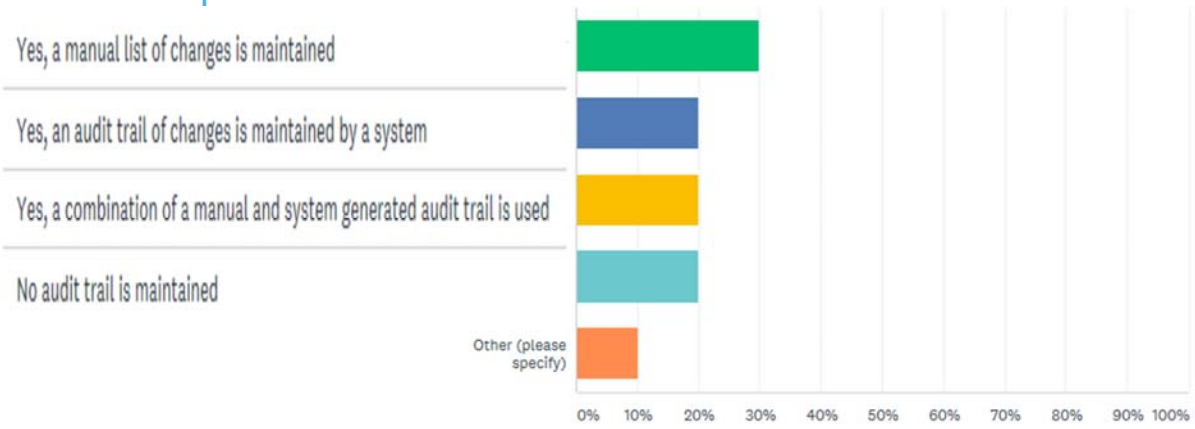
*69. Did the organisation use the DRIVE Code Book to guide the data entry in relation to the vaccine effectiveness studies from which the data was used in DRIVE?



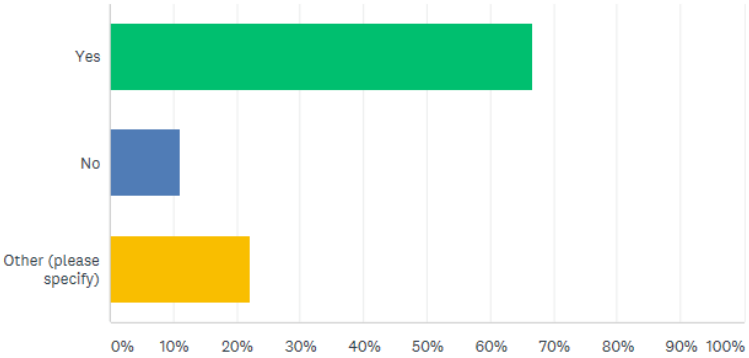
71. In addition to the quality and consistency checks devised by the “DRIVE Electronic Study Support Application”, does the organisation perform any additional local quality and data consistency checks?



*73. Does the organisation maintain a historical list of any revisions of the data points in the database?



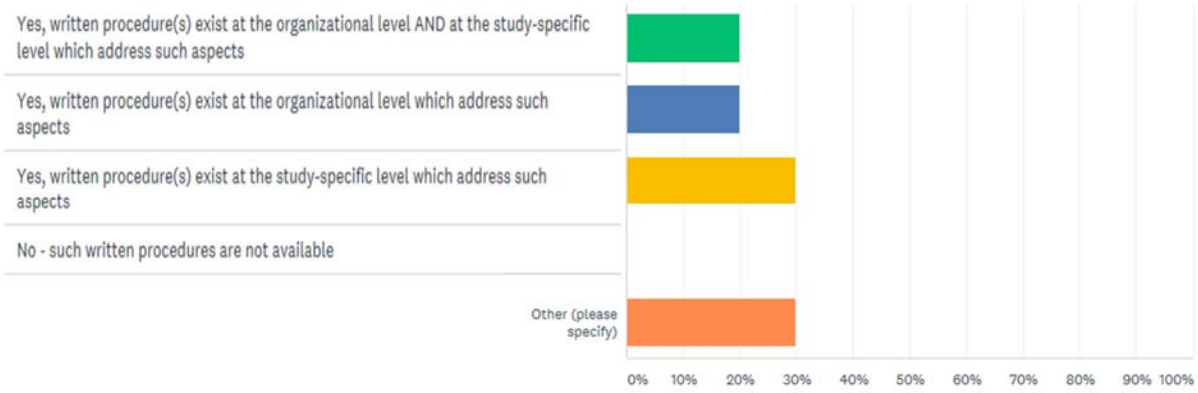
75. Does the organisation maintain a Data Management Report during the study conducts (i.e. a report which describes the events (i.e. identified inconsistencies, applied changes etc) which occurred in relation to the database?



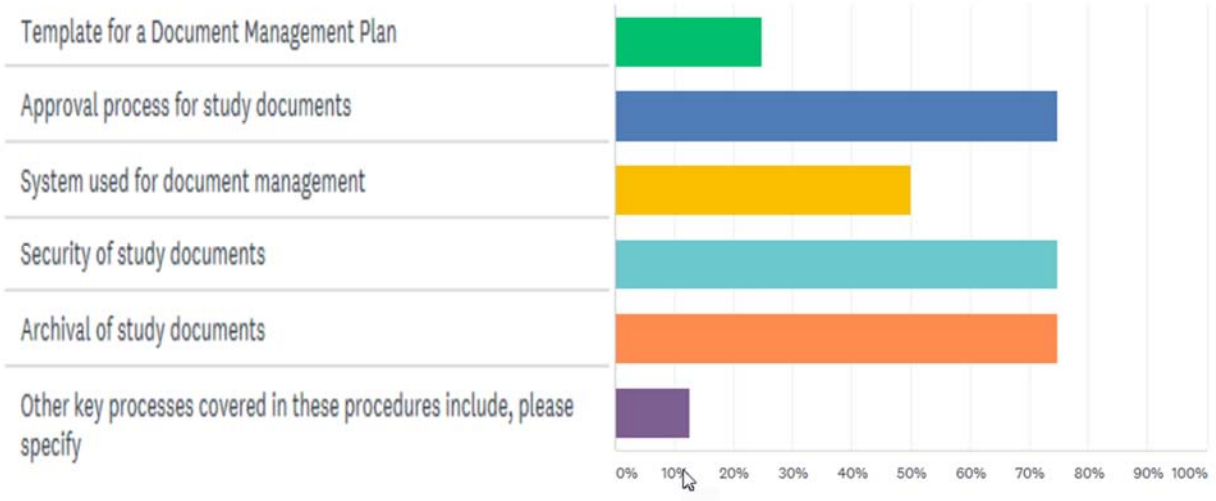
Document management

* 77. Does the organisation have any written procedures covering document management?

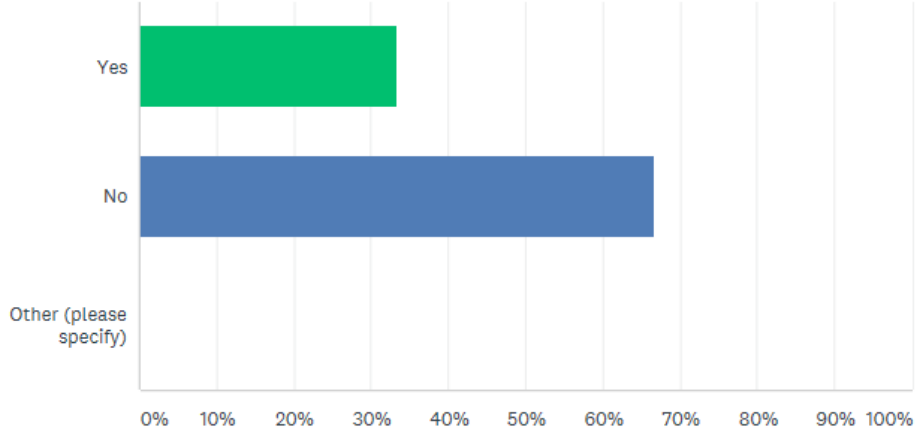
(i.e. a procedure which describes how electronic or paper documents are stored, retrieved, processed, distributed, secured etc), how documents are made accessible to authorized personnel etc.)



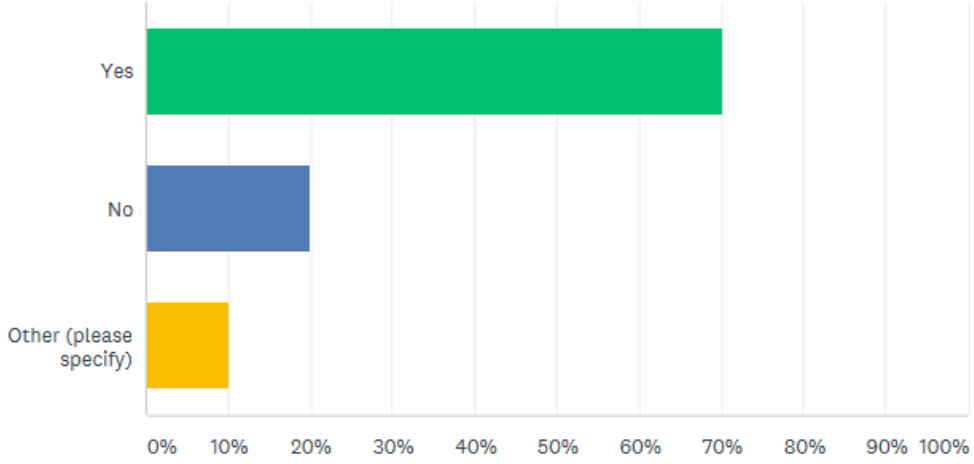
79. If your organisation has any written procedures covering document management, please detail the processes covered by the written procedures (tick all that apply)



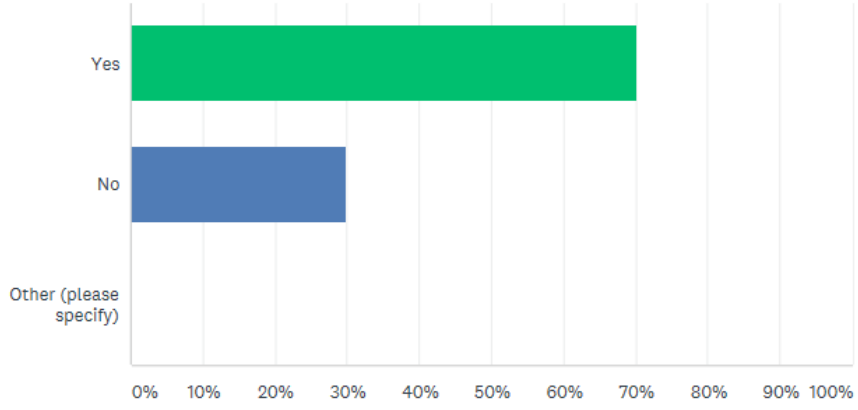
80. Does the organisation use a study-specific Document Management plan?



*82. Has the organisation defined which documents should at minimum be retained in the study archive?

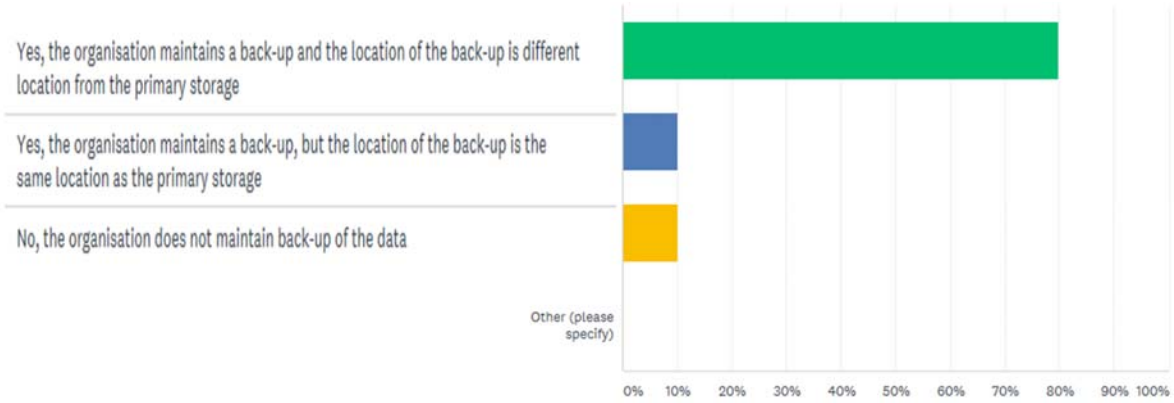


*85. Does the organisation maintain an index/list of archived study materials, documents and data?

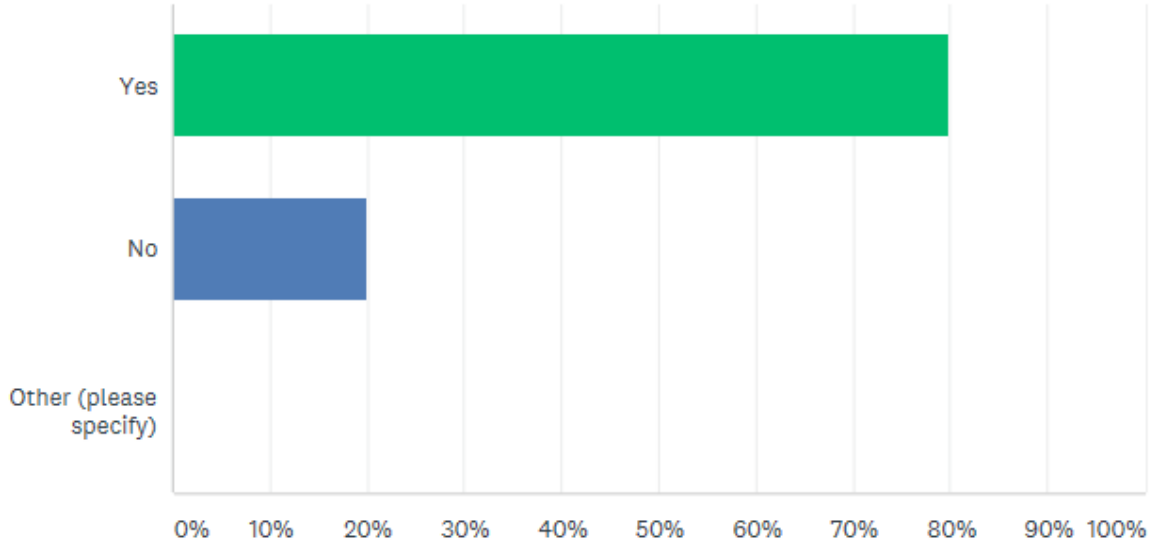


Security and confidentiality

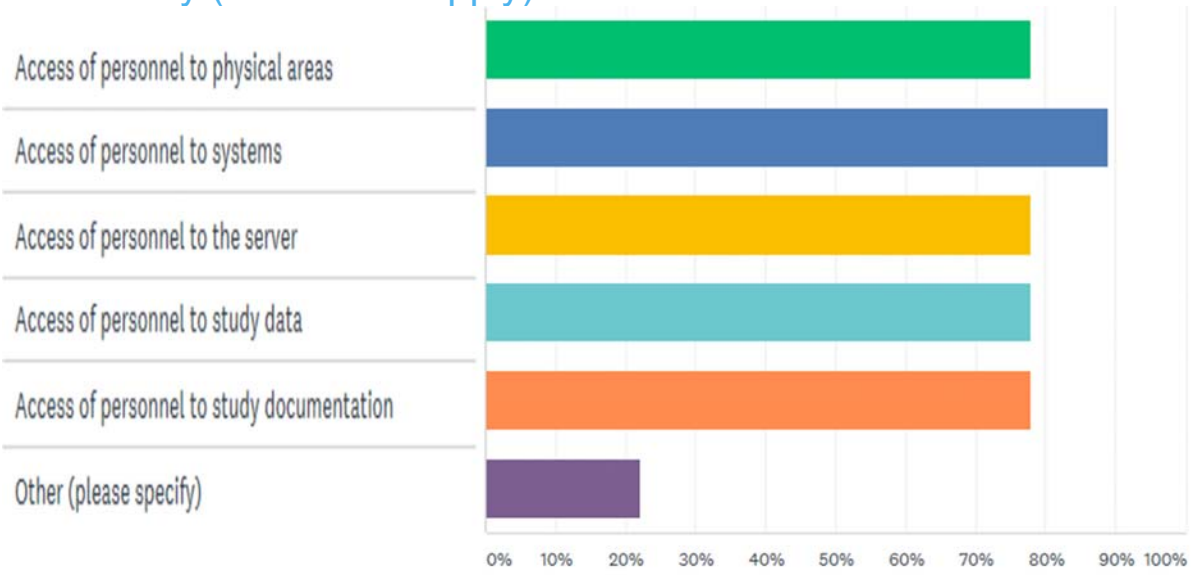
*87. Does the organisation maintain a regular back-up during the study conduct of the electronic data (i.e. server) and is this back-up in a different location than the location of the primary data server?



*89. Does the organisation have any written procedure(s) covering security? (i.e. a processes which describes protection of data, physical storage areas etc)

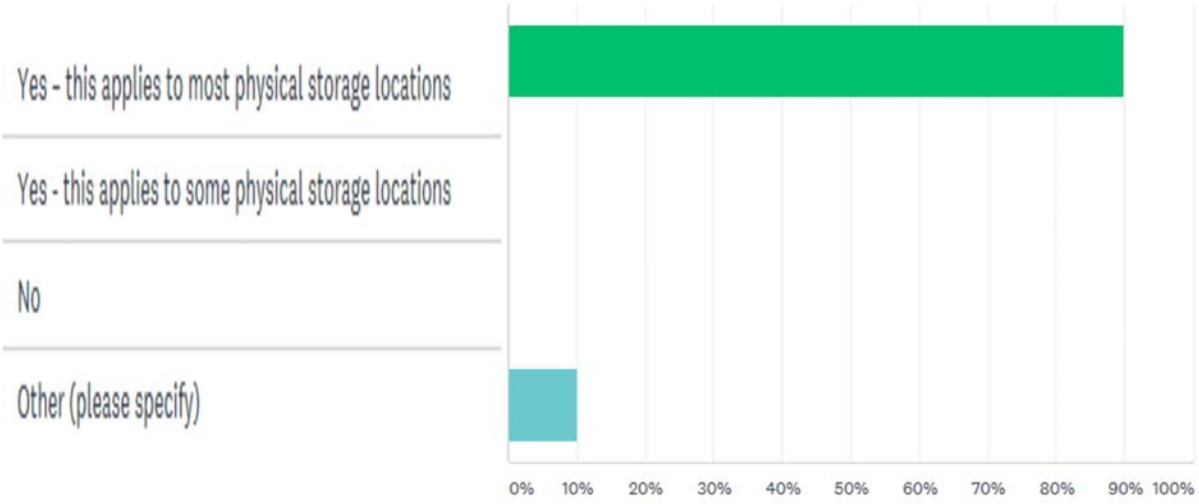


91. If your organization has any written procedure(s) covering security, please detail the processes covered by written procedures for security (tick all that apply)



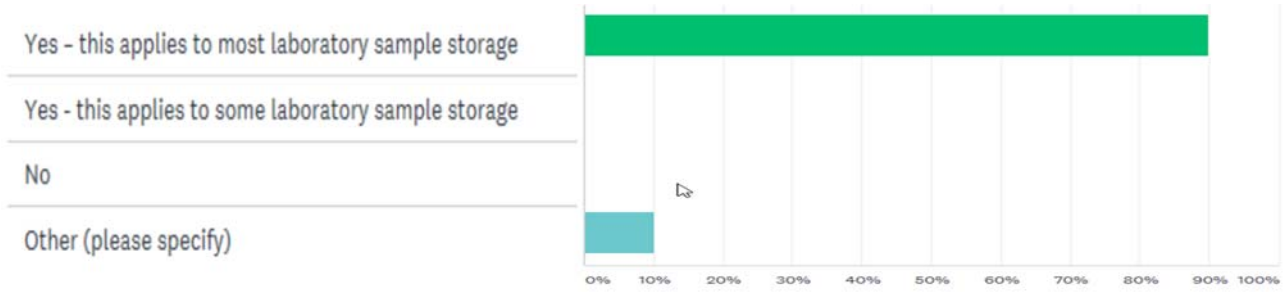
92. Is access to physical storage locations of paper study documents “controlled”?

(i.e. controlled meaning that it is possible to restrict access to authorized personnel to a place or other resource, that previous access is logged (manually or by a system) etc)



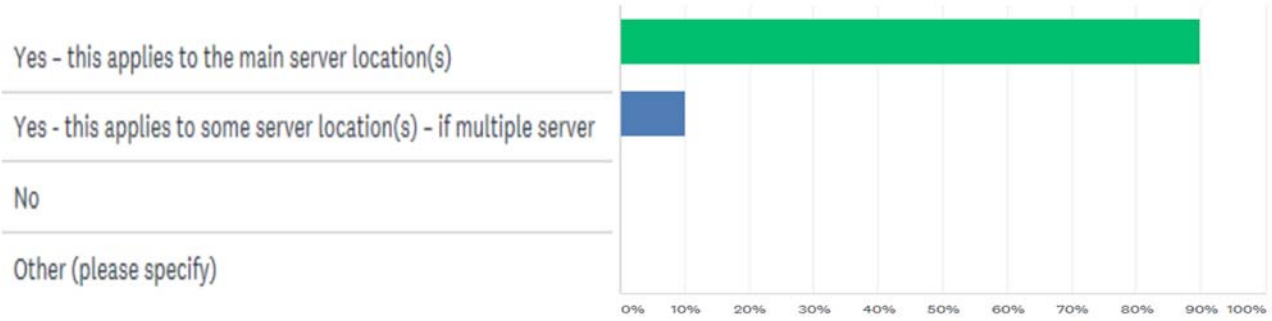
94. Is access to laboratory sample storage “controlled”?

(i.e. controlled meaning that it is possible to restrict access to authorized personnel to a place or other resource, that previous access is logged (manually or by a system) etc)

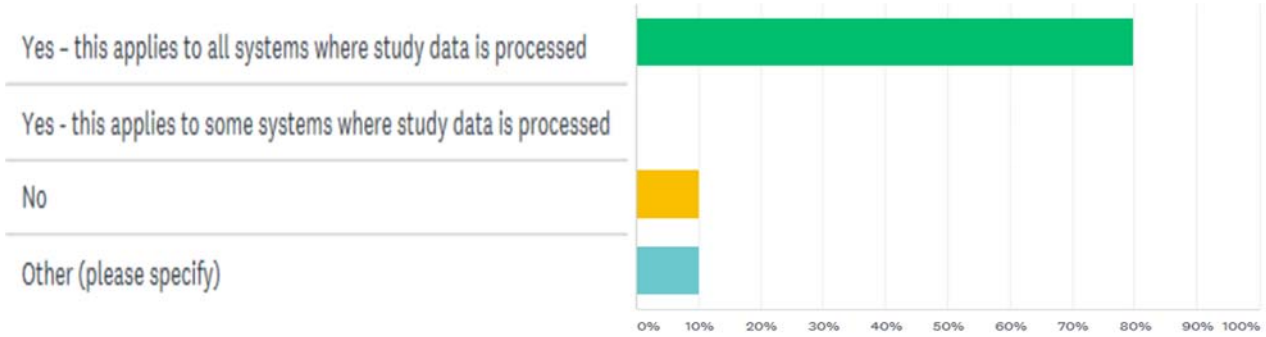


*96. Is access to the main server locations “controlled”?

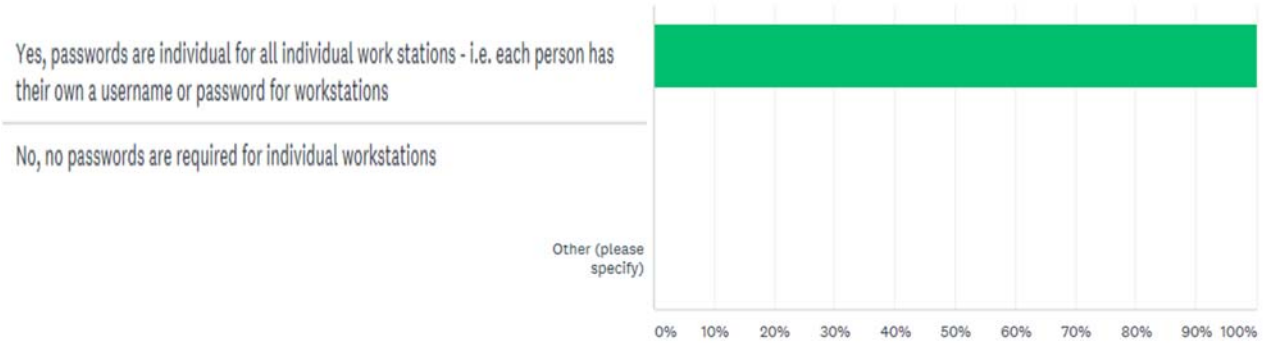
(i.e. controlled meaning that it is possible to restrict access to authorized personnel to a place or other resource, that previous access is logged (manually or by a system) etc.)



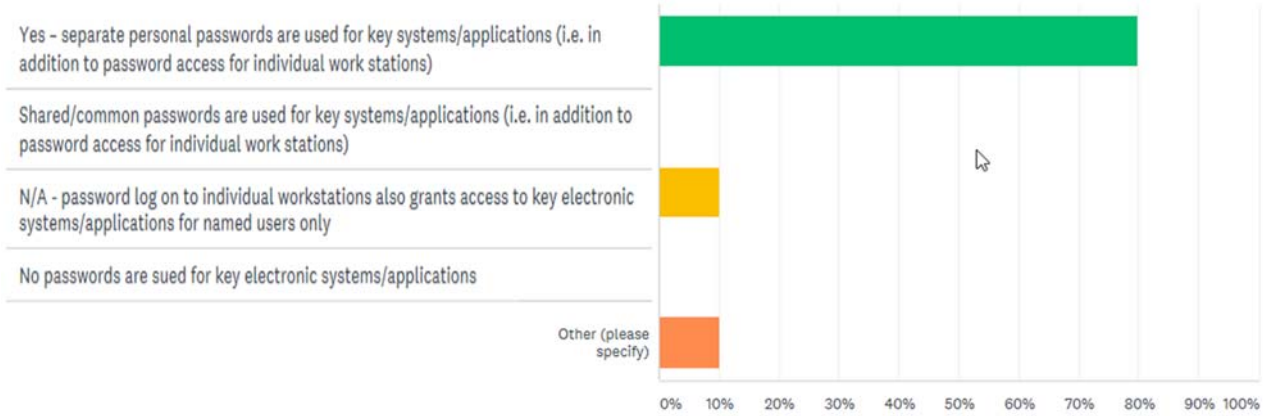
* 98. Does the organisation maintain access logs for systems where study data is processed (excluding applications provided by DRIVE)?



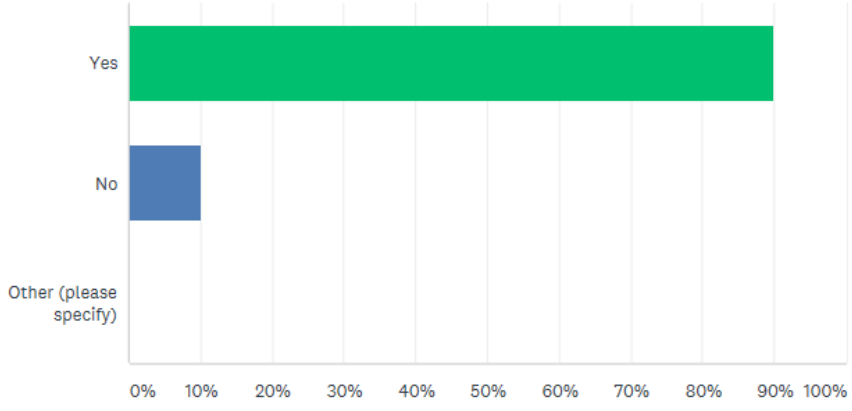
* 100. Does the organisation apply password access for individual work stations (i.e. laptops, desktops)?



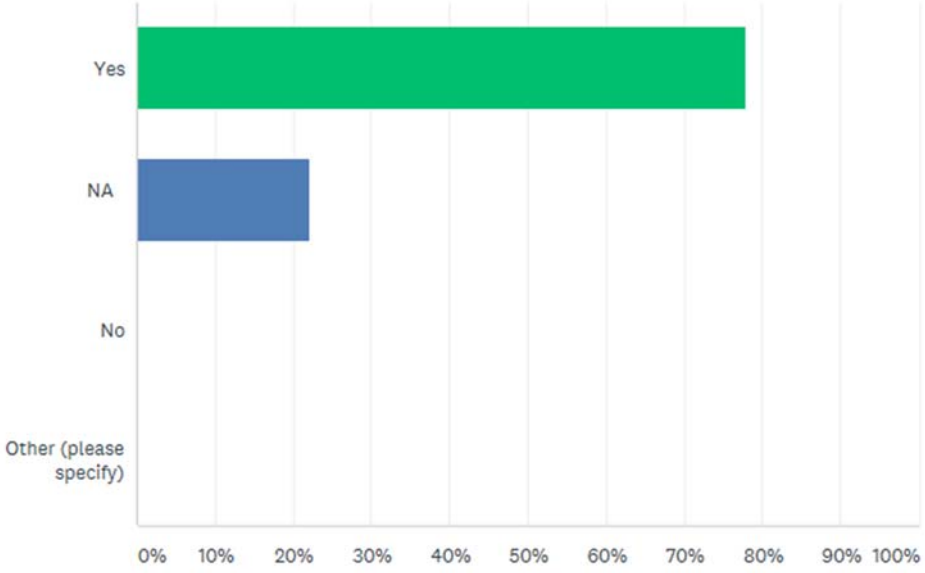
* 102. Does the organisation require password access to electronic systems/ applications relevant for study conduct (not considering the applications provided by DRIVE)?



*104. Does the organisation obtain confidentiality agreements of the study team members (as part of their contract or as separate agreements)?



106. Does the organisation obtain confidentiality agreements of collaborating partners if they have access to study data?



108. Does the organisation obtain confidentiality agreements of commercial suppliers if they have access to study data?