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Navigating eConsent Submissions: Who, What, Where and Why?

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Unraveling eConsent Ethics Committees and Health Authorities Submission Document Requirements to Foster Wider Adoption

eConsent is a hot topic within the clinical trial industry, but it is also a subject that gives rise to multiple interpretations and uncertainties. In this article we will focus on unraveling the information required by Ethics Committees (ECs) and Health Authorities (HAs).

Current clinical trial regulatory requirements[1,2,3,4,5,6,] and expectations are that participant-facing informed consent material and how informed consent will be obtained, must be reviewed, and approved by ECs. However, they are rather silent on various other aspects and processes linked with eConsent, especially those not seen by the participant, and the needs of HAs.

The non-profit, multistakeholder, European Forum Good Clinical Practice (EFGCP) eConsent Initiative wants to change this[7]. Experts from over 50 pharma, vendor and academic institutions launched two surveys to understand industry's thinking and understanding regarding EC and HA requirements for eConsent submission documents. The target audiences were primarily sponsors (pharma, academic institutions) and CRO/technology vendors. Nevertheless, a few ECs and HAs were also included in both surveys to consider their perspectives and see whether those aligned with industry perceptions.

Exploring eConsent Submission Needs: Platform and Operational Aspects

Two identical surveys focusing on eConsent study documents and information requirements for either EC or HA submission were distributed. Questions were grouped into eConsent platform and operational aspects (Table 1). Depending on the respondents' answers to the 28 survey questions, sub-questions about the rationale, type of submission document, and need for approval were triggered.

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Category	Sub-Category	Should ECs (or HAs) be informed about the following aspects
eConsent Platform Aspects	Digital Features	Participant's use of digital features
		Participant's type of digital features*
		Site's use of digital features
		Site's use of digital features
	eSignature/Wet Ink Signature	Use of eSignature
		Type of eSignature*
		Participants' access to a fully eSigned form*
		Use of wet-ink signature
		Electronic storage of wet-ink signed document*
		Linkage of wet-ink signature with electronic consent record*
	Remote Identification Methods	Participants' remote identification methods
	Remote Consent withdrawal	Participants' remote consent withdrawal
	Electronic Data Storage	Electronic data storage of PII data
		Electronic data storage of metadata metrics (non-PII data)
	Platform validation	Platform validation
	Platform integration	Platform integrations with study systems
		Platform integrations with site systems
eConsent Operational Aspects	Location	Location of consent discussion
	Training	Participants' training
		Sites' training
	Helpdesk	Participants' access to a helpdesk
		Participants' helpdesk measures linked to privacy*
		Sites' access to a helpdesk
	Device Deployment	Use of participants' own mobile device
		Use of provisioned mobile device
		Details of provisioned mobile device*
	Remote Monitor Access	Remote monitor access to PII data
		Remote monitor access to non-PII data

***Table 1**: Overview of the EC and HA submission docs survey questions. Questions marked with an asterisk (*) indicate additional questions triggered by a positive response to the related core question. PII refers to Personal Identifiable Information.*

Surveys were anonymous, but optionally, contact details could be provided in order to clarify unclear answers. The recommendation to respondents was to complete one survey per organization.

High Consensus: ECs Should be Informed About Most Aspects of eConsent

63 organizations completed the EC-focused survey (Graph 1). The majority (71%) were sponsors (pharma, academic institutions) and CROs/vendors, in line with the core audience of the survey. Additionally, 21% represented ECs and 8% indicated “Other”, which included a non-profit organization, a consultant and other research centers. Pharma and vendors predominantly had “global” experience (+90%) and the majority had at least piloted eConsent (+80%). ECs had more “local” expertise with 60% having piloted eConsent. Academic institutions had mainly “exploration or no” experience with eConsent (+70%).

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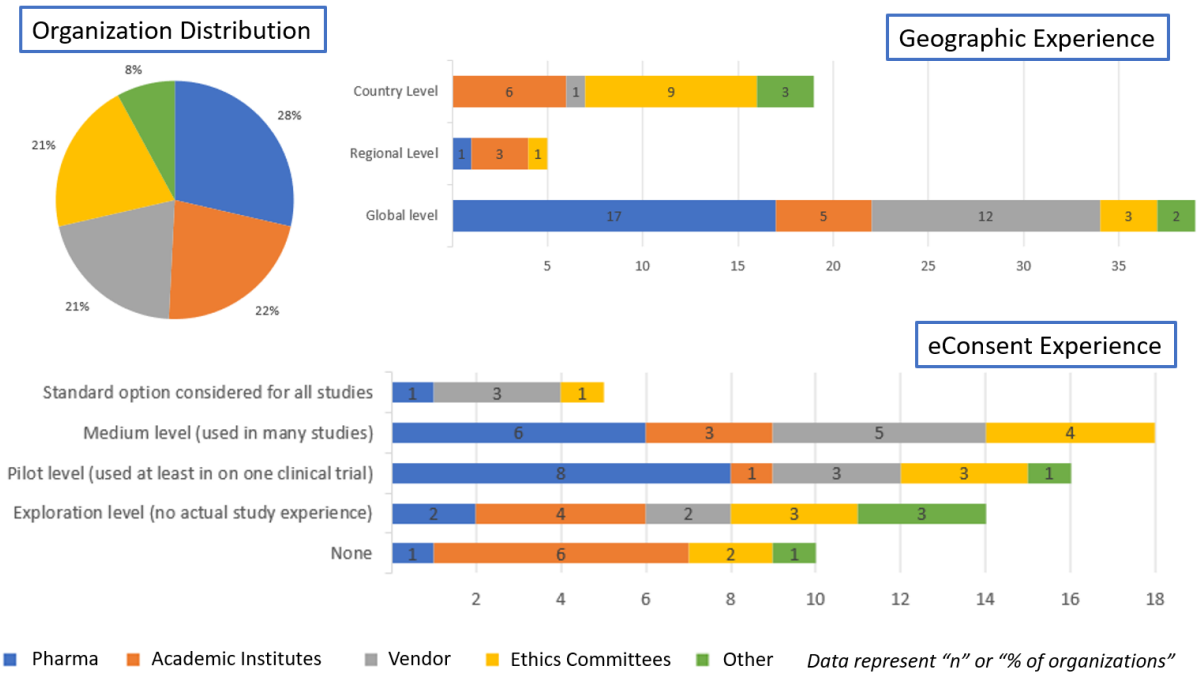

Graph 1: *Organization distribution, geographic and eConsent experience of EC survey respondents.*

There was a common opinion among all organizations that ECs should be informed about platform and operational aspects of eConsent (75% of core questions). Depending on the responses provided by respondents, the data was further categorized into high (+70% of organizations), medium (60-70% of organizations) and low (50-60% of organizations) levels of consensus.

- There was a **high** consensus that ECs should be informed about:
    - Participants' use of digital features, use of eSignature, remote consent withdrawal, remote identification methods, location of consent discussion, training, and access to a helpdesk.
    - Participants'/sites' use of a provisioned mobile device.
    - Sites' use of digital features.
    - Electronic data storage of personal identifiable information (PII) data.
- There was a **medium** consensus that ECs should be informed about the use of wet-ink signature, use of participants' own mobile device, and remote monitor access to PII data.
- There was a **low** consensus that ECs should be informed about platform validation and integration with site systems.

10% of core questions had a medium consensus that ECs should NOT be informed. These were questions related to sites' training and sites' access to a helpdesk.

15% of core questions had no consensus about whether an EC should be informed (or not) and those were related to electronic data storage of non-PII, platform integration with study systems and remote monitor access to non-PII.

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There was an 80% alignment of the responses of the participating ECs (n=13) with the responses of the organizations surveyed. Non-aligned responses (10%) were on questions related to platform validation (ECs scored this as NOT to be informed) and platform integration with study systems (EC scored this as to be informed). There was no consensus (10%) between ECs related to questions about electronic data storage of non-PII and remote monitor access to non-PII, which reflected the same lack of consensus among all organizations.

Limited differences in responses were observed to be linked with the geographic experience (75% alignment between local and regional/global) and eConsent experience (85% alignment between exploration/no experience and pilot/medium/standard experience).

It is important to emphasize that there was no unanimous consensus on any of the questions, not even within the same organization type, nor within the same country. As an example, 5 different ECs of the same European country completed the survey but 55% of the core questions were answered differently.

Clarity in Participants' Activities: Why ECs Should Know

More than 50% of organizations selected "It provides additional clarity allowing ECs to have a better understanding of participants' activities" and "It is important information for ECs to be aware of" for all questions as the rationale why ECs should be informed. Followed by "Required by regulations", which was also selected for all questions and by +50% of organizations for questions related to remote monitor access to PII and non-PII, electronic data storage of PII and non-PII, and participants' training.

"Not relevant for ECs" and "Not part of EC responsibilities" were scored as the key rationale why ECs should not be informed, next to some limited free text comments, such as "It is a sponsor responsibility (not ECs)" on the platform validation question.

Overall, all organization types gave comparable rationales.

Crucial Documents Requiring EC Approval with High Consensus that ECs Should Approve

Both "EC submission docs (e.g., patient-facing material)" and "protocol" were selected for all questions as the core documents where these aspects of eConsent should be described, with a slightly higher preference for the first option. A wide variety of "Other EC submission docs" was also given, such as recruitment documents, SOPs, data management plans, monitoring plans, etc.

Among the different organization types, academic institutions had an overall strong preference to document eConsent aspects in the "protocol" (85% of core questions selected by +50% academic institute respondents), while vendors selected the protocol in a very limited way as the EC submission document where aspects of eConsent should be documented (15% of core questions selected by +50% of vendor respondents) (Table 2).

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% of organizations per organization type that selected "Protocol"					
eConsent Platform and Operational Aspects	All	EC	Pharma	Acad Instit	Vendor
Participants' use of digital features (high-level reference)	64%	69%	41%	93%	50%
Participants' type of digital features*	49%	69%	24%	77%	9%
Sites' use of digital features (high-level reference)	58%	58%	42%	75%	44%
Sites' type of digital features*	45%	58%	30%	56%	0%
Use of eSignature (high-level reference)	47%	50%	25%	77%	36%
Type of eSignature*	37%	50%	29%	45%	25%
Participants' access to fully eSigned form*	29%	40%	13%	55%	10%
Use of wet-ink signature	28%	50%	20%	33%	11%
Electronic storage of wet-ink signed document*	37%	50%	17%	50%	20%
Linkage of wet-ink signature with electronic consent record*	36%	60%	17%	50%	20%
Electronic data storage of PII data	50%	80%	27%	83%	25%
Electronic data storage of non-PII data	47%	83%	33%	56%	0%
Participants' remote identification methods	46%	64%	23%	73%	33%
Location of consent discussion	64%	69%	33%	100%	60%
Use of provisioned mobile device	64%	58%	54%	92%	33%
Details of provisioned mobile device*	32%	30%	33%	38%	0%
Use of participants' own mobile device	44%	36%	50%	43%	33%
Remote monitor access to PII data	67%	56%	58%	100%	50%
Remote monitor access to non-PII data	76%	67%	75%	100%	33%
Participants' remote consent withdrawal	47%	42%	45%	88%	18%
Platform validation	51%	33%	42%	78%	25%
Platform integrations with study systems	75%	67%	57%	86%	33%
Platform integrations with site systems	52%	44%	56%	56%	25%
Sites' training	50%	40%	60%	67%	40%
Participants' training	34%	44%	20%	64%	17%
Sites' access to a helpdesk	44%	25%	60%	80%	0%
Participants' access to a helpdesk	28%	20%	27%	44%	22%
Participants' helpdesk measures linked to privacy*	31%	29%	22%	67%	14%

Multiple Answer Categorization		
High (+70% of organizations)	Partial (between 25-50% of organizations)	Not selected (0%)
Moderate (between 50-70% of organizations)	Low (less 25% of organizations)	

Table 2: *Comparison between the different organization types on selecting "protocol" as the EC submission document where eConsent aspects should be described. % represents the percentage of organizations per organization type.*

There was also a high consensus between all organizations and organization types, that ECs also need to approve the platform and operational aspects of eConsent (85% of the core questions), in addition to being informed.

High Consensus: HAs Should NOT be Informed on Most Aspects of eConsent, the 3 HAs Disagreed

58 organizations completed the HA-focused survey, with 81% representing sponsors (pharma, academic institutions) and vendors. Additionally, 3 HAs (5%), 2 ECs (3%) and 6 "Other" (10%) respondents also gave their perspective. "Other" represented similar organizations as the EC survey. Geographical and eConsent experience amongst the organizations was comparable with the EC survey respondents.

75% of core questions had consensus that HAs should NOT be informed about platform and operational aspects of eConsent, while 15% indicated that HAs should be informed and 10% lacked consensus (Table

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3). Participants' use of digital features (including type of digital features), sites' use of digital features (including type of digital features), use of eSignature (including type of eSignature and participants' access to a fully eSigned form) were the only questions with consensus that HAs should be informed.

However, these responses were NOT aligned (75%) with the responses of the 3 HAs, who scored 80% of core questions that HAs should be informed. The only questions with alignment that HAs should NOT be informed were about participants' training and sites' access to a helpdesk. Of note, 40% of core questions were not uniformly answered by the 3 HAs.

Pharma and vendors scored +75% of questions as HAs should not be informed versus 50% by academic institutions. A similar high score that HAs should not be informed was observed for regional/global level experience (75%) versus local experience (30%), and pilot/medium/standard eConsent expertise (85%) versus no/exploration level experience (35%) respondents.

The 2 ECs answered all questions as HAs should NOT be informed (85%) or "Don't know (15%)" with the rationale "HAs should only be informed if the eConsent tool would also be used by the participant to notify on adverse event reactions" (EC 1) and "eConsent is not allowed in my country, whatsoever" (EC 2).

Similar to the EC survey, none of the HA questions had 100% consensus between the organizations.

Organization Type	% of Core Questions That HAs Should be Informed, Not Informed or No Consensus		
	Inform	Not Inform	Not Consensus
All (n = 58)	15%	**75%**	10%
HAs (n = 3)	**80%**	10%	10%
ECs (n =2)	0%	**90%**	10%
Pharma (n =17)	5%	**85%**	10%
Academic Institutes (n =10)	40%	**50%**	10%
Vendors (n =20)	20%	**75%**	5%
Other (n =6)	30%	35%	35%

Table 3: *Overview of responses, divided per organization type, on whether HAs should be informed or not.*

Rationale for HA Non-Involvement and the Role of the Protocol

"Not part of HA responsibilities" and "Not relevant for HAs" was selected for most of the questions, often by +40% of organizations, as the key reasons why HAs should not be informed.

Additional free text comments included "It is an EC responsibility," "No information should be provided upfront to a HA but it needs to be available to review, upon request, during inspections," "It is a sponsor

responsibility when they audit the technology vendor," "HA only needs to be informed if it concerns pure personal data protection," and "HA only needs to be informed if the mobile device will also be used for medical monitoring".

The rationale given by the 3 HAs (who answered most questions as they should be informed) was "It provides clarity that can avoid queries in future inspections". "Required by regulations" was selected by 2 of the 3 HAs for questions related to participants' use of digital features, sites' use of digital features and the use of eSignature - all limited to a high-level reference, with no need for detailed information about type or participants' access to a fully eSigned form.

For respondents who indicated that HA should be informed, the "protocol" was selected as the key document where this information should be described, followed by the "submission cover letter". A variety of other HA submission documents were provided, comparable with comments on the EC survey, as well as free text comments such as "Only remote consenting should be covered in the protocol (high level)".

Of the limited questions with consensus that HAs should be informed, sites' use of digital features and use of eSignature (both only high-level references) were the only ones where respondents had consensus that HAs need to approve.

The Need for Further Guidance and Alignment

While overall there was some common perspective that ECs should and HAs should NOT be informed about most aspects of eConsent, none of the questions had 100% consensus between the organizations, nor even within the same type of organization.

Questions related to the platform, operational aspects of eConsent in relation to participants, and PII data, had overall high consensus that ECs should be informed, while questions about platform validation, platform integrations, electronic data storage and remote monitor access fell in the grey zone, with either low consensus or no consensus between organizations. Additionally, sites' training and sites' access to a helpdesk had consensus that neither ECs nor HAs should be informed about these aspects of eConsent.

In general, the participating ECs (13) were aligned with EC survey responses, while the participating HAs (3) were not aligned with HA survey responses. While there was only a small number of HAs involved, the overall difference in opinion between the 3 HAs gives an indication that there is a lack of related understanding and guidance.

The "protocol" was often selected as the submission document for both EC and HA surveys where most of the platform and operational aspects relating to eConsent should be documented. EC respondents even suggested that the details about participants' and sites' use of digital features should be reported in the protocol. However, having such detailed information within the protocol, much of which is operational in nature and/or derived following protocol finalization, might impose unnecessary complexities (in particular relative to country and regional, regulatory differences), delay study start, or even increase the rate of protocol amendments.

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Several of the free text comments showed that there are many unknowns and disconnects regarding eConsent. Some comments were even contradictory. For example, one EC claimed "eConsent is not allowed in my country" (HA survey) while another EC of the same country indicated "eConsent is a standard option considered for all studies" as per their eConsent experience (EC survey). In addition, when consulting current regulatory guidance[2] the use of eConsent seemed to be supported within that European country.

Clearly, the surveys have provided valuable initial insights, but they also highlight that there are still numerous gaps to bridge in terms of basic understanding, addressing uncertainties, and harmonizing eConsent document submissions for ECs and HAs. A call for more practical guidance was recently also raised by a thorough analysis of eConsent in UK academic-led clinical trials[8].

As next steps, the EFGCP eConsent team will use these survey insights to generate tailored questions for ECs and HAs, to enable a unified eConsent guidance for EC and HA needs. In this effort, we will also consider and build further on existing guidelines[9, 10, 11]. We believe that as a multi-stakeholder, non-profit initiative, we are poised to elevate eConsent to its rightful place, maximizing its support for participants, sites, and all stakeholders in clinical trials.

Supplemental Information

The detailed results of the eConsent EC Submission Documents Survey and eConsent HA Submission Documents Survey, and a layout of the 2 surveys, are available at the EFGCP eConsent website Access to the Supplemental Information.

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