

# UNDERSTANDING AND ADDRESSING REGULATORY QUESTIONS IN THE USE OF TECHNOLOGY SOLUTIONS TO COLLECT PATIENT REPORTED OUTCOMES DATA

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## INTRODUCTION

Patient reported outcomes (PRO) data can be an important component of efficacy evidence in regulatory drug submissions. These data can represent the primary study endpoints where there are no objective markers of symptoms (eg. rhinitis) or no objective measures of the impact of symptoms (eg. sexual dysfunction). PRO data are also valuable secondary endpoints in therapy areas where diseases can be characterized by several possible measures (eg. asthma).

This poster explores the benefits of electronic PRO (ePRO) data collection and associated regulatory questions, and their potential solution, with particular reference to the use of Interactive Voice Response (IVR) systems.

## BENEFITS OF ELECTRONIC SOLUTIONS

The most common application of PRO utilizes paper diaries, instruments and questionnaires. The limitations of paper have been well documented and can result in erroneous data collection, invention of data as well as low (true) compliance levels [1,2].

Electronic solutions are acknowledged to address many of the quality and integrity concerns of regulators associated with paper diaries:

- The timeliness of diary entry can be measured
- Retrospective data entry can be limited
- Prospective diary entry can be prohibited
- Conflicting and ambiguous data can be eliminated

Common ePRO solutions include IVR systems [3] and hand-held devices (PDAs). IVR ePRO data have been submitted successfully to FDA as a component of new drug applications [4].

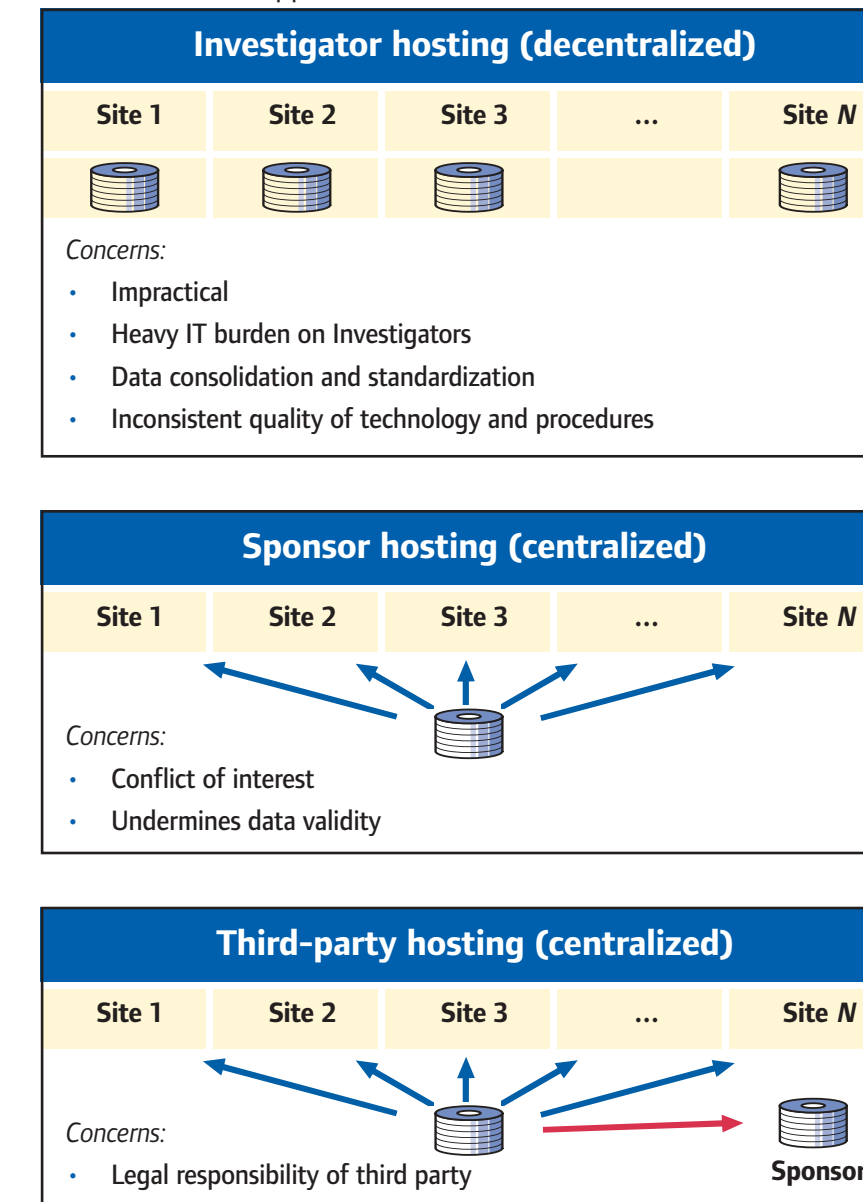
## SOURCE DATA RESPONSIBILITIES

Diary data are defined as source data in ICH GCP. This means Investigators are responsible for these data, should review these data along with other clinical data, and should be able to make these data available to an on-site regulatory auditor.

### What defines the source data

With IVR ePRO systems, the source data are the data stored on the central database server. This is the case with hand-held devices when data transfer from device to server is shortly after data capture. However, with hand-held devices it is necessary to prove that all data entered on each device will reach the central server. This requires a validated data transfer routine and IQ/OQ of every device used by patients.

FIGURE 1. ePRO application models



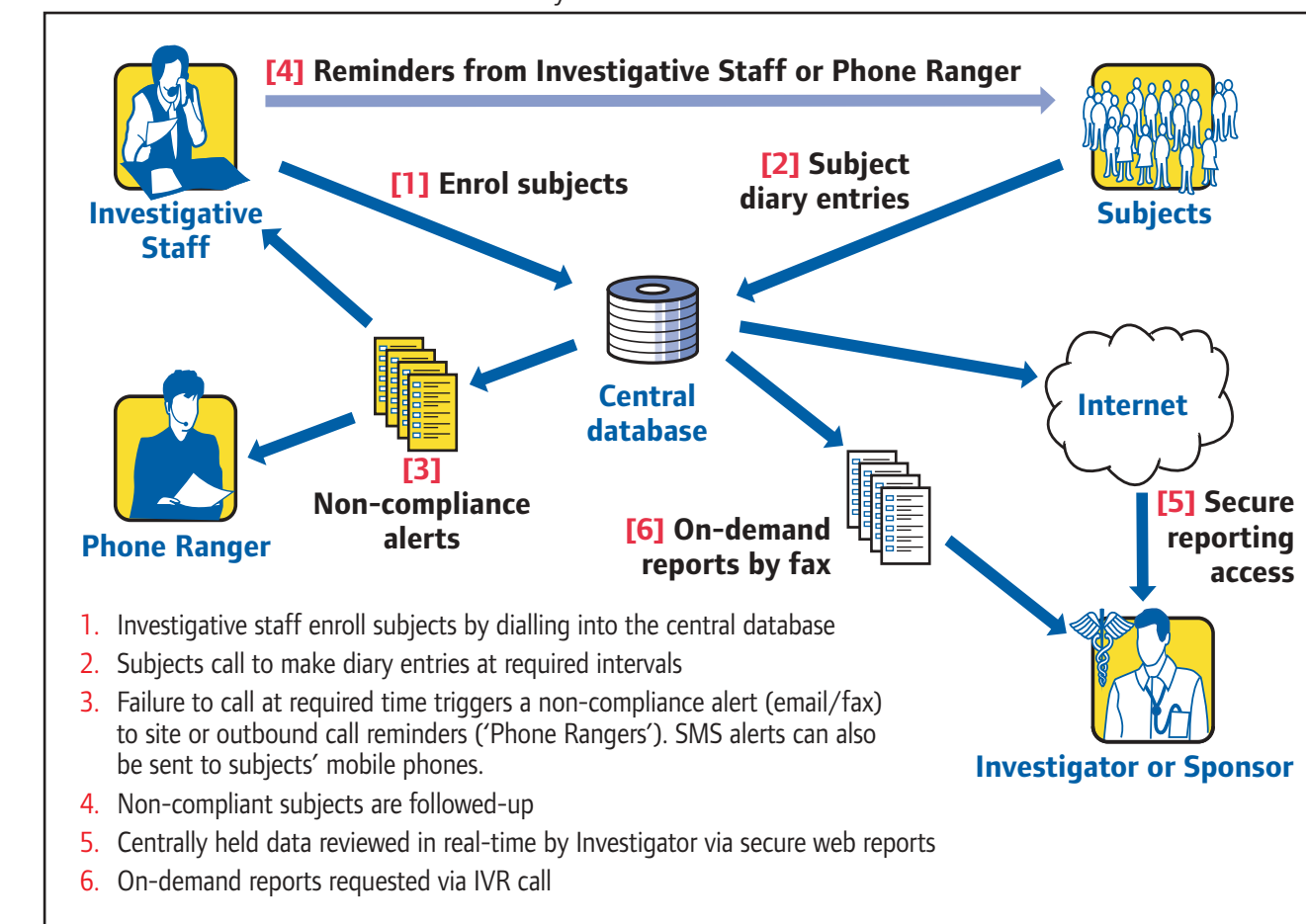
## ePRO considerations

Models for administering ePRO are described in figure 1. Centralized solutions hosted by Sponsors or third parties that ensure a seamless audit trail and prevent any manipulation of data outside the system, enable an investigator to retain “ownership” of these data.

To ensure this, Investigators should be given:

- An understanding of the data capture process, security features, patient authentication control and data quality processes
- Full access to the data during the study
- A certified copy of the data for site archive

FIGURE 2. IVR ePRO solution functionality



## IVR ePRO SOLUTION

Figure 2 illustrates how IVR provides an effective means of patient recorded data collection. IVR has successfully been used in a variety of therapy areas including irritable bowel syndrome [5], insomnia [4], depression [6] and for cognitive function testing [7].

### Patient authentication

(figure 2, steps [1] and [2])

Investigators confirm the identity of the patient during the enrolment IVR call (step [1]). Patients access the system via a unique usercode and self-defined PIN number known only to the patient (step [2]). Full 21 CFR part 11 compliance can be achieved by asking subjects to sign a declaration upon receipt of their ePRO account; however, few Sponsors consider this to be a requirement.

## Data quality and integrity enhancement

- Built-in data logic and consistency checks can improve data quality.
- Retrospective and prospective data entry can be limited or prohibited, enhancing data integrity.
- Real-time data access enables diary compliance to be assessed. Proactive encouragement of patients to comply with the diary schedule can be achieved by site reminders, out-bound telephone operators, SMS and email (step [3]).
- Sophisticated branching and question-skipping is possible.

## Investigator data access

(figure 2, steps [5] and [6])

IVR ePRO data can be made available to Investigators in a variety of ways to suit the needs of the study site (table 1). Importantly, solutions should enable effective data access to sites with (A, F) and without (B, C, D, E) internet connectivity. Post-study certified copies of ePRO data should be supplied on CD-ROM in secure PDF files including study data, metadata and audit trail.

TABLE 1. Methods of site data access using IVR ePRO

Data Report	Medium	Frequency
A Web report	Internet. Secure access. Downloadable if required	Real-time.
B On demand report (requested via IVR call made by site)	Fax / secure email	Real-time.
C Per event notification	Fax / secure email	Real-time.
D Scheduled data report	Fax / secure email	As defined. (E.g. Weekly).
E Scheduled data report	PDF on secure CD-ROM	As defined. (E.g. Weekly).
F EDC integration	Secure XML transfer.	Real-time.

## CONCLUSIONS

ePRO solutions offer enormous potential to improve the quality and integrity of patient self-report data. This benefits Investigators, Sponsors and Regulators. Appropriate application of ePRO can maintain Investigator “ownership” of PRO data. FDA are currently discussing formal guidance on the use of ePRO.

## REFERENCES

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