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The eClinical Forum¹
and PhRMA EDC Task Group

Present this Discussion Document on

***The Future Vision of Electronic Health
Records as eSource for Clinical
Research***

D R A F T

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*Comments welcome before March 31, 2006
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¹ Formerly the Electronic Data Management Forum (EDM Forum)

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D R A F T

741 **EXECUTIVE SUMMARY**

75

76 **Healthcare Industry and Bio-pharmaceutical industry both strive for efficiency and quality**
77 **while managing cost of patient data.**

78 The Health Care industry (physicians, hospitals, etc.) and the Bio-pharmaceutical industry
79 (pharmaceutical, biological, and medical device industry), while having different goals, have
80 many similar needs. Both record and manage information on patient experiences, and both are
81 looking to leverage technology to manage efficiency, quality, safety and cost.

82 **Today's multiple data entry environment is a step backwards.**

83 The expansion and government-encouraged use of electronic health record (EHR) systems in
84 hospitals and physician offices means that patient data are increasingly being entered and
85 maintained electronically. At the same time, clinical trial sponsor-supplied electronic data capture
86 systems are often used by healthcare professionals for entry of this same patient data.
87 Unfortunately, the data in these EHR systems cannot be used directly for clinical research
88 purposes because of the variability of the data and systems and because the systems are not under
89 the control of clinical research regulations. Conversely, the sponsor-maintained EDC system
90 cannot be used as the only source for the data because of regulations requiring that the
91 investigator, and not the sponsor, be responsible for the source data. The result is the creation of a
92 third record of information (either via paper or investigator-controlled, regulatory-compliant
93 eSource system) in order to meet regulatory requirements. The duplication of tasks and associated
94 costs will grow with the increasing use of electronic data sources.

95 **Planning must happen today for tomorrow's needs.**

96 The ideal would be an environment where regulatory authorities can rely upon data from all
97 electronic sources in carrying out their statutory duties and where data exchange between
98 healthcare and research systems can occur in a manner compliant with both data protection and
99 international research regulations. Such an environment would lead to efficient and robust
100 methods of data collection and exchange, would ensure that research data is of high quality, and
101 that regulatory approval of future therapies are based upon reliable and secure data sources.

102 The vision is for shared systems and processes that would allow the use of patient electronic
103 medical data for clinical research in a way that meets data protection, regulatory, and ethical
104 research requirements and thereby minimize the challenges of clinical research for healthcare
105 professionals.

106 In meeting this challenge, three areas need to be addressed:

- 107 1. A mechanism to utilize electronic medical information to support both routine treatment
108 and outcomes for research purposes while satisfying regulatory and research requirements
- 109 2. Data standards such that the data can be consistently collected, interpreted and exchanged
110 within the medical and research communities
- 111 3. Controlled, secure processes for releasing and transferring data from and to the EHR,
112 device and research systems that are consistent with personal data privacy, clinical trial
113 regulations, and bioethical considerations

114

115

1162 **INTRODUCTION**

1172.1 **Background and Rationale**

118 The adoption of electronic health records (EHRs)² in both hospitals and private practice is on a steady
119 incline. Recent reports suggest that 20-25% of US healthcare practices use electronic medical/health
120 record systems (1). Within Europe these figures vary greatly between country and can be as high as
121 90% in Sweden or The Netherlands to 60% in the UK or Denmark to as low as 17% in Greece (2). The
122 growth is being driven by the need to manage healthcare cost drivers and to deliver more efficient and
123 higher quality healthcare, while enhancing the safety of the patients. While there has been much
124 media attention given to the national efforts of the US and the European Union (EU) to develop
125 nationwide electronic health networks (eHealth), the following countries are in varying stages of
126 planning and implementing systems and processes for capturing, maintaining and sharing electronic
127 health records: Australia, Austria, Canada, Cyprus, Czech Republic, Denmark, France, Germany,
128 Greece, Italy, Latvia, Lithuania, Luxemburg, Malta, Netherlands, Norway, Poland, Slovenia, Spain,
129 Sweden, United Kingdom, United States (3).

130 Alongside the growth in EHR, Electronic Data Capture (EDC) systems are today used in an estimated
131 27-30% of clinical trials (4), again in both hospitals and private practices. The use of electronic data
132 capture technologies provides the opportunity to significantly enhance clinical trial conduct through
133 improved efficiency and accuracy as well as real-time response to potential adverse situations. The
134 data captured in clinical trial systems may be based upon a prior electronic source (eSource), such as
135 EHR. Unfortunately, many of the EHR systems that manage the electronic source today cannot be
136 used reliably for clinical research purposes because of the variability among these systems and the fact
137 that they are not required to meet regulatory requirements for clinical trials. Therefore the data that
138 are in the EHR system has to be re-entered into the EDC system. The duplication of tasks, generation
139 of paper and associated costs and inefficiencies, will only grow with the increasing use of electronic
140 data sources. This could in turn put undue burden on offices performing both patient care and
141 investigative clinical trials such that the quality of execution of associated tasks could be
142 compromised.

143 The challenge is to develop a non-redundant environment where the bio-pharmaceutical and
144 healthcare industries can benefit from data exchange in a manner compliant with both data protection
145 and research regulations and where regulatory authorities can rely upon data from electronic sources in
146 carrying out their statutory obligations. Such an environment will lead to efficient and robust methods
147 of data collection and exchange, will ensure that research data are of high quality, and that regulatory
148 approval of future therapies is based upon reliable and secure data sources.

1492.2 **Purpose of this Document**

150 This document is intended to 1) expand the discussion on the current EHR and EDC environments and
151 2) convince governmental (US, EU, etc.) and private groups involved in the planning and architecting
152 of national eHealth initiatives that there is great value in involving the bio-pharmaceutical industry
153 and that this value is consistent with the goals of national eHealth initiatives for improved patient care
154 and accelerating the pace at which scientific discoveries in medicine are disseminated into medical
155 practice. In particular, involving clinical trial professionals from this industry in the early planning
156 can result in EHR data structures, infrastructure, and processes that are geared for long-term use in

² Also commonly referred to as EMR (electronic medical records), however future trends are toward a more encompassing health record and for the purpose of this paper, we will use only the term EHR to refer to both EHR and EMR systems and records.

157 multiple industries. We hope to persuade designers of government-sponsored eHealth initiatives and
158 providers of EHR systems (private market vendors), of the feasibility and practicality of the vision and
159 to persuade them to include requirements for integration of clinical studies. We will identify the
160 benefits that implementation of this vision can realize, as well as identify regulatory needs and
161 potential next steps towards achieving this goal.

162 Several industry presentations and position papers have discussed the role of the bio-pharmaceutical
163 industry in national eHealth initiatives. In particular

- 164 • the PhRMA IMPACC paper on the Role of the Biopharmaceutical Industry in the Growth and
165 Adoption of HIT in the US Healthcare System (27) seeks to inform industry leaders about HIT and
166 persuade them to participate in the development and adoption of HIT, and
- 167 • the CDISC Electronic Source Data Interchange paper (19) reviews the regulatory requirements for
168 paper and electronic source and explores the potential roles of the CDISC standards given several
169 compliant eSource scenarios.

170 We offer this paper in addition, to present a future vision of how patient data, already collected by
171 physicians and entered into electronic systems, might be leveraged for clinical research in conjunction
172 with trial-specific data collected in the same efficient and regulatory-compliant manner thus benefiting
173 healthcare professionals, patients, and sponsors of clinical trials. The authors of this paper are experts
174 in the area of electronic data capture of patient data used in clinical trials and can lend valuable insight
175 into the future of clinical data capture, given the continued progress of national efforts towards
176 individual electronic health records and the sharing of this data among healthcare providers.

1772.3 About the eClinical Forum

178 The eClinical Forum (formerly the Electronic Data Management Forum) is a transatlantic, not-for-
179 profit and non-commercial, technology independent group representing members of the
180 pharmaceutical, biotechnology, and allied industries. The eClinical Forum mission is to serve these
181 industries by focusing on those systems, processes and roles relevant to electronic capture, handling,
182 and submission of clinical data. For further information: eClinical Forum, 68 rue de Rhin, 67860
183 Friesenheim, FRANCE
184 <http://www.eclinicalforum.com>.

1852.4 About the PhRMA EDC Task Group

186 The PhRMA (Pharmaceutical Research and Manufacturers of America) Clinical Trial Electronic Data
187 Capture (EDC) Task Group was initially chartered in August 2000 by the PhRMA/FDA Electronic
188 Regulatory Submission (ERS) Working Group to identify ways to advance the use of electronic
189 clinical data capture. Sponsorship was transferred in 2003 to PhRMA's Biostatistics and Data
190 Management Technical Group (BDMTG). The mission of the EDC Task Group is to facilitate the
191 adoption of EDC for clinical trials and the inclusion of EDC data in regulatory submissions, with the
192 intent of allowing clinical investigators, bio-pharmaceutical sponsors, and regulators to fully realize
193 the benefits of EDC. Membership includes industry representatives from Data Management, Clinical
194 Informatics and Regulatory groups of PhRMA member companies, and liaisons from PhRMA's Bio-
195 Research Monitoring Committee (BRMC) and Health Outcome Technical Group (HOTG). This
196 group has had meetings with FDA representatives from CDER, CBER, and the Division of Scientific
197 Investigations (DSI) to discuss their work and ideas.

1982.5 Providing Feedback

199 Your feedback and input will help us continue to develop the document and to maintain the currency
200 of the information it contains. If you have opinions or information that you feel would be of benefit to
201 groups working with electronic clinical trials, please contact:

202 **eClinical Forum**
203 Email: info@eclinicalforum.com

2043 CURRENT SITUATION AND TRENDS

205 In order to evaluate the feasibility and practicality of making changes to any environment it is
206 important to first understand all areas of that environment. When conducting clinical trials, the
207 environment includes the healthcare system, the clinical researchers, the source data, the regulations
208 that govern clinical research and research data, and the standards that prescribe formatting for data
209 content, data integration, and data exchange.

2103.1 The Current Healthcare Environment

211 There is currently a global movement towards the transformation of healthcare through the use of
212 information technology. Many countries have community or national initiatives underway and are
213 struggling to expand their adoption rate. This is driven by projected and perceived improvements in
214 patient safety, general healthcare delivery, and overall cost. Healthcare payers also have a vested
215 interest in these initiatives since billing and payment efficiencies will be a by-product of an all-
216 electronic healthcare record system.

217
218 The agreement on and introduction of data standards at the local, state, country, and international
219 levels is needed to increase computer utilization and awareness in physician's offices and hospitals
220 and to help spur the desire to move to a paperless environment. In some areas, data standards have
221 been approved, but cross-boundary agreements and implementation are still desired. Concerns over
222 the perceived disruption in the doctor-patient relationship imposed by computer use during their
223 sessions, can be minimized through use of devices such as tablet PCs and PDAs. Still, there are
224 concerns that current privacy regulations are not stringent enough to ensure patient data confidentiality
225 in all cases, particularly in an electronic world. And of course, implementation cost of moving
226 towards a paperless environment needs to be justified.

228 3.1.1 Objectives of eHealth Initiatives

229
230 While there are many eHealth initiatives around the world with varying approaches, all share a
231 common desire to:

233 a) Enhance patient safety

234 Medical errors may account for tens of thousands of preventable deaths in hospitals each year:

- 235 • The Committee on Quality Healthcare in America (5) estimates that medical errors could
236 account for 44,000 – 98,000 deaths in the US alone.
- 237 • In the UK, the National Patient Safety Agency has been set up with the goal of improving the
238 safety and quality of care through reporting, analysing and learning from adverse incidents
239 and 'near misses' involving National Health Service (NHS) patients.

240 Many of the deaths and other incidents are thought to be the result of a lack of collated patient-
241 specific information and/or accessibility of experienced-based medical best practises. Medical
242 staff cannot be expected to remember all aspects of every single potential problem that a person

243 may present with – it is just not humanly possible. The ability to access all data pertinent to an
244 individual person at any one time through a networked EHR allows the medical practitioner the
245 most comprehensive view of their patient’s condition and supports fully informed decision
246 making. In addition, the use of electronic systems storing and presenting information about
247 medications, available dose amounts and indications can substantially reduce prescribing errors
248 caused by poor handwriting and similarities in names between certain drugs.
249
250

251 b) Improve quality of healthcare delivery

252 At no time in history has the growth in knowledge and technologies in medicine been so profound,
253 yet health care delivery systems are floundering in their ability to provide consistently high-quality
254 care (17).
255

256 A patient's healthcare is largely dependent on the collection of past and present health status
257 information and the healthcare provider’s ability to retain and retrieve learned medical information
258 and updates. These form the basis for the healthcare provider’s decision regarding a course of
259 treatment. Paper-based collection of this data with its inherent legibility, accuracy and
260 completeness issues provides a poor platform for making these healthcare decisions. Electronic
261 healthcare can help improve the quality and completeness of the information by implementing
262 rules that proactively identify potential errors and interdependencies and alert the healthcare
263 provider. Based on this now more accurate information and experience-based treatment templates,
264 intelligent healthcare decision support systems can go so far as to suggest a course of appropriate
265 clinical treatment not otherwise considered by the healthcare provider.
266

267 Treatment assessments can be made much more broadly once patient health records reside in
268 electronic databases. Organizations can use the electronic data to analyze treatment approaches
269 across the patient spectrum rather than independently. Based on these analyses viable treatment
270 options can be presented to the Healthcare provider to identify the best course of treatment for a
271 patient.
272

273 c) Reduce health care costs.

274 Paper-based healthcare systems are expensive and unable to consistently deliver recommended
275 patient care, particularly for chronic diseases, due to the fact that the information is scattered
276 throughout numerous files/locations and not easily gathered or viewed as a whole. In the US,
277 investment in standardized electronic healthcare information exchange would deliver an estimated
278 \$77.8 billion in annual healthcare savings (6). This is mainly derived from reducing redundancies
279 between different services, such as duplicate records with basic details for the same patient being
280 maintained at multiple locations, and reducing the large amounts of resources and time taken to
281 support and administer all these independent records. The EU has invested many hundreds of
282 millions of Euros in preparing the framework for an interoperable network of EHR systems, and
283 contracts have been awarded in many countries to begin implementation. The savings are expected
284 to be substantially greater than the investment, with the clinical benefits of improved safety and
285 quality outweighing the financial gains.
286

287 d) Develop Person-Centered Health systems

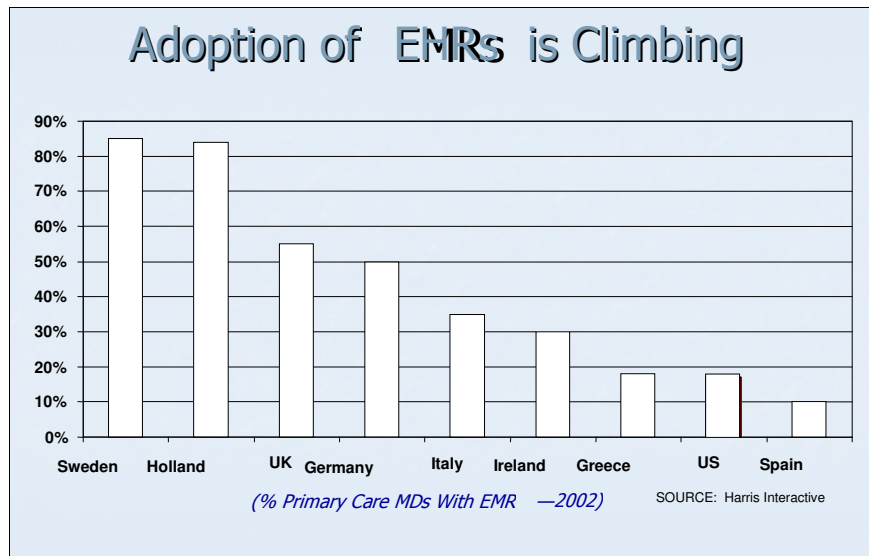
288 In such a system, information would move with an individual across healthcare facilities, regions
289 and countries, providing comprehensive knowledge of any medical conditions and facilitating
290 appropriate treatment regimens.
291

292 **3.1.2 Adoption of Electronic Health Records**

293 Within the EU, the recent Action Plan for Health mandates that each member country will have an
294 outline for interoperability of electronic health records in place by the end of 2006 (7). Many European
295 countries are moving rapidly towards this goal with extensive restructuring, development of
296 technology infrastructures and changes in procedures and policies. In the US, the Office for National
297 Coordination for Health IT (ONCHIT) launched a range of activities during 2004 which are designed
298 to provide direct technical assistance to states and regions.

299 Within the US and Europe, not everyone has moved at the same pace. Consequently, as Figure 1
300 illustrates, even within Europe, where EU-wide agreements and socialized healthcare provide a
301 framework for co-ordinated development and implementation, some countries are more advanced than
302 others in the introduction of an electronic healthcare environment. The US has seen a slower
303 movement towards electronic health records, attributed to a healthcare environment based on multiple
304 private-practice providers and reimbursement schemes (8). However, what is clear is that all countries
305 are accelerating the transformation so that throughout Europe and the US, the intent is to have a high
306 level of interoperable EHRs implemented by 2007 – 2014 (9).

307
308



309
310
311

Figure 1: The Adoption of Electronic Medical Records Is Growing Globally³

312 As institutions move towards electronic patient records, the use of a computer during consultations
313 becomes the norm. The formerly perceived barrier of the computer in the doctor-patient relationship is
314 being eroded as practices change with a new generation of computer-aware physicians and patients. As
315 a result, it has become not only possible, but in many institutions commonplace, for the physician to
316 access and enter patient notes directly from the computer in front of the patient. This trend is also
317 likely to have an impact on the comfort of physicians with the direct entry of patient data for clinical
318 trials.

³ See footnote 2 for difference between EMR and EHR

3193.2 The Current Clinical Research Environment

320 Bio-pharmaceutical companies have faced increasing pressure to bring new, innovative products to
321 market faster and in a more cost-conscious manner than ever before. At the same time, increasing
322 concern over product safety has resulted in the need for more and longer trials, causing costs and time-
323 to-market to increase. The use of EDC by the bio-pharmaceutical industry to conduct clinical trials on
324 new drug candidates is growing as sponsors make commitments to improve data quality and drive
325 efficiency in their research & development organizations. However, the transition from paper to EDC
326 has not been a smooth one, and the bio-pharmaceutical industry is realizing that EDC is not the whole
327 answer.

3.2.1 Electronic Data Capture

329 EDC is a technique for collecting clinical trial data in such a way that they are delivered to the sponsor
330 in electronic form instead of paper. This includes the following scenarios:

- 333 ■ Information that is first recorded on paper by the investigator's staff or the patient, is subsequently entered
334 into a computer at the investigator's site, and is delivered electronically to the sponsor or sponsor's
335 representative (such as a CRO) without a hand-written case report form. The computerized system into
336 which the site enters the clinical trial data is generally provided and maintained by the sponsor or a third-
337 party vendor. It is customized for each trial and may include data entry support mechanisms which
338 validate the data against protocol and other logical requirements as the data are being entered, thus
339 resulting in cleaner data compared to paper CRFs.
- 340 ■ Clinical laboratory data that are transmitted to the sponsor electronically and batch-loaded into the
341 sponsor's database
- 342 ■ Patient data that are directly captured by instrumentation
- 343 ■ Electronic patient reported outcome (ePRO) i.e., information that is entered by the patient directly into an
344 electronic device, such as personal digital assistant (PDA)

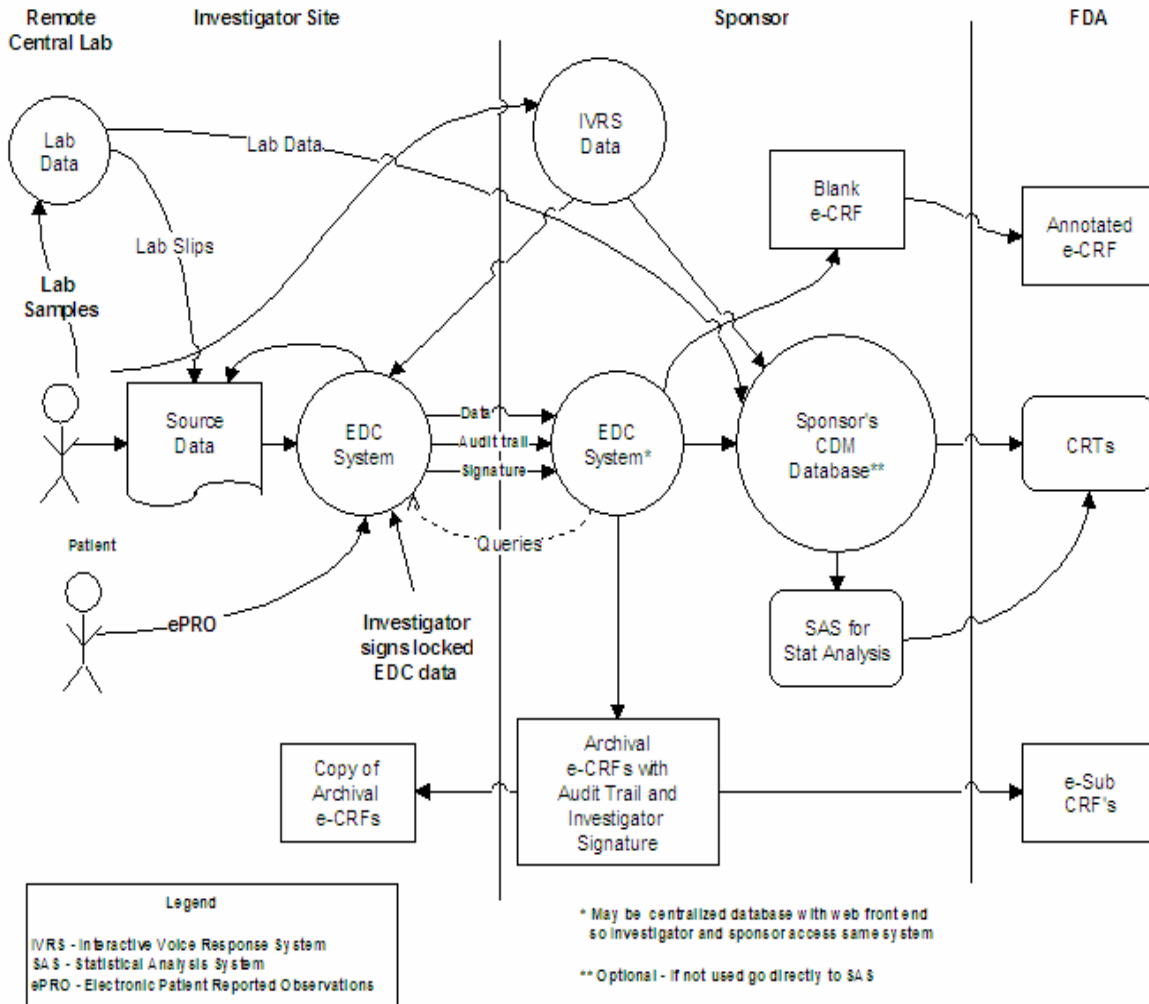
3.2.2 The Concept of Source Data

345 At the center of data collection and data management for all clinical trials, regardless of the use of EDC or
346 paper, is the concept of source data. Source data, as defined by the ICH Harmonised Tripartite Guideline for
347 Good Clinical Practice (ICH E6) (21), is all information in original records and certified copies of original
348 records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction
349 and evaluation of a trial. Source data are contained in source documents (original records or certified
350 copies). Examples of source documents include hospital records, patient charts, laboratory notes and
351 pharmacy dispensing records.

353 In clinical research, it is these source data that are transcribed onto paper case report forms (CRFs) or
354 into the EDC system. During the trial, it is the physician's responsibility to secure and maintain the
355 source data, and the sponsor's responsibility to ensure the reported trial data are accurate, complete
356 and verifiable from source documents. To ensure the accuracy of this process, sponsors usually carry
357 out a process called Source Data Verification (SDV), in which CRF records are manually compared to
358 the corresponding source data in the charts. This source data is required to be under the control of the
359 investigator (Part 312.62b) and through an investigator signature is deemed to be accurate. The
360 creation, modification, maintenance, archival, retrieval and transmission of data in the CRFs and its
361 subsequent manipulation, analysis and submission to the FDA are subject to the detailed regulations.
362 Further, regulatory agencies and auditors require access to the source data in order to reconstruct a trial
363 and ensure overall accuracy and integrity of the data. So, as electronic health records become more
364 common and data are recorded directly into systems (creating an electronic source, or 'eSource'), it is
365 necessary to continue to evaluate the processes and regulations related to source to ensure continued

366 data integrity for clinical research purposes. CDISC's eSDI paper provides an excellent overview of
 367 the current regulatory requirements applicable to source data and eSource which we will not duplicate
 368 here. The following sections will review selected aspects of the current regulatory requirements in
 369 more detail, and further explore the concept of 'source' and 'eSource'.
 370

371 Figure 2 below shows an example of data flow within EDC and associated systems, highlighting Source
 372 Data as a central component in the process.



373
 374 Figure 2: An Example of the Data Flow in an EDC System

375 From: Position Paper on Electronic Data Capture-Revision 1, PhRMA EDC Task Group, 2005 (21)

376
 377 **3.2.3 Growth of EDC in Clinical Research**

378 While EDC is not a new technology, its adoption by bio-pharmaceutical companies is a relatively
 379 recent effort. In the 1990's, many companies tried to deploy EDC as a pure technology solution, with
 380 only limited process changes. At the same time, the EDC vendor market place was immature and
 381 fragmented. The tools themselves were somewhat unstable and did not fully meet sponsor needs.

382 Over time, the EDC vendor market place has matured, and while it is still fragmented, there has been
383 significant consolidation and several market leaders have emerged. In parallel to this evolution in the
384 market place, bio-pharmaceutical sponsors have learned that the real key to making EDC successful is
385 to leverage the technology to redesign business processes. The result has been that EDC is no longer
386 seen as a tool, but rather as a capability consisting of optimized processes combined with supporting
387 technology. Many investigative sites and bio-pharmaceutical sponsors are now using EDC to realize
388 significant benefits in resource efficiency, data quality, and time to market. Today, EDC usage is at
389 steady-state in several bio-pharmaceutical companies, with many others scaling up aggressively.
390 Overall, roughly 27-30% of all clinical trials are currently conducted using EDC, with this percentage
391 rising year to year (4).

392
393 **3.2.4 Benefits of EDC**

394 For bio-pharmaceutical sponsors and regulators, the primary benefits of EDC include:

- 395 ■ Significantly reduced lag time between a patient visit and the time when the data become available
396 for review by the sponsor. Data are accessible as soon as they are entered by the investigator site
397 into the system.
- 398 ■ Timely review of accumulated data for decision-making made possible by the reduction of the data
399 availability gap. Of particular importance is the ability to detect potential safety issues in as close to
400 real time as possible.
- 401 ■ Significantly increased data quality through the inclusion of data validation checks in entry screens.
- 402 ■ Reduced sponsor data entry and cleaning costs.
- 403 ■ Database lock and delivery for interim or final analysis in a shorter timeframe by speeding up data
404 capture and query resolution, thus offering the potential for maximizing time on patent.

405
406 EDC also delivers significant benefits for investigators and their patients:

- 407
408 ■ Provides site personnel with immediate feedback during data entry through on-line, automated
409 checks, They are prompted to correct illogical/erroneous entries immediately, while they still have
410 the patient's chart at hand, rather than weeks or months later as occurs with paper, thus eliminating
411 later re-work
- 412 ■ Rather than retaining large volumes of paper Case Report Forms (CRFs), at the end of the study,
413 sites receive copies of their electronic CRF data and associated audit trail on CDs.
- 414 ■ Accelerates delivery of new drugs to the patients who need them by allowing study sponsors to
415 analyse the data faster.

416
417 **3.2.5 Why EDC is not the perfect answer**

418 Unfortunately, despite these benefits, the process associated with EDC still includes some
419 inefficiencies for investigator sites:

- 420 ■ Despite the consolidation of the EDC market place, sponsors use a variety of EDC systems.
421 Investigators and site staff are often required to learn how to use multiple EDC systems, and may
422 need to have multiple computers at their sites to accommodate the various systems. The typical
423 active investigative site is estimated to have an average of three disparate EDC systems provided by
424 the sponsors of the clinical trials they participate in (22). In the coming years, this number may
425 grow as the adoption of EDC by bio-pharmaceutical companies continues to increase.
- 426 ■ As described previously, some clinical trial data are first recorded, as part of the patient's normal
427 care, in paper or electronic patient charts which constitute the source documents, and must then be
428 transcribed into the EDC system. Indeed, even if the patient's charts are available at the site as
429 electronic health records (EHR), they cannot today be used directly for research purposes because of

430 the variability of these systems and the fact that they are generally do not comply with the
431 regulations that governs systems used for clinical trials (see Section 3.3).
432 ■ In most clinical trials, a variable portion of the data is specific to the trial and would not normally be
433 recorded in the patient's paper or electronic chart. For those data, the regulatory obligation to have
434 source documents for all clinical trial data results in the need to create a separate record in addition
435 to entering the data in the sponsor's EDC system.

436
437 Thus, a significant percentage of electronic CRF data are entered into multiple electronic and paper
438 systems resulting in extensive duplication of data entry and, occasionally, lack of clarity on what was
439 the original source. Based on current regulations, processes for the use of EDC still result in
440 duplicative recording of data, which may explain the finding that 25% of sites surveyed (22) believe
441 EDC is increasing their workload, despite the advantages of on-line data discrepancy management,
442 streamlined archiving, and other tools of major EDC systems.

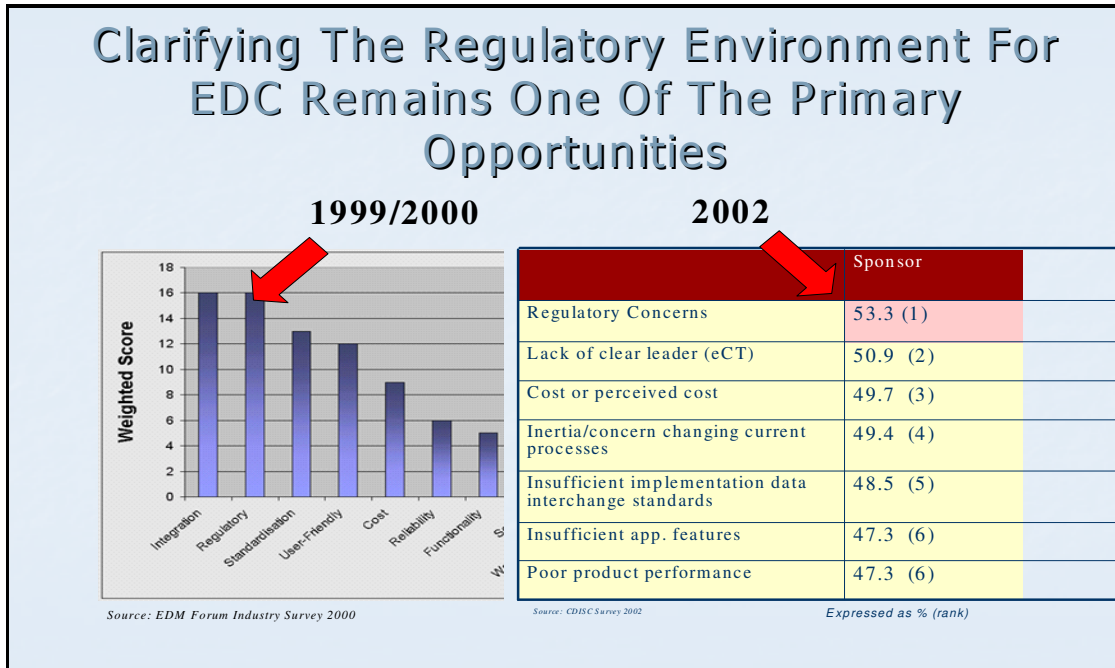
443
444 This duplication of tasks and associated costs will grow with the increasing use of electronic data
445 sources (such as EHR), diminishing the efficiency of both healthcare professionals and clinical
446 research organizations. Better integration of the healthcare and clinical research environments,
447 systems and processes can lead to further efficiency.

4483.3 Current Regulatory Environment and Implications for eSource

449 A 2002 industry survey reported by the Electronic Data Management Forum (now eClinical Forum)
450 indicated that clarifying the regulatory environment for EDC was one of the primary issues facing
451 clinical research. A more recent survey reported by the Clinical Data Interchange Standards
452 Consortium (CDISC) in 2003 confirms that the situation is unchanged with 53% of sponsors still
453 regarding regulatory concerns as the primary cause of delay in the implementation of EDC (Fig 3).
454 The PhRMA EDC Task Group position paper (20) released in 2005 highlights the regulatory issues
455 that are problematic for EDC. Many of these issues have been addressed by the draft CSUCT
456 guideline (13) (Sept 2004), however, to date this guideline has not been finalized. Some of the
457 highlighted regulatory issues (e.g., the need to identify all computer systems used in clinical trial,
458 password expiration requirements) apply to the use of the EDC system as eSource and these same
459 issues would apply to the use of the EHR system as eSource.

460

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461
462

463

Figure 3: Clarifying the regulatory environment for EDC

464

3.3.1 Applicable Regulations

465 Both the FDA and ICH provide requirements for clinical trials records and the systems and
466 processes that maintain them. The same responsibilities of the investigator towards the accuracy of
467 source data would exist whether that data is hand-written on paper or entered and stored electronically.
468 The source data must follow the ALCOA principles and the above regulations and if they are entered
469 and stored into an EHR or EDC system as the sole source then that system must be compliant with
470 these regulations as well.
471

472

473 Applicable regulations are:

- 474 • U.S. FDA, 21 CFR 312.62b Investigational New Drug Application: Investigator
475 recordkeeping and record retention
- 476 • U.S. FDA, Guidance for Industry, Part 11, Electronic Records; Electronic Signatures, and
477 Guidance on 21 CFR Part 11 Scope and Application
- 478 • U.S. FDA, Guidance for Industry-Computerized Systems Used in Clinical Trials
479
- 480 • ICH (International Conference on Harmonisation), E6 Good Clinical Practice:
481 Consolidated Guidance
482

483

3.3.2 Challenges for using Electronic Health Records as eSource

484 If source data for clinical research are collected electronically in an EHR system, without duplication
485 into a second system, all the requirements for compliant electronic systems as described above will
486 extend to EHR systems leading to a number of practical challenges which will have to be overcome.
487 The intent of the following sections is to start exploring the current gap between the realities of EHR
488 data and existing regulatory requirements pertaining to clinical research.
489

490

491 1. Data collection processes at the point of care are minimally controlled

492 This section addresses issues from 21 CFR Part 11.

493

494 Health care is under tremendous time and cost pressure, patient records predominantly serve the
495 purpose of the medical care of the patient and are optimized towards this purpose. It would be
496 inefficient and costly for a hospital or physician's office to carry out the meticulous documentation
497 that are common in the bio-pharmaceutical industry.

498

499 If data in EHR systems are used as eSource for clinical trials, authority checks (as expected under 21
500 CFR Part 11) will have to be applied to ensure that only authorized persons can access the system and
501 an electronic audit trail will be required. This may collide with practices such as generic user names or
502 passwords shared by multiple staff, particularly in small physician's offices. It will also create the need
503 for a substantial redevelopment of the EHR products on the market, especially for those which do not
504 have clinical research-compliant audit trail capabilities today. The enforcement of a requirement like
505 this may cause adoption problems and might take a longer period of time to occur if not given
506 appropriate encouragement and incentive.

507

508 2. Source data are far from perfect

509 This section addresses ALCOA principle from CSUCT and GCP issues from ICH E6.

510

511 Patient data are collected mostly when medical treatment is necessary. Depending on the
512 circumstances and nature of the condition, the quality of the records may suffer substantially. For
513 example, in emergency situations, the medical staff of ambulances and emergency rooms will
514 exclusively focus on rapid intervention rather than accurate record keeping. In addition, recordings
515 are made by a variety of staff of different qualifications: physicians, nurses, phlebotomists, etc. In
516 the medical practice, these shortcomings are usually mitigated when the physician responsible for
517 the treatment produces a discharge summary: In this case one could legitimately question what is
518 the source, the notes or the summary. All data are then subject to professional judgment and a
519 representative selection of the key data are provided. The question as to what is the source data
520 then needs to be tackled: Should the notes from each of the consecutive caregivers be considered
521 source data or is the summary from the overseeing physicians the only valid source data? This
522 ambiguity was acknowledged by the FDA's Division Scientific Investigation (DSI) representatives
523 who met with the PhRMA EDC Task Group in January 2006. They noted that the regulations do
524 not equate source data with initial data.

525

526 However, it is well known that this piece-meal record-keeping approach is notoriously flawed and
527 leads to a great number of treatment errors (6). In fact, the improvement of this situation and easy
528 accessibility to the information is one of the reasons for the introduction of the EHR systems, however
529 without process and control changes similar to clinical research controls, the reality of improvement in
530 the accuracy of healthcare information may not be seen.

531

532 3. Control and ownership of data is difficult to clearly identify

533 This section addresses issues from 21 CFR Part 312.62b.

534

535 Since the investigator is responsible to keep records of the case history of the patient (11). Therefore,
536 it is inferred that the sponsor must not have exclusive controls of these records.

537 The FDA's current position on sponsor hosting of such eSource data is defined in the Feb 2006 Draft
538 Guidance on Patient Recorded Outcomes (23, page 26). It states that the sponsor should not have
539 exclusive control of the source document, there must not be only one database, and the investigator

540 must be accountable for the accuracy of the data. In other words, the sponsor cannot have
541 responsibility for maintenance or custody of source records.

542
543 Current EDC systems, however, are often hosted by the sponsor over the public internet.
544 However, if such EDC systems or modules develop into or integrate with EHR systems, this
545 model becomes no longer viable, as it would make the sponsor the custodian of the sole dataset.

546
547 There has recently been strong argumentation from the FDA in support of the theory that eSource data
548 are vulnerable to potential fraud in the hands of a sponsor, and as such should therefore be hosted by a
549 Trusted Third Party (TTP), which have traditionally been providers of eDiary and eCRF-software
550 solutions. However, the potential conflict of interest is still questioned as the TTP may be paid by the
551 sponsor. CDISC's document (19) endorses the idea of TTP as one of several solutions to providing a
552 separation between investigator and sponsor.

553

5543.4 Data Standardization Initiatives

555 The emergence and evolution of marketed electronic health record systems and marketed
556 electronic clinical data systems has been completely separate. While these systems are
557 functional they are not interoperable. Only recently have organizations like HL7,
558 representing healthcare data standards, and CDISC, representing research data standards,
559 participated in collaborations to work towards integration.

560

561 Below are listed some of standards initiatives, however we acknowledge that there are many
562 other organizations focusing on this area.

563

564 3.4.1 Healthcare Data Standards: Health Level 7 (HL7)

565

566 Health Level Seven (HL7) is a global, non-profit organization started in 1987 that produces
567 standards for clinical and administrative data. "Level Seven" refers to the highest level of the
568 International Standards Organization's (ISO) communications model supports such functions as
569 security checks, participant identification, availability checks, exchange mechanism negotiations
570 and data exchange structuring.

571

572 HL7's mission is to "create standards for the exchange, management and integration of electronic
573 healthcare information, to promote the use of such standards within and among healthcare
574 organizations to increase the effectiveness and efficiency of healthcare delivery for the benefit of
575 all." In 2002, the HL7 Electronic Health Record (EHR) Special Interest Group was established
576 with the mission of "designing standards to support the exchange of information for clinical
577 decisions and treatments, and help lay the groundwork for nationwide interoperability by
578 providing common language parameters that can be used in developing systems that support
579 electronic records."

580

581 3.4.2 Research Data Standards: Clinical Data Interchange Standards Consortium

582

583 In the bio-pharmaceutical industry, the Clinical Data Interchange Standards Consortium (CDISC),
584 begun in 1987, is an open, multidisciplinary, non-profit organization committed to the
585 development of industry standards to support the electronic acquisition, exchange, submission and
586 archiving of clinical trials data and metadata for medical and biopharmaceutical product
587 development. The mission of CDISC is to "lead the development of global, vendor-neutral,

588 platform independent standards to improve data quality and accelerate product development in this
589 industry”.

590
591 3.4.3 Joint CDISC / HL7 Charter

592
593 In 2004 a partnership was formed between CDISC, HL7 and FDA/HHS to have one overarching
594 standard model for data interchange for healthcare information and clinical trial/clinical research
595 data and to produce models harmonized to yield value for both clinical research and healthcare.
596 They have some joint Advisory Board seats and incentives for joint organizational memberships.
597 In addition, HL7 has created a Board-appointed Clinical Research Outreach Committee that will
598 include CDISC representation.

599
600 The HL7 clinical document architecture (CDA), based on the HL7 RIM, and the CDISC
601 operational data model (ODM) provide a joint interface to clinical and research systems. The
602 ultimate goal is a single overarching data model to support both clinical research and healthcare
603 (25).

604 One of the HL7 technical committees is RCRIM (Regulated Clinical Research
605 Information Management). Their mission is to develop standards to improve or enhance
606 information management during research and regulatory evaluation of the safety and
607 efficacy of therapeutic products or procedures worldwide. This committee intends to
608 facilitate the development of common standards for clinical research information
609 management across a variety of organizations -- including government agencies (FDA,
610 CDC, NIH), private research efforts, and sponsored research -- and thus improve the
611 availability of safe and effective therapies by improving the processes and efficiencies
612 associated with regulated clinical research.

613 3.4.4 Biomedical Research Integrated Domain Group

614
615 The Biomedical Research Integrated Domain Group (BRIDG) is an open model collaboration
616 between CDISC, HL7, National Cancer Institute (NCI) and FDA to develop a model to support
617 standards within the clinical research domain. This structured information model is being used to
618 support development of data interchange standards and technology solutions that will enable
619 harmonization between the biomedical/clinical research and healthcare arenas.

620
621 3.4.5 Healthcare Information Technology Standards Panel (HITSP)

622
623 The Healthcare Information Technology Standards Panel (HITSP) is sponsored by the American
624 National Standards Institute (ANSI) in cooperation with strategic partners such as the Healthcare
625 Information and Management Systems Society (HIMSS), the Advanced Technology Institute
626 (ATI) and Booz Allen Hamilton and funded by a contract award from the U.S. Department of
627 Health and Human Services.

628
629 The Panel is comprised of members from standards development organizations (SDOs), non-SDO
630 stakeholder organizations (e.g., clinicians, providers, health IT vendors, national organizations
631 with an interest in healthcare information technology standards), governmental bodies, and
632 consumers.

633

634 The Panel’s objective is to “achieve widely accepted and readily-implemented consensus-based
635 standards that will enable and support widespread interoperability among healthcare information
636 technology, especially as they would interact in a Nationwide Health Information Network
637 (NHIN) for the United States”.

638
639 3.4.6 openEHR Foundation

640 The *openEHR* Foundation, established in 2003, “works in an open manner, based on active
641 relationships with domain experts and users, with national and international standards bodies,
642 including ISO, CEN, and HL7, with software and system developers, and with educational
643 institutions and researchers”.

644 The *openEHR* Foundation is “committed to supporting relevant government-sponsored and
645 industry-based standards bodies as a means of encouraging the widespread and effective adoption
646 of interoperable EHRs”.

647 As is obvious by the number of standards organizations and the long period that some of these have
648 been in existence, this is not an area that is easily defined or agreed upon. In order for electronic
649 health records to be shared among different healthcare providers and/or clinical research it is critical
650 that a small number of standards are agreed upon globally and implemented.
651
652
653

654 3.5 Overview of eSource Initiatives

655 Despite limitations as noted in previous sections such as an unclear regulatory environment and the
656 lack of accepted standards across all regions and platforms, groups are still interested in finding ways
657 to use eSource within the current environment. In an effort to provide a clear picture of the
658 convergence of the environments for electronic healthcare and electronic clinical data capture, it is
659 necessary to outline some current eSource pilots. While a few are described below, we recognize
660 there may be many more that have not yet been published.

- 661 ○ Johnson & Johnson (J&J) is performing Phase I trials using tablet PCs (10). This allows the
662 investigator to move around the clinic/hospital and collect the data directly as it is generated.
663 While J&J sees definite benefits to this, they are using the tablet PCs much like any other
664 EDC system except that the mobility makes it easier to enter data directly and thus eliminate a
665 separate source. The data entered into the tablets do not reside there, but go directly to a local,
666 on-site server. Data are then transmitted from the local server to the sponsor’s (J&J’s) a
667 central server.
- 668 ○ Pilots involving retrospective mining of data to be used for analysis to determine trends and
669 information for future clinical trials were reported by the Karolinska Institute (28). In these
670 pilots, large amounts of data were retrieved from pre-existing electronic medical records
671 databases and analyzed in a short timeframe. Although these pilots used retrospective
672 collection of data, they did demonstrate that transfer of eSource data to a sponsor for clinical
673 trial analysis is feasible and also that efficiencies can be seen using this process. The authors
674 of this paper wish to draw the readers’ attention to the distinction between retrospective data
675 mining and prospective clinical research: Academic and other researchers frequently use data
676 from EHR systems to conduct retrospective and epidemiologic research. The requirements for
677 this type of research are far less stringent than those governing the work of researchers
678 conducting prospective clinical trials to test the safety and efficacy of new drug candidates
679 (referred to as ‘clinical research’ in this paper), which are subject to regulatory oversight.

- 680 ○ Siemens Medical Systems, an EHR vendor, is conducting a pilot with the University of
681 Munich to allow entry of clinical trial data through one integrated portal during trial conduct
682 (24).
- 683 ○ CDISC is conducting a proof of concept pilot (called “Single Source”) using standards for
684 healthcare information (HL7) and standards for clinical research (CDISC) for the electronic
685 source documentation of clinical trial data and the generation of medical records for patient
686 care from a single point of entry. This takes the approach of an entry application prior to
687 either EHR or EDC systems in which both patient data and clinical research data enter under
688 regulatory control and from there are populated to the appropriate databases (25).
- 689 ○ Lundbeck, a sponsor company, is allowing eSource into their EDC systems by creating a
690 controlled PDF copy of the data as it is saved or updated and automatically storing this PDF
691 off-site in a secure facility outside the sponsor’s direct control (i.e., controlled by a trusted
692 third party (TTP)). These controlled PDFs may be viewed but not modified or overwritten by
693 both the sponsor and the site and used to verify data integrity should any questions arise. In
694 this way, the sponsor has access to the data immediately, yet there is still a separate source for
695 verification. These measures are taken in order to meet current regulatory guidelines (26).

696 Regulatory agencies are also showing interest in furthering eSource as demonstrated during the
697 January 11th, 2006 meeting between CDER’s Division of Scientific Investigations and the PhRMA
698 EDC Task Group. At that meeting, DSI representatives expressed their interest in exploring eSource
699 options and associated issues. They also stressed that investigator’s control over the source data—
700 whether it is maintained in paper records or electronically—remains a fundamental requirement.

701 These recent initiatives demonstrate that there is interest in further exploring the potential of eSource.
702 As vendors, sponsors and regulatory agencies work out the issues surrounding the use of eSource, we
703 will move closer to the vision of having the variety of data collection systems currently in use being
704 able to directly share data for a variety of purposes (e.g., EHR, clinical trials).
705

7064 **IDEAL FUTURE ENVIRONMENT**

7074.1 **The Challenge: EHR/CR**

708 The eHealth initiatives thus far have been strongly healthcare-centric. As a result, the transformations
709 that are ongoing have not been considering the requirements of secondary users of healthcare data
710 such as clinical researchers. This oversight has occurred despite the desire of regulators to speed up
711 delivery of new medicines, reduce the cost of new and improved treatments and to deliver improved
712 patient care based upon best practices.

713 Significant benefits can be accrued through collaboration of both the healthcare and research worlds in
714 effectively and efficiently sharing data. Without such collaboration, as the use of EHRs grows, both
715 the healthcare sector and the bio-pharmaceutical companies will be obliged to spend valuable
716 resources on duplicate tasks. The challenge is to develop systems and processes that will allow the
717 direct use of patient electronic medical data for both prospective and retrospective clinical research⁴ in
718 a way that meets data protection, regulatory and ethical research requirements. For purposes of this
719 paper, we are using the term “EHR/CR” to mean a system that is capable of supporting both electronic
720 healthcare and electronic clinical data capture. In meeting this challenge, three areas will need to be
721 addressed:

⁴ See discussion of prospective and retrospective clinical research in section 3.5

- 722 ○ A mechanism for satisfying regulatory and clinical research requirements for system validation
723 and data reliability will need to be created, or adapted from existing clinical research systems
724 ○ Data standards for electronic data collection, interpretation, and exchange will need to be
725 determined based upon needs of both the medical and clinical research communities.
726 ○ Controlled, secure processes for releasing and transferring data from and to EHR, device and
727 research systems will need to be developed, consistent with personal data privacy, clinical trial
728 regulations and bioethical considerations.
729
730 It is acknowledged that this is likely to be an evolutionary process over a number of years.

731 4.2 Attributes of the Ideal Environment

732 The ideal future environment for the capture and exchange of electronic data for clinical trials include
733 attributes that would be part of a quality nation-wide network of interoperable patient health records
734 with additional requirements for the use of these records for clinical trials. Following is a list of
735 requirements needed for a successful EHR/CR system. It includes requirements that we are assuming
736 would already be a part of a nation-wide EHRS, followed by requirements that would be specific to
737 the needs of collecting clinical research via this nation-wide EHRS. It should be noted that interim
738 solutions towards this ideal goal (such as investigators using certified, standard EHRs) will also have
739 benefit. Some interim solutions are discussed by the CDISC Electronic Source Data Interchange
740 (eSDI) paper (19).

741 *System and System Design*

742 *Requirements for a successful nation-wide EHRS:*

- 743 ○ EHR systems will share common data standards and features such that data can be interchanged.
744 ○ A mechanism will be defined to allow the exchange and/or access of data from different health
745 locations
746 ○ Systems will be certified via a formal accreditation process (e.g. similar to what is currently
747 available for lab systems)
748 ○ The EHR system must be non-intrusive to the doctor-patient relationship
749 ○ The performance and reliability of the systems must be very high
750 ○ Access points must be secure
751 ○ System must be easy to use by different types of staff (physicians, nurses, administration, even
752 patients)
753 ○ Physicians must be able to use the system to access centrally collected data (labs, ECG, etc.)
754 ○ Potential privacy issues must be managed
755 ○ Direct data transfer mechanism/protocol from medical devices must exist such that this
756 information can be part of the patient's EHR
757 ○ Access to patient electronic records is available at every location where a patient is seen (e.g.
758 physician's office, hospital, lab, etc.) to avoid the creation of paper records and subsequent-entry
759 of this information
760 ○ Widespread use of certified EHR systems (that comply with defined data standards and agreed
761 regulatory standards)
762

763 *Additional requirements for EHR/CR:*

- 764 ○ EHR systems must be able to collect all required research data and provide support for clinical
765 workflow at the investigator site. Once a patient signs informed consent for a clinical trial, then
766 additional trial screens and information would appear when that patient's records are accessed
767 ○ Systems must be compliant with regulatory research requirements (e.g. access control, audit
768 trail, backup, and ALCOA properties)

- 769 ○ Regulators must accept data sourced from accredited EHR systems for research purposes
- 770 ○ System must differentiate and handle both clinical trials patient data and private patient data.
- 771 ○ Study sponsor only has access to the part of the patient's data that are relevant to the clinical
- 772 trial
- 773 ○ Data security methods preserve requirements for data blinding
- 774 ○ The source of data within the system will be clearly documented
- 775 ○ An accepted process is available to approve research access to EHR data in a way that meets
- 776 data privacy and bioethical considerations
- 777 ○ Chain of custody is managed (who is responsible for data at different points)

778 **Data Standards**

779 *Requirements for a successful nation-wide EHRS:*

- 780 ○ Open data standards and open interchange standards are agreed on and adopted
- 781 ○ Translation requirements are minimized through the use of standard templates and dictionaries
- 782 (rules for dictionary use limit untranslatable text information)

784 *Additional requirements for EHR/CR:*

- 785 ○ Standards for both Bio-Pharmaceutical and eHealth initiatives converge such that common data
- 786 exchange standards allow for flexible data interchange between EHR and clinical research
- 787 systems
- 788 ○ Common data standards are adopted extensively across clinical research sponsors
- 789 ○ A digital identity standard that allows organizations to meet the requirements of document
- 790 authentication, legally binding digital signatures, integrity, uniform liability controls and privacy
- 791 (e.g., SAFE Initiative)

792 **Quality System**

793 *Requirements for a successful nation-wide EHRS:*

- 794 ○ Formal accreditation process for EHR systems allows confidence in system compliance towards
- 795 data integrity and security

797 *Additional requirements for EHR/CR:*

- 798 ○ eSource through use of EHR must be part of a system with appropriate validation and built-in
- 799 security and audit features and under system life cycle control
- 800 ○ Record showing investigators have completed training on responsibility and accountability for
- 801 the integrity of the data, and system functionality and SOPs

802 **Regulations**

803 *Requirements for a successful nation-wide EHRS:*

- 804 ○ Applicable privacy regulations will be met

806 *Additional requirements for EHR/CR:*

- 807 ○ EHR systems required to meet yet-to-be-determined regulatory guidance for e-source as well as
- 808 21 CFR Part 312.62b, ICH E6, 21 CFR Part 11, and CSUCT
- 809 ○ Changes required in regulations/regulatory positions to accommodate eSource (e.g. 21 CFR Part
- 810 11, CSUCT) (See section 3.3)

8114.3 **The Vision: EHR/CR System**

812 In order to streamline the capture of clinical trial data and to realize the associated economic and time
813 savings, redundant data collection must be eliminated and communication between different areas of

814 the sponsor and investigator sites must be clear, non-redundant, timely, and effective. Such a
815 framework will allow data exchange in a manner compliant with both data protection and other
816 research specific regulations and will lead to innovative and efficient methods for data collection and
817 data use.

818 Following is one possible scenario of what *might* be possible as technology in both the Bio-
819 Pharmaceutical and Health Care industries evolve and merge. *This is not a recommendation, but*
820 *rather an example for illustration and to foster discussion.*
821

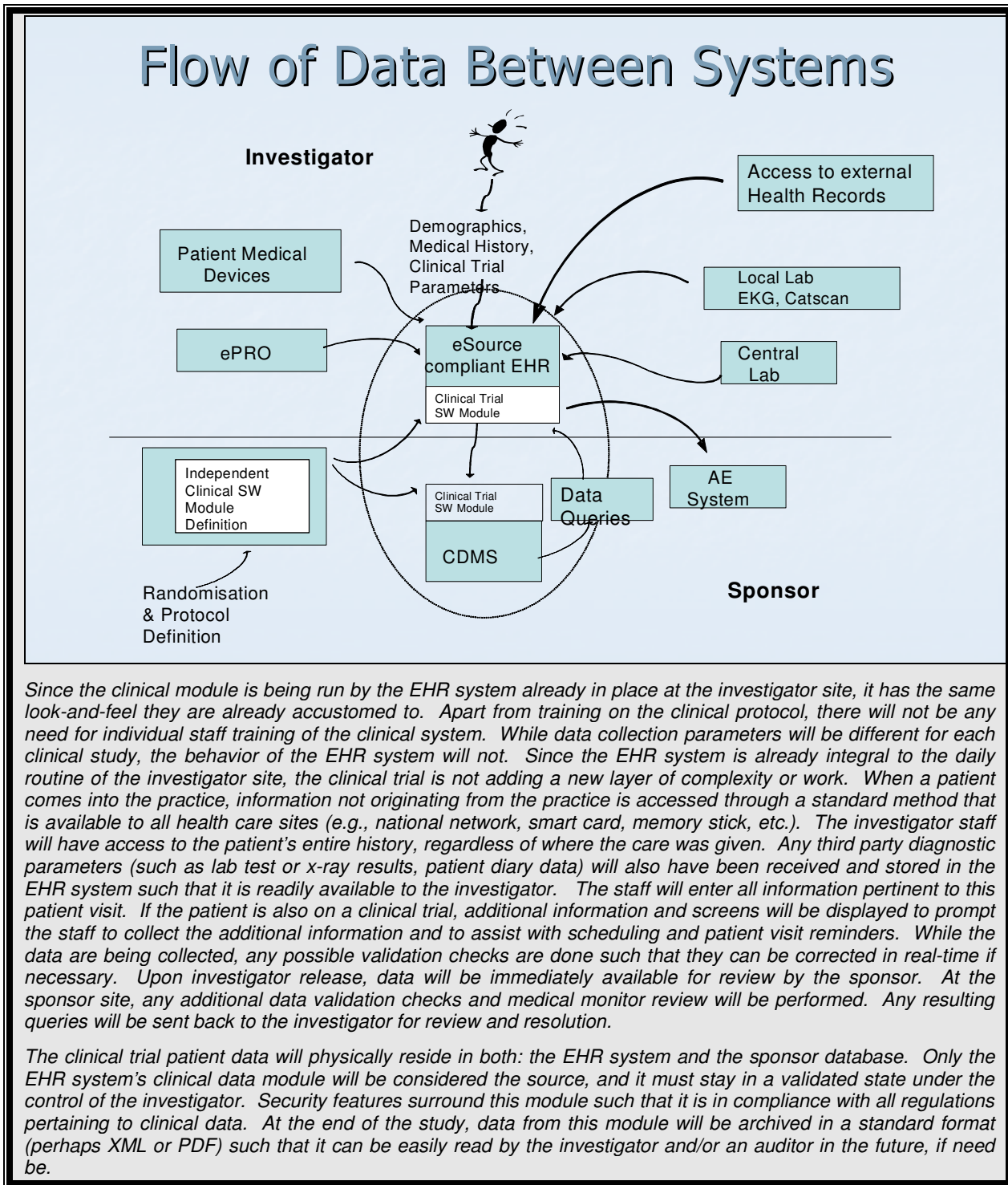
822

823 **Possible Future Scenario**

824 *Patients are being seen at hospitals, clinics and private practices in many countries, and the health information is*
825 *being entered and retrieved from computer databases during these visits. At the same time, within a*
826 *pharmaceutical company, a clinical study is being planned. The protocol parameters are entered into a standard*
827 *form or program and distributed electronically for approval. Once approved, these parameters are used by a*
828 *program (possibly vendor-provided) to set up the data capture system and database for this study. It will utilize a*
829 *library of standard data elements and associated edit checks that has been previously set up and augmented*
830 *over time. Once all standard database tables, data entry screens and validation checks have been set up and*
831 *approved, necessary validation on the study screens and database structure is performed.*

832 *The study is now ready to be deployed to the study investigators. It is in the form of an independent software*
833 *module that employs standard interface definitions developed by a standards committee within the Bio-*
834 *Pharmaceutical and Healthcare industries. Using the standard interface definitions, the independent clinical*
835 *module can be recognized by any certified electronic health record (EHR) system being used by the investigator*
836 *sites. When the investigator staff receives the module for the new study, it is installed and a self-check program*
837 *runs to verify that it is working properly, and logs the results. These results are automatically transmitted to the*
838 *study sponsor for storage with the validation documentation for that study. This constitutes the technical*
839 *qualification of the site and signals to the sponsor that the site is ready to enter clinical patient data for this study*
840 *as soon as all other site initiation steps are completed (e.g., regulatory document filing, IRB approval, etc.).*

D R A F T



8645 BENEFITS AND BUSINESS IMPACT FOR STAKEHOLDERS

865 This section highlights the benefits and potential business impact that could be realized through a
866 combined EHR/CR system in which clinical research data could be collected and stored with the same

867 mechanism used for other patient data. Section 5.6, Potential Roles and Responsibilities with
868 EHR/CR is provided as “*food for thought*” on how roles and responsibilities could be affected.

869
870 EDC as currently adopted in about 27-30% of clinical trials provides acknowledged benefits over
871 paper CRF data capture. Since much of the clinical data needed for the trial will already be available
872 in an electronic form through the EHR, the introduction of the EHR/CR technologies and processes
873 will extend and accelerate the existing benefits of EDC into an increasingly higher number of clinical
874 trials, and an increasingly higher number of hospitals and healthcare clinics. Additionally, one major
875 hurdle to participating in clinical research, clinical data capture, will already be overcome by those
876 facilities that have adopted EHR systems that include EHR/CR technology.

877
878 Necessary business process changes will affect all involved in clinical research. We envision that the
879 healthcare centers involved in clinical research and clinical trial participants will benefit the most
880 through improved patient safety. Clinical sites will be able to devote quality time to their patients and
881 not be distracted by sponsor-supplied EDC systems that do not fit their common practices. Trial
882 sponsors, CROs, regulatory agencies, and other stakeholders will also benefit. It is therefore
883 advantageous for the bio-pharmaceutical industry to become an important participant in the
884 development of EHR and in particular EHR/CR technologies.

885.1 Patients

886 All patients whose healthcare provider participates in a nation-wide EHR system will reap
887 benefits of that system facilitating clinical research. These benefits are:

- 888 ○ Potential to address underserved populations through clinical trial recruitment and
889 participation
- 890 ○ Greater possibility of being identified for a clinical trial because their physician will
891 have better ability to search his/her patient population for inclusion criteria
- 892 ○ New therapies get to market and reach patients faster due to more efficient clinical
893 research process

894 In addition, patients participating in a clinical trial will see more immediate benefits. All
895 clinical trial safety data relating to the patient will be immediately available to their physician,
896 the medical monitor and the sponsor, allowing safety issues to be identified in real time.
897 Additionally, the sponsor will be able to easily pool data in real-time across multiple
898 geographies, racial and ethnic populations (prospective /retrospective), and pool safety data on
899 compound and classes of compounds, allowing possible drug interactions to be detected
900 sooner.

901 Clinical trial patients’ benefits:

- 902 ○ Improved safety monitoring on an individual trial basis as well as longer term (pre-
903 approval and post-approval)
- 904 ○ In Phase IV safety trials on approved, marketed drugs, the sponsor could look across a
905 larger number of patients and more easily identify less frequently observed
906 unexpected adverse events
- 907 ○ Potential for improved patient:physician interaction due to efficiency of process in
908 investigator’s office leading to a less hurried timeslot
- 909 ○ Patient’s health records offer a complete picture of all patient events

910.2 Investigator Staff

911 For Sites and Investigators, data contained within their patients’ database can be used to
912 identify those who may benefit the most from a new therapeutic drug compound or device.

913 Trial-specific inclusion and exclusion criteria will be readily assessed. Additionally, clinical
914 sites benefit as collection of data required for clinical studies will be incorporated within their
915 daily work routine. Essentially, as sites see patients who are participating in a clinical trial
916 they will use the same computerized systems adopted by their practice to enter data, address
917 queries, report any safety concerns and adverse events and schedule trial-specific visits and
918 procedures. EDC has already introduced many benefits as well as positive process changes
919 that would increasingly be seen in more investigational sites.

920 Clinical / investigational site benefits:

- 921 ○ Patients recruitment – EHR records could be searched for patients satisfying
- 922 inclusion/exclusion criteria
- 923 ○ The time required to check-in a patient and complete the medical record will be
- 924 significantly reduced:
 - 925 ● Data entry will be simplified and more efficient due to a one-time data entry into
 - 926 the EHR system (instead of today's multiple entries) and improved record
 - 927 retrieval
 - 928 ● Direct transfer of validated data to research systems will be simplified and more
 - 929 efficient due to a common validated interface
- 930 ○ Information storage will be more efficient as data will be stored electronically saving
- 931 on space requirements currently needed for multiple trial/sponsor hardware
- 932 ○ Serious Adverse Event (SAE) reporting and management may be simplified and
- 933 improved as SAEs could be sent to sponsor and regulatory authorities at the same
- 934 time, impacting the way both react to this information
- 935 ○ Regulations and controls surrounding clinical data capture can improve overall quality
- 936 of all data managed by the EHR system
- 937 ○ Potential to perform more trials with same level of in-house resource due to efficiency
- 938 in trial management
- 939 ○ Investigators will access their data through the use of an EHR portal rather than
- 940 through different sponsor/vendor developed front-ends, reducing training and ongoing
- 941 support issues
- 942 ○ Efficiency in presentation of patients' entire medical history, including data from
- 943 clinical trial participation
- 944 ○ Standards will enable data integration to be more consistent so investigator will not
- 945 have to learn multiple ways of dealing with multiple sponsors

946 5.3 Government-Sponsored eHealth Initiatives

947 Collaborative efforts between Government, Bio-pharmaceutical Companies as well as other
948 clinical research bodies (e.g., academia, National Cancer Institute (NCI)) will be increasingly
949 possible with the establishment of nationwide electronic health records. Processes need to be
950 established to ensure that government and the clinical research community can work together to
951 identify national / global health care issues that need to be addressed. Access to patient data will
952 be readily available for both prospective and retrospective analysis. This will enable identification
953 of future health care needs and has the potential to address those needs before they become urgent.

954 Benefits for government sponsored initiatives:

- 955 ● Potential for bio-pharmaceutical industry to assist in funding of national eHealth
- 956 initiatives
- 957 ● Improved population health through improved clinical research processes leading to better
- 958 understanding of emerging population health needs
- 959 ● Facilitation of getting new therapies to market faster
- 960

9615.4 Regulatory Authorities

962 Auditing clinical sites (i.e., comparing source data with that provided by the sponsor), evaluating
963 sites for potential fraudulent activity, and early monitoring for safety issues will be made easier
964 with a national EHR/CR system. A key responsibility of regulatory authorities is ensuring that the
965 data provided to support approval of a new drug or medical device truly represents that collected
966 at the clinical site. Regulators have had concerns with electronic data capture, in particular
967 electronic source, if that source data is maintained by the sponsor. It has been stated, by the FDA
968 Division of Scientific Investigation (DSI), that there must be two independent data sets, one
969 maintained by the investigator and one maintained / submitted by the sponsor. Regulators want to
970 ensure that data can be audited. With an EHR system that is under the investigators' control, data
971 is independent from the sponsor's study data and will be readily available for comparison.

972
973 Benefits for regulatory authorities:

- 974 • With a nation-wide network, regulatory authorities could have the capability to review
975 and/or audit sites' electronic source data against the data provided by the sponsor, thus
976 reducing the need for actual site visits by auditors while giving more transparency to the
977 authorities
- 978 • Refocus workload – the reduction of paperwork will allow for auditors to focus more on
979 key areas

9805.5 Sponsor / Bio-Pharmaceutical Industry

981 The Sponsor / Bio-pharmaceutical industry has already benefited from the use of EDC and EDC
982 processes in studies where this technology has been possible. With EHR/CR, the Sponsor will see
983 the EDC benefits in an increasing number of trials. In addition, they will benefit from better
984 availability to target patient populations. Because the sponsor's data comes directly from the
985 source (i.e., the EHR), queries will be kept to a minimum and source data verification will be
986 reduced or eliminated. The process for conducting clinical trials and collecting patient data will
987 evolve into one that is more collaborative with the practices of the investigational site.
988 Additionally, this will ensure compliance with 21 CFR 312.62b: Investigator recordkeeping and
989 record retention.

990 When standard clinical research requirements/functions are built into EHR systems, development
991 and support of today's EDC systems will go away. This has the potential to lower the cost of
992 clinical research and enable a greater number of clinical trials and sponsors to participate. In
993 general, redundant systems and overhead are eliminated.

994 Benefits for Bio-pharmaceutical Sponsors:

- 995 ○ With the ability to compare safety data from a clinical trial to a much larger baseline (i.e.
996 all EHR patients, not just clinical trial data), there is a potential for improved analysis and
997 projection of long-term safety through the sponsor's ability to do large retrospective trials
998 to identify potential safety issues or to review post-market product use via access to
999 information on patients who are using these products, keeping in mind privacy regulations
1000 for the patients
- 1001 ○ Better access to target patient populations
- 1002 ○ Ease study execution:
 - 1003 • Utilization of standardized EHR Clinical Research components
 - 1004 • As data transferred to research is a transaction copy of the source data no source data
1005 verification (SDV) will be required and queries will be reduced
- 1006 ○ Eliminates redundant computer systems and overhead:
 - 1007 • Application and hardware support, helpdesk, and training will be reduced

- 1008 ○ Archiving requirements will be significantly reduced:
- 1009 • More of the Trial Master file will be electronic
- 1010 • Sites will already hold research data (as source) therefore preparation of an archive
- 1011 copy for retention at the site may not be required
- 1012 ○ Pharmacy and patient records will be integrated within the EHR environment allowing
- 1013 drug accountability to be performed electronically via electronic access to dispensing and
- 1014 usage, monitoring of supplies, automated ordering, etc.
- 1015 ○ Transcription errors are reduced or eliminated
- 1016 ○ EHR/CR will lead to reduction in trial costs and time savings
- 1017 ○ Potential for not maintaining data in a sponsor database but rather to access source
- 1018 through the EHR/CR
- 1019 ○ Potential investigator list is expanded to include any physician with a certified EHR/CR
- 1020 system

1021 **5.6 Potential EHR/CR Roles and Responsibilities**

1022 This section provides discussion on clinical research roles and responsibilities that may evolve with
1023 the onset of national electronic health record systems capable of use for clinical research data
1024 collection. It is provided to prompt additional discussion and thinking with regard to the nature of
1025 clinical research in the future.

- 1026 1. Roles & responsibilities in all areas will evolve:
 - 1027 • Clinical Research Associate (CRA): The traditional work of the CRA will migrate into
 - 1028 more of a site relationship management role. The EHR/CR system removes the need for
 - 1029 much of the CRA's time to be spent checking and managing paper CRFs allowing time
 - 1030 on-site to be spent more effectively providing protocol and safety training, ensuring GCP
 - 1031 compliance, etc. The EHR/CR software gives the CRA access to the patient data when
 - 1032 not at the site, allowing for more targeted preparation of visits. The need for source
 - 1033 document verification will largely be replaced by verification that the data points extracted
 - 1034 to the eCRF are the correct data points. More complex interrogation of the EHR may
 - 1035 allow the detection of omitted information such as non compliance with exclusion criteria,
 - 1036 non-reporting of prohibited concomitant medications, etc. Quality of remote monitoring
 - 1037 tools and processes allows change in focus of monitoring effort
 - 1038 • Data Manager role changes to be far more site oriented, as they become the liaison
 - 1039 between the data and the site staff communicating primarily via the EHR/CR system.
 - 1040 Preparation of ongoing reports for safety and review purposes and programming of
 - 1041 extraction algorithms may move this towards a more technical role. New tasks might
 - 1042 involve transferring research data back to EHR (e.g., laboratory data). In addition, Data
 - 1043 Managers will have more involvement in protocol development as data definitions will
 - 1044 need to be built into the protocol to assist Ethics Committees/IRBs in determining data
 - 1045 collection requirements and to enable the development trial-specific EHR modules
 - 1046 • IT Support Personnel will need to be more aware of the total process of clinical trials from
 - 1047 eSource through Submissions. Study protocol will become more Information Technology
 - 1048 (IT)-oriented (it will need to specify electronic methods of data collection and identify
 - 1049 electronic source)
 - 1050 • Quality Assurance must audit EHR/CR systems to ensure appropriate controls exist such
 - 1051 that investigators can make the assurance that they are accountable for the integrity of the
 - 1052 data (eSource) they provide
- 1053
- 1054 2. The informed consent process will change. This will include all that are involved in the
- 1055 process (e.g., sponsor, site, patients and IRB (ethics committees):

- 1056
- 1057
- 1058
- 1059
- 1060
- 1061
- 1062
- 1063
- 1064
- Data is moving to patient ownership. The Informed Consent documentation will need to be adapted to collect patient approval for clinical trial participation
 - Informed Consent can be given electronically
3. Some financial costs may be shifted from sponsors to investigator sites or built into the amount that sites may charge for conducting clinical trials due to a shift in some responsibilities from sponsor to investigator, such as data hosting, on-site validation (data/system), trial module development/configuration
- 1065
- 1066
- 1067
- 1068
- 1069
- 1070
- 1071
- 1072
- 4. Review of data for FRAUD will change:
 - Fraudulent data will likely be reduced (never eliminated) as sponsors will be able to monitor the timeliness of the data entry and any changes
 - Since the EHR is usually accessible to many medical and nursing staff, it is less vulnerable to fraudulent changes by an individual
 - Sponsor will look for data trends, in order to detect fraud

10736 CRITICAL SUCCESS FACTORS AND RISKS

10746.1 Critical Success Factors for an EHR/CR System

1075 While we recognize the magnitude and priority of the national eHealth initiatives to implement
1076 national health networks that will drive the cost of healthcare down while bringing up healthcare
1077 quality, we feel strongly that the earlier in this process that the needs of clinical research are
1078 considered, the better for the entire healthcare community. Encouraging the growth of EHR systems
1079 without consideration to the regulatory requirements and efficiency needs of clinical research could
1080 bring unwanted consequences to the healthcare industries and to the patients themselves, by reduced
1081 efficiencies in the clinical research process, and therefore potentially decreasing the introduction of
1082 new therapies while increasing their costs.

1083

1084 The next evolutionary step for EDC in clinical trials is eSource and the elimination of duplicate record
1085 keeping. This is paralleling the national eHealth initiative efforts to move all clinical practices
1086 towards electronic source for all patient health records. In order for these electronic health records to
1087 be used for clinical research purposes there are some critical issues that must be addressed. The time
1088 is right for discussing these issues. Capturing patient data so that it can be used for both healthcare
1089 and research purposes can only be accomplished through the use of common data standards, and
1090 common regulatory guidelines for privacy, security, and record integrity. Collaboration between the
1091 healthcare industry and the bio-pharmaceutical industry is critical for influencing the goals of the
1092 eHealth initiatives, communicating with the stakeholders, and determining the details of the records,
1093 systems, networks, and processes. Not only can the data be captured in such a way as to facilitate
1094 both needs, but a strategic alliance between the two industries can be made thus facilitating ongoing
1095 communication and collaboration towards timely research of critical healthcare needs as they arise.

1096

1097 The following defines what we believe are critical success factors for accomplishing this vision and
1098 will position both healthcare and clinical research for success:

- 1099
- Convince governmental decision makers that there is value in incorporating the facilitation of
1100 prospective clinical research as a goal of the National Electronic Health Initiatives

- 1101 • Collaboration between the bio-pharmaceutical and healthcare industries and associated
- 1102 vendors to expand and adapt the structure of EHR and the associated systems, networks, and
- 1103 processes
- 1104 • Collaboration on common data standards (including EHR narratives) and data transfer
- 1105 standards to support both national health record and clinical research needs (e.g., support for
- 1106 the CDISC/HL7 joint initiative)
- 1107 • Development and testing of an AHIC (American Health Information Community) use case
- 1108 that incorporates clinical research data collection
- 1109 • Regulatory guidelines supporting the use of eSource
- 1110 • Modification to data privacy laws to enable clinical research while maintaining patient
- 1111 anonymity (e.g., HIPAA), EU Data Protection Directive)
- 1112 • Application of 21 CFR Part 11 Electronic records and signatures rule to EHR systems
- 1113 • Security for electronic transfers and transactions (e.g., 21 CFR Part 11, and SAFE)

11146.2 Concerns with Current eHealth Plans Towards Meeting the EHR/CR

1115 Vision

1116
1117 The priority for implementing national health information networks has been driven by the ever
1118 increasing costs of health care and associated services. While the requirements of the bio-
1119 pharmaceutical industry have a lower priority, accounting for these needs now is critical to the future
1120 advancement of quality and cost effective clinical research. This will enable clinical researchers to
1121 identify, attract and manage patients and patient data and speed delivery of breakthrough medicines,
1122 therapies and devices.

1123
1124 If clinical research is not incorporated into EHR system plans now, there is the potential for difficulty
1125 in recruiting investigators. The additional workload of clinical research data collection on top of the
1126 already-imposed requirement to collect healthcare data electronically makes clinical research
1127 economically impractical especially in the current cost-containment climate in the healthcare industry.
1128 If the redundancy of collecting data via the EHR as well as a clinical-research-appropriate system
1129 (either electronic or paper) is not imposed in the case where there is no EHR/CR, there is the concern
1130 that the only source of data could be EHR systems that are not suitable for clinical research and which
1131 do not meet clinical data regulations. Thus, without a suitable means to collect clinical research
1132 quality data within the EHR, clinical research will become more inconvenient and more expensive due
1133 to a redundant and less efficient process.

1134
1135 If clinical research becomes economically prohibitive due to the cost of running clinical trials coupled
1136 with the already crippling effects felt through the introduction of generic drugs and current patent
1137 laws, the impact to national health and to individual patients could be immense. This could very well
1138 inhibit the discovery of breakthrough drugs or research on diseases affecting small populations. While
1139 dealing more effectively with routine healthcare issues and improving the ability of a nation to identify
1140 an emergent healthcare crisis through a nationwide network of electronic health records, the ability of
1141 the research community to quickly conduct research and development to combat an emergency such as
1142 a new or evolved disease strain could be hampered. An increase in the cost and time it takes to do
1143 clinical research will only result in more costly and fewer medications available on the market which
1144 will increase the cost of healthcare overall. The economic savings gained through a more efficient
1145 national healthcare network would be lost on the higher cost of medications while access to new
1146 therapies would be reduced.

1147

1148 In countries where the eHealth initiative has gone past the design phase and into implementation, the
1149 lack of common EHR data standards, code sets, and vocabularies, within and across countries, may
1150 make it difficult if not impossible to access and integrate this data efficiently for clinical research.
1151 While electronic health records may come under existing federal regulations (e.g., HIPAA, Federal
1152 Rule of Evidence, EU Data Protection Directive) to ensure their security and integrity, these may fall
1153 short of what is needed for clinical research, and so it is critical that EHRs are governed by the same
1154 regulations that govern clinical research (e.g., 21 CFR Part 11, 21 CFR 312).

1155
1156 A further concern is that EHR system vendors and service providers do not have economic incentive
1157 and lack the knowledge of clinical data workflow to build EDC-like capabilities (see section 3.2) into
1158 their products. There are efforts being made to address this and to better define the value and cost
1159 associated with incorporating clinical research needs within EHR systems (16). It is critical that
1160 clinical research professionals be included in the design and implementation phases of EHR such that
1161 the result is an EHR/CR.

1162

11637 STEPS TOWARD IMPLEMENTING THE VISION

1164 It is not possible to develop and implement EHR/CR technology with its full potential at this time.
1165 However, by collaboration of members from the bio-pharmaceutical and healthcare industries,
1166 regulators, and vendors of EHR and EDC systems towards this common EHR/CR vision, a smooth
1167 evolution towards this state as an acceptable reality is possible. Following are steps in this direction
1168 that could be taken now.

1169

11707.1 Technology Industry

1171 Collaboration between EHR and EDC system vendors needs to occur for either of them to compete in
1172 the market for clinical research money. Both have knowledge, software, processes, and services that
1173 need to be combined in order for the EHR/CR vision to become an acceptable and beneficial reality
1174 for all stakeholders. A new business model for these industries, targeted at a combined EHR/CR,
1175 needs to be developed. While interim steps may include multiple bridges and interfaces to existing
1176 applications, only an integrated solution will ultimately be beneficial and successful.

1177

1178 It is recommended that both EHR and EDC vendors:

- 1179 ○ Work together with members from the bio-pharmaceutical and healthcare industries, regulators
1180 and other government agencies towards a common vision for EHR/CR.
- 1181 ○ Work towards integrating the “parallel universe” of clinical research and physician health records
1182 when designing/upgrading their products
- 1183 ○ Continue to support CDISC/HL-7 standards:
 - 1184 ■ Integrate these standards when designing/upgrading EHR and EDC products
 - 1185 ■ Add support for import and export using these standards
- 1186 ○ Incorporate features into existing products to allow the secure use of eSource in today’s
1187 environment
- 1188 ○ Incorporate into applications the ability for secure, encrypted data to be passed over the World
1189 Wide Web
- 1190 ○ Continue to support SAFE(18) initiative

11917.2 Bio-Pharmaceutical Industry

1192 The bio-pharmaceutical industry cannot just sit back and wait to see what happens with the eHealth
1193 initiatives and the onset of more and more healthcare data being collected via eSource. They must be
1194 proactive in ensuring their ability to attract and keep investigators, that the investigators will continue
1195 to collect quality research data, and that the process of developing new drugs and bringing them to
1196 market continues to be cost-effective.

1197

1198 It is recommended that the bio-pharmaceutical industry:

- 1199 ○ Work together with vendors of EHR and EDC systems, healthcare industry, regulators, and other
1200 government agencies towards a common vision for EHR/CR
- 1201 ○ Continue to support the joint work of the CDISC/HL-7 committee
 - 1202 • Request clinical data transfers using CDISC standards
 - 1203 • Use CDISC standards in internally developed applications
- 1204 ○ Maximize the number of studies conducted with EDC in order to prepare all clinical data
1205 management and investigator staff for an electronic environment
- 1206 ○ Audit investigators who are already using EHR to determine the level of ALCOA associated with
1207 their patient data and make recommendations on improving this data such that it might be used as
1208 eSource for clinical trials
- 1209 ○ Urge investigators who are considering purchasing/implementing EHR systems to only consider
1210 systems that provide for a secure method for eSource collection and other clinical research data
1211 capture functionality
- 1212 ○ Plan for changing business processes surrounding clinical trial data collection and management to
1213 accommodate EHR/CR vision
- 1214 ○ Continue involvement and feedback of eSource pilot projects
- 1215 ○ Work with regulatory agencies to be sure that regulations can support whatever model is being
1216 designed for eSource

12177.3 Government Agencies

1218 Government agencies dealing with either national healthcare or bio-pharmaceutical drug control need
1219 to realize that the health of the overall population is best served through supporting a national
1220 electronic healthcare network that includes clinical research.

1221

1222 It is recommended that government agencies:

- 1223 ○ Work together with members from the bio-pharmaceutical and healthcare industries and vendors
1224 of EHR and EDC systems towards a common vision for EHR/CR
- 1225 ○ Allow use-cases for the national network to include functionality needed for clinical trial data
1226 capture (i.e. as a Clinical Trials use-case or part of a Bio-surveillance use-case)
- 1227 ○ Work together across regulatory agencies to ensure they are addressing common and/or
1228 complimentary regulations
- 1229 ○ Provide guidance on using electronic data as source for clinical trials
- 1230 ○ Collaborate with both Healthcare and Bio-Pharmaceutical industry groups when setting EHR
1231 technical and record content standards such that clinical research needs and regulations are met
1232 (i.e. endorse joint CDISC/HL-7 standards for EHR systems)
- 1233 ○ Determine how to uniquely identify all individuals who may use a national health network
- 1234 ○ Continue work on developing a certification process for EHR systems to determine adherence to
1235 approved standards for architecture, record content and validation
- 1236 ○ Provide incentives for health care provider associations (both government sponsored and private
1237 sector) to follow set EHR standards and employ EHR systems

- 1238 ○ Modify privacy regulations in order to provide for structure for informed consent at different
1239 levels such that it can accommodate needs of access to patient data for both clinical trials research
1240 and data mining

12417.4 Healthcare Providers

1242 In most developed countries, initiatives for national electronic healthcare systems are under
1243 development and healthcare providers will be required to collect and maintain patient health records
1244 via an electronic record system. This will require a change in the way healthcare data is recorded,
1245 handled, and stored and can affect the processes in all areas of patient care.

1246 It is recommended that members of the healthcare industry:

- 1247 ○ Work together with members from the bio-pharmaceutical industry, regulators, and vendors of
1248 EHR and EDC systems towards a common vision for EHR/CR
1249 ○ Start planning now for moving to an electronic environment.
1250 ○ If not currently participating in any EDC clinical studies, request to run a trial using EDC. The
1251 training in processes and systems along with the ongoing support from EDC professionals
1252 provided by the sponsor will be invaluable in adjusting to an electronic records environment
1253 ○ When researching EHR systems for purchase/implementation, insist on a model that enables
1254 capturing electronic health records along with clinical research data
1255
1256

12578 CONCLUSION

1258 **Clinical research requirements must be included in current plans for nation-wide eHealth** 1259 **initiatives in order to achieve cost-effective and timely new therapies.**

1260 In the current environment where approximately 27% of clinical research is conducted using
1261 electronic data capture, a significant number of these sites are also using electronic health records
1262 systems. This duplicative environment results in inconvenient and costly procedures for both
1263 healthcare and clinical research. As the use of EHR systems grows, the number of sites with this
1264 costly and inconvenient process will grow to encompass all studies and all sites. This will drive
1265 up the cost of clinical research immensely and could result in difficulty in recruiting investigators
1266 due to the added workload. This is especially significant during a time when the cost-containment
1267 climate in the healthcare industry is resulting in pressure on the bio-pharmaceutical industry to
1268 also contain costs.

1269 **Bio-Pharmaceutical Industry needs to find a voice in the National eHealth Initiative debate.**

1270 Healthcare and research automation efforts are for the time being sector-centric. We need to
1271 collaborate and integrate if we are to improve the efficiency of data collection, minimize the effort
1272 from healthcare professionals in conducting clinical research, exchange reliable data, and ensure
1273 that regulatory approval of future therapies is based upon reliable and secure data sources. To
1274 achieve this, the bio-pharmaceutical industry needs to find a voice in the EHR/ Healthcare
1275 Technology debate.
1276

12779

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1372 9.2 Websites

1373 The following websites may be instrumental in getting information on current initiatives that could
1374 further benefit or affect this vision:

1375 9.2.1 Standards Initiatives

- 1376 ○ CDISC Single Source project: http://www.cdisc.org/single_source
1377 ○ Joint CDISC / HL-7 Standards Initiative: <http://www.cdisc.org/indexnew.html>

1378 9.2.2 National and Community eHealth Initiatives

- 1379 ○ Open Clinical: EMR National Deployment Strategies and Programmes (links from this site to
1380 sites of national eHealth initiatives): <http://www.openclinical.org/emrDeployment.html>
1381 ○ US Health & Human Services (HHS), Office for the National Coordination for Health Information
1382 Technology (ONCHIT) : <http://www.hhs.gov/healthit>
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1387 ○ Action Plan for the European eHealth Area:
1388 http://europa.eu.int/information_society/doc/qualif/health/COM_2004_0356_F_EN_ACTE.pdf
1389 ○ Regional Secure Healthcare Networks (RESHEN): <http://www.biomed.ntua.gr/reshen/>
1390 ○ European Institute for Health Records (Eurorec): <http://www.eurorec.org/>
1391 ○ WideNet: <http://www.sadiel.es/Europa/widenet/acceso.htm>
1392 ○ NPfIT (UK National Programme for IT): <http://www.npfit.nhs.uk>
1393 ○ Danish Center for Health Telematics: <http://cfstuk.temp.fyns-amt.dk/default.asp?id=150961>
1394 ○ National Cancer Institute (NCI) Cancer Biomedical Informatics Grid (caBIG)

1395 9.3 Glossary of Terms

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Term	Description
ALCOA	The principal that all data and data updates recorded in electronic format can be shown to be Attributable, Legible, Contemporaneous, Original and Authentic. This requirement is set forth in the CSUCT Guidance (13)
CDMS	Clinical Data Management System (clinical trial sponsor's database used to collect and maintain clinical research data)
CRA	Clinical Research Associate (a member of the clinical trial sponsor's staff responsible for overseeing that the clinical trial is conducted according to protocol)
CRF, eCRF	Case Report Form (form used to present clinical research data) Electronic Case Report Form
EDC	Electronic Data Capture of clinical research data via systems that provide electronic support for data capture and management at the investigator site and communication between the site and the sponsor
eDiary, ePRO	Electronic Patient Reported Outcomes - Patient-entered experience data that is entered into a device often referred to as eDiary or ePRO device
eHealth	Government initiatives focused on developing nation-wide electronic health

	networks
EHR/CR	Term coined in this paper. Refers to a system that is capable of supporting both electronic healthcare and electronic clinical data capture.
EHR	Electronic Health Records managed through an EHRS – Electronic Health Record System
eSource	“When original observations are entered directly into a computerized system, the electronic record is the source document.” FDA Guidance on Computerized Systems Used in Clinical Trials section III.D (note: also commonly referred to as “direct entry”)
Hosting	In this paper, hosting means providing the computer facilities (servers) and procedures for a safe custody/storage of clinical data in such a way that data are protected against un-authorized access during and after a trial. The host is responsible for ensuring the ALCOA-principle.
SAFE	The Secure Access for Everyone (SAFE) initiative, supported by group of major bi-pharmaceutical companies in cooperation with regulators and industry associations, is a collaborative effort to create an industry-wide e-signature standard. SAFE’s mission is to provide an open global standard for secure and legally enforceable digitally signed e-documents exchanged among biopharmaceutical companies and with regulatory bodies.
Source Data	ICH GCP Guideline E6: ‘All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).’

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