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CONCEPT PAPER

RISK MANAGEMENT PROGRAMS

DRAFT

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For questions on the content of this draft document contact Christine Bechtel, 301-594-5458.

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CONCEPT PAPER: RISK MANAGEMENT PROGRAMS

If you plan to submit comments on this concept paper, to expedite FDA review of your comments, please:

- *Clearly explain each issue/concern and, when appropriate, include an alternative proposal and the rationale and/or justification for employing the alternative.*
- *Identify specific comments by line numbers; use the pdf version of the document whenever possible.*

1 **I. INTRODUCTION**

2
3 In accordance with Section VIII of the PDUFA III Reauthorization Performance Goals
4 and Procedures, the CDER/CBER Risk Management Working Group is drafting
5 guidance for industry on the development, implementation, and evaluation of drug and
6 biological product¹ risk management programs. This concept paper is intended to
7 facilitate public discussion on the content of the draft guidance by outlining FDA’s
8 proposed approach and requesting comment. Specifically, this concept paper presents
9 FDA’s preliminary thoughts on:

- 10
- Considerations for initiating and designing a risk management program
 - The selection and development of risk management tools
 - The evaluation of risk management programs
 - The recommended elements of a risk management program submission

11
12
13
14
15
16 **II. IMPORTANT RISK MANAGEMENT CONCEPTS**

17
18 **A. What is risk management?**

19
20 FDA approval of a product means FDA believes that it is safe and effective for its labeled
21 indications under its labeled conditions of use. FDA’s determination that a product is
22 safe, however, does not suggest an absence of risk. Rather, a product is considered to be
23 safe if the clinical significance and probability of beneficial effects outweigh the
24 likelihood and medical importance of its harmful or undesirable effects. In other words, a
25 product is considered safe if it has a positive benefit/risk balance on a population and
26 individual patient level.

27
28 Risk management is the overall and continuing process of minimizing risks throughout a
29 product’s lifecycle to optimize its benefit/risk balance. Risk information emerges
30 continuously throughout a product’s lifecycle, during both the investigation and
31 marketing phases through both labeled and off-label uses. FDA considers risk
32 management to be a continuous process of (1) learning about and interpreting a product’s

¹ For ease of reference, this concept paper uses the term *product* to refer to all products (excluding blood products other than plasma derivatives) regulated by the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER). Similarly, for ease of reference, this concept paper uses the term *approval* to refer to both drug approval and biologic licensure.

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33 benefits and risks, (2) designing and implementing interventions to minimize a product's
34 risks, (3) evaluating interventions in light of new knowledge that is acquired over time,
35 and (4) revising interventions when appropriate.

36

37 **B. What aspects of risk management are addressed in this concept**
38 **paper?**

39

40 This concept paper defines and discusses risk management programs and submissions.
41 Risk management programs are one result of the overall process of risk management
42 planning, which also encompasses good risk assessment and pharmacovigilance. These
43 latter two topics are covered in separate concept papers entitled: (1) *Premarketing Risk*
44 *Assessment*, and (2) *Risk Assessment of Observational Data: Good Pharmacovigilance*
45 *Practices and Pharmacoepidemiologic Assessment*.

46

47 **C. What is risk management planning?**

48

49 FDA proposes that the sponsor of every product submitted for approval consider how to
50 minimize risks from the product's use. Risk management planning generally
51 encompasses all efforts by a sponsor to minimize the risk from its product's use and may
52 include product labeling, risk assessment, pharmacovigilance, and special studies or
53 interventions. All products have some kind of risk management planning. For most
54 products, traditional risk management planning consists of professional product labeling
55 (i.e., the package insert or PI) and postmarketing surveillance. However, the PI alone is
56 not always sufficient to minimize a product's risks. In these cases, FDA proposes that
57 sponsors submit a risk management program (RMP) as defined below.

58

59 **D. What is a risk management program (RMP) and what are its goals**
60 **and objectives?**

61

62 FDA is defining a risk management program (RMP) as a strategic safety program
63 designed to decrease product risk by using one or more interventions or tools beyond the
64 package insert.² Examples include (1) specialized educational materials for health care
65 practitioners or patients, (2) processes or forms to increase compliance with reduced -risk
66 prescribing and use, and (3) systems that modify conventional prescribing, dispensing,
67 and use of the product to minimize specific risks.

68

69 An RMP could be considered similar to a clinical development program with one or more
70 risk reduction (or safety) goals as its endpoint. We believe the best risk reduction goals
71 would be tailored to the specific risk(s) of concern and, to the extent possible, evidence-
72 based methods would be used to target the achievement of critical processes, behaviors,
73 and human factors to increase safety. For example, if product safety can be increased by
74 judicious patient selection for therapy, one goal might be appropriate prescribing and
75 dispensing to the appropriate patient group. Another example would be if a product's risk

² The package insert (PI) is that portion of approved product labeling described in 21 CFR 201.57 that is directed primarily to health professionals. The PI should not be confused with approved product labeling which may incorporate RMP materials such as Medication Guides and patient agreements in addition to the PI.

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76 increases due to patient factors such as misuse or poor self-monitoring; in this case, a
77 goal of adequate patient education regarding product use could be established.

78

79 Much like a clinical development program's goals are translated into individual protocols
80 each designed to measure achievement of a particular outcome, RMP goals would be
81 translated into pragmatic, specific and measurable program objectives that result in
82 processes or behaviors leading to RMP goals being achieved. Objectives can be thought
83 of as intermediate steps to achieving the overall RMP goal. An RMP goal could be
84 translated into a variety of objectives depending upon the type and severity of the specific
85 risks being managed. For example, an RMP goal could specify that no patient with
86 condition A will be given product B. Illustrative examples of objectives for achieving
87 such a goal could include one or more of the following:

88

89 1. Physicians will be fully knowledgeable about the need to withhold product B
90 from patients with condition A

91

92 2. Candidate patients for product B will be fully knowledgeable that condition A is
93 a reason not to take product B, and will know how to (1) inform their prescriber,
94 or (2) help their prescriber detect if they have condition A

95

96 3. Pharmacists will confirm that patients with a product B prescription do not have
97 condition A.

98

99 **III. WHEN WOULD AN RMP BEYOND THE PACKAGE INSERT BE** 100 **APPROPRIATE?**

101

102 Since risk characterization (through identification and evaluation) is an ongoing process
103 throughout a product's lifecycle, a perceived need for an RMP may emerge pre- or post-
104 approval. Ideally, an RMP would be developed, submitted, and modified as risk
105 reduction needs are identified in a product's lifecycle.

106

107 At any point in product development or approval, a sponsor could voluntarily submit a
108 proposed RMP for Agency review and comment. Alternatively, FDA may propose to the
109 sponsor that an RMP merits consideration and discussion with the Agency. Both
110 sponsor- and FDA-initiated approaches would be based on the benefits as well as the
111 demonstrated risk profile of the drug product as characterized by the clinical development
112 program, postmarketing surveillance, phase IV studies, or other risk information. Ideally,
113 an RMP would be broached when the number or severity of a product's risks appears to
114 undermine the magnitude of its benefits in an important segment of potential or actual
115 users.

116

117 Benefits and risks can result in corresponding positive and negative effects on patient
118 outcomes that may be cosmetic, symptomatic, curative, or affect mortality. Benefits and
119 risks are numerous, varied, and measured in different units. No ready formula currently
120 exists to determine when risks exceed benefits. As such, FDA anticipates that the
121 decision to develop, submit, and implement an RMP will be made on a case-by-case
122 basis. FDA anticipates that for most products that risk management planning will be

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123 handled by the information contained in the PI. Submissions to FDA to revise the PI for
124 adverse events would not automatically lead to an RMP being proposed.

125

126 **IV. WHAT INTERVENTIONS OR TOOLS ARE AVAILABLE FOR USE IN**
127 **ACHIEVING RMP GOALS AND OBJECTIVES?**

128

129 A risk management intervention or tool is a process or system intended to enhance safe
130 product use by reducing risk. There are a number of available tools, one or more of which
131 could be used when designing and implementing a risk management program.

132 Professional product labeling is an important tool used to communicate risks and
133 benefits. However, we plan to focus the draft guidance on risk management tools and
134 strategies that a sponsor may implement above and beyond the package insert.

135

136 **A. How are tools related to RMP objectives and goals?**

137

138 RMP tools serve specific risk management program objectives. This relationship can be
139 illustrated using the previous example of an RMP goal that no patient with condition A
140 will be given product B. Examples of tools related to each of the sample objectives could
141 include the following:

142

143 Objective: Physicians who are fully knowledgeable about withholding product B from
144 patients with condition A.

145 Tools: Potential tools to achieve this objective could include:

- 146 1. Educating physicians with product labeling, detailing, CME, or other methods
- 147 2. Having physicians self-attest or be tested/certified that they possess the
148 appropriate knowledge
- 149 3. Requiring documentation that condition A is not present prior to prescribing and
150 dispensing
- 151 4. Limiting prescribing only to registered practitioners who meet certain
152 requirements including being skilled in recognizing and monitoring condition A

153

154 Objective: Patients who are fully knowledgeable that condition A is contraindicated with
155 product B and are able to help their prescriber know if they have condition A.

156 Tools: Potential tools to achieve this objective could include:

- 157 1. Patient education or self-assessment materials about condition A and its
158 contraindication with product B
- 159 2. Office use of a checklist that actively solicits patient history or symptoms
160 consistent with condition A

161

162 Objective: Pharmacists who confirm that a patient with a product B prescription does not
163 have condition A.

164 Tools: Potential tools to achieve this objective could include:

- 165 1. Educational materials and training of pharmacists to ask patients if they have
166 condition A
- 167 2. Having the pharmacist check for documentation from the prescriber that
168 condition A is absent

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169 3. Having the pharmacist check pharmacy records for evidence that condition A is
170 likely to be present
171

172 The severity, reversibility, and rate of the risk being prevented will influence the extent
173 and impact of risk management tools used to achieve specific objectives.
174

175 **B. What interventions or tools are being used in current RMPs?**
176

177 FDA is considering how best to describe the various types of tools that could be
178 considered for use in a risk management program. Instead of specific tools being
179 presented as part of a guidance document, FDA may maintain a more easily updated
180 resource on its Website that describes tools that currently are in use.
181

182 In general, tools are employed to facilitate or constrain prescribing, dispensing, and/or
183 use of a product to the most appropriate situations or patient populations. Tools used in
184 current RMPs include but are not limited to the following:
185

186 1. Generalized education and outreach to health professionals and consumers/patients
187 (beyond the package insert):

- 188 • health care professional letters
- 189 • training programs
- 190 • CME and CE
- 191 • public notices
- 192 • patient package inserts
- 193 • Medication Guides
194

195 2. Systems that guide the circumstances of individual prescribing, dispensing, and/or
196 use:

- 197 • patient agreements/ informed consent
- 198 • certification programs for practitioners
- 199 • enrollment of physicians, pharmacies, and/or patients in a safety program
- 200 • limited supply or refills of product
- 201 • specialized product packaging
- 202 • specialized systems or records that attest to safety measures having been
203 satisfied (e.g., stickers, physician attestation of capabilities)
204

205 3. Restricted access systems designed to enforce individual compliance with program
206 elements

- 207 • prescribing only by registered physicians
- 208 • dispensing only by registered pharmacies or practitioners
- 209 • dispensing only to patients with evidence or other documentation of safe
210 use conditions (e.g., lab test results)
211

212 4. Marketing suspension with or without application withdrawal
213

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214 Additional interventions or tools can be added to this list and FDA encourages the
215 suggestion and development of other tools for inclusion.

216

217 **C. How can tools be best selected or developed?**

218

219 We believe that the best tools would be those that are predicted to have a high likelihood
220 of achieving their objective based on documented performance in other RMPs or in
221 similar settings and populations. Relevant non-RMP evidence and experience may be
222 found in health care quality initiatives, public health education and outreach, marketing,
223 and other outcomes-based research.

224

225 Tools can be developed, selected, and negotiated based on their individual impact and/or
226 for their impact when used in coordination with other tools. Some considerations in
227 choosing the most effective tools include the following:

228

- 229 1. Input from key stakeholders such as physicians, pharmacists, patient groups, and
230 third party payers on the feasibility of implementing and accepting the tool in
231 usual healthcare practices, disease conditions, or lifestyles
- 232 2. Consistency with the existing tools that are familiar to and accepted by the
233 targeted groups (e.g., physicians, pharmacists, patients)
- 234 3. Documented evidence of effectiveness³ in achieving the specified objective (e.g.,
235 tools effectively used in pregnancy prevention)
- 236 4. Documented evidence of effectiveness in a related area that supports the
237 rationale, design, or method of use (e.g., tools applied in modifying patient or
238 health care professional behaviors in medical care settings)
- 239 5. Degree of variability, validity, and reproducibility in either method and/or results

240

241 Methods and considerations in developing evidence of effectiveness are discussed in the
242 section V.

243

244 **D. How does the choice of tools for an RMP lead to its broad**
245 **categorization?**

246

247 For ready description and comparison of RMPs, FDA recommends they be broadly
248 categorized into one of several “levels” to reflect how much the tools used in the RMP
249 diverge from conventional prescribing, dispensing, and use. Increasing RMP levels
250 would be related to increasing severity, frequency, or duration of the product’s risk(s). A
251 proposed classification scheme for RMP levels follows:

252

253 Level 1: Package insert only

254 Level 2: Level 1 + education and outreach to health professionals and
255 consumers/patients (examples in Section IV.B.1)

³ Evidence may be based upon population studies, surveys, or qualitative methods such as focus groups.

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256 Level 3: Level 2 + systems which guide the circumstances for practitioners and/or
257 patients to prescribe, dispense, or receive a product (examples in Section
258 IV.B.2)

259 Level 4: Access to product requires adherence to specific program elements from
260 levels 2 and/or 3 (examples in Section IV.B.3)

261

262

263 **V. HOW AND WHEN CAN RISK MANAGEMENT PROGRAMS BE**
264 **EVALUATED?**

265

266 As discussed above, good risk management requires ongoing efforts to minimize a
267 product's risks. As a result, evaluation is essential to monitor the effectiveness of risk
268 management interventions. Through evaluation efforts, areas of improvement may be
269 identified. Timely evaluation offers the opportunity to further minimize the product's risk
270 and to improve the benefit/risk balance.

271

272 **A. Why is evaluation of risk management programs important?**

273

274 Several studies have documented that previous risk communication and risk management
275 interventions to reduce safety problems have been variably effective.^{4,5,6} As such, FDA
276 considers pretesting and evaluation of the effectiveness of an RMP to be very important.
277 FDA is considering recommending that risk management tools be pretested prior to the
278 implementation of the RMP and that a post-implementation evaluation plan be part of
279 RMP submissions.

280

281 RMP evaluation is important for two reasons: (1) to predict the likelihood of whether an
282 RMP will work before its full-scale implementation and (2) to determine whether or not
283 an RMP, once implemented, is meeting its desired objectives. Stakeholder input,
284 pretesting, pilot testing or drawing from previous similar product safety issues can
285 increase the potential for good comprehension, acceptance, and feasibility of RMP
286 components fitting into patient lifestyles and the everyday practices of physicians,
287 pharmacists, and third party payers. After implementation of an RMP, periodic
288 evaluations may lead to RMP alterations or redesign to increase or decrease the level of
289 the RMP.

290

291 FDA recognizes that more than one evaluation method may be necessary to assess an
292 RMP and that trade-offs of validity, accuracy, timeliness, representativeness, biases,
293 societal impositions, and costs may occur. In the ideal situation, evaluation
294 measurements (or metrics) will be of actual health outcomes. That is, the metric would
295

296

297 ⁴ Graham DJ, Drinkard CR, Shatin D, Tsong Y, Burgess MJ. 2001. *Liver enzyme monitoring in patients treated with troglitazone.*
298 *JAMA* 286(7):831-3.

299

300 ⁵ Smalley W, Shatin D; Wysowski D; Gurwitz J, Andrade S, Goodman, M, Chan, A, Platt, R, Schech, S, Ray, WA. 2000.
301 *Contraindicated Use of Cisapride: Impact of Food and Drug Administration Regulatory Action* *JAMA* 284(23):3036-3039.

302

303

⁶ Weatherby LB, Nordstrom BL, Fife D, and Walker AM. 2002. *The impact of wording in "Dear Doctor" letters and in black box labels.* *Clin Pharmacol Ther* 72:735-742.

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304 capture the outcome itself rather than some surrogate event or process. If process, rather
305 than outcome, metrics are chosen, it will be important to review the scientific and other
306 bases that link them to the ultimate outcome of interest. The ultimate goal of each
307 evaluation is to ensure that efforts and costs involved in an RMP are expended on
308 effective processes that achieve a positive benefit/risk balance.

309

310 RMP evaluation may be directed to assess both (1) the individual tools and (2) overall
311 RMP effectiveness in achieving their prespecified objectives and goals.

312

313

314

315 **B. What are the considerations for the overall approach to evaluation of**
316 **risk management tools and programs?**

317

318 Ideally, an overall approach to RMP evaluation would:

319

320 1. Select well-defined, validated metrics. A sample outcome metric for reducing the
321 occurrence of an adverse event could be analysis of the number or rate of
322 hospitalizations for that event in an administrative data system. A sample process
323 metric would be to measure how many patients prescribed a product get lab
324 monitoring to reduce their risk of serious sequelae.

325

326 2. Use at least two different evaluation methods for key RMP goals or objectives.
327 Preferably, the different evaluation methods would be both quantitative and
328 representative to offset the biases that are intrinsic to any single evaluation process.
329 For example, hospitalization data on an adverse event would not capture deaths that
330 occurred out of the hospital; in such an instance, death certificate surveillance would
331 offer complementary and more complete ascertainment of mortality risks. If it is not
332 possible to implement two complementary representative methods, FDA suggests
333 using other quantitative methods such as multiple site sampling or audits.

334

335 3. Use qualitative data collected from a large and diverse group of patients when
336 quantitative data are either not available or not applicable to the evaluation
337 measurement. Qualitative data such as focus group testing may be useful in assessing
338 the effectiveness of education and comprehension about safety and risk information.

339

340 4. Consider using evaluation methods to assess if each RMP tool is performing as
341 intended.

342

343 **C. How can RMP effectiveness be measured?**

344

345 RMP objectives or goals can be evaluated for effectiveness using outcomes that measure
346 whether targeted changes or levels of patient health outcomes were achieved (e.g., an
347 acceptably low or reduced rate of an adverse event such as agranulocytosis.). If patient
348 outcomes cannot be practically or accurately measured, closely related measures can be
349 used such as the following:

350

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- 351 1. Surrogates of health outcomes measures (e.g., co-prescribing of contraindicated
352 medications)
353
354 2. Process measures that reflect desirable safety behaviors (e.g., performance of
355 recommended laboratory monitoring)
356
357 3. Assessments of comprehension, knowledge, attitudes, and/or desired safety
358 behaviors about drug safety risks (e.g., provider, pharmacist, or patient surveys)
359

360 If risk communication or education is part of an RMP, pretesting materials in the target
361 audience(s) is highly desirable to help ensure good comprehension and acceptance of the
362 communication method and contents. A variety of testing methods such as focus groups,
363 convenience samples, and surveys can be used as long as testing design ensures that
364 participants are recruited in ways to minimize potential biases.
365

366 **D. What are the strengths and limitations of different evaluation** 367 **methods?**

368 We do not recommend using spontaneous adverse event data as an outcome measure
369 since reporting of adverse events varies due to many factors and represents an unknown
370 and variable fraction of the adverse outcomes that are actually occurring. Continuing
371 reports of adverse events may signal a persistent safety problem. A decrease in reporting
372 does not constitute assurance that a safety issue has been resolved.
373

374 Some evaluation methods measure performance via administrative data systems that
375 capture service or payment claims. Such systems often have limitations for evaluation
376 purposes since the data are not collected with that purpose in mind. Generally, good
377 evaluation design considers which individuals are covered and which are excluded from
378 data systems and sampling methods. Excluded populations often experience higher risks
379 by virtue of the same characteristics (such as poor health) that exclude them.
380

381 In addition to administrative claims data from various insurers, purchasing groups, or
382 networks, surveys using various modes (in-person, mail, telephone, electronic) are
383 another useful form of active surveillance. Reporting biases as well as sampling errors of
384 such active surveillance systems merit consideration.
385

386 **VI. WHAT ARE THE DESIRED ELEMENTS OF A RISK MANAGEMENT** 387 **PROGRAM SUBMISSION?**

388
389 An RMP submission would describe (1) the background of the overall risk reduction
390 goal(s) and rationale for the planned approach, (2) the targeted goals, objectives, and
391 RMP level, (3) one or more proposed tools with a rationale and implementation plan for
392 each, and (4) an evaluation plan for component tools and overall RMP objectives or
393 goal(s) detailing the analyses that will be conducted and the plan for reporting the
394 evaluation results to FDA.
395
396

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397 **A. What information would the Background section contain?**

398
399 The Background section would characterize all the risks to be managed and the
400 corresponding RMP goals for each. This section would address the rationale for why a
401 risk management program is being considered and created. Sample questions to discuss
402 would include:

- 403 1. What is the safety risk?
- 404 2. Who is at highest risk?
- 405 3. Are specific populations at risk (e.g., children, pregnant women, age, gender)?
- 406 4. Are the risks predictable?
- 407 5. Are the risks preventable?
- 408 6. Why is a program needed?

409
410 **B. What information would the Goals, Objectives, and Level section**
411 **contain?**

412
413 This section would describe the goals and objectives of the RMP (as defined in section
414 II.C) and their relationships to each other.

415
416 In addition, FDA recommends that this section describe and categorize the overall RMP
417 into a level that reflects the severity, frequency, or duration of the product's risk(s) (see
418 Section IV.D). The rationale for choosing that particular level over other levels would be
419 addressed. Conditions or outcomes that would lead to revising an RMP to another level
420 would be invited in this section, particularly when a product has serious or difficult-to-
421 manage risks. For example, if risk education and communication were proposed for an
422 RMP (a Level 2 program under the proposed categorization scheme) the sponsor would
423 address the metric and the corresponding value of that metric that would prompt
424 development of a Level 3 or higher RMP.

425
426 Where applicable and possible, the goals, objectives, and level section of the RMP would
427 discuss potential unintended and untoward consequences of the RMP, particularly if there
428 are therapeutic alternatives with similar risk profiles. In such a situation, an extensive
429 RMP for one product in a therapeutic class may unintentionally encourage the use of
430 equally risky products that do not have an effective RMP. Anticipating such situations
431 will assist FDA in considering whether similar products should have an RMP. Yet
432 another unintended consequence is that an RMP with component tools perceived to be
433 burdensome by practitioners or patients could result in illicit access via the Internet or
434 other outlets that circumvent the RMP.

435
436 **C. What information would the Tools section contain?**

437
438 The Tools section would:

- 439
440 1. Identify the risk management interventions or tool(s) that would be used and
441 provide a rationale for choosing them to achieve the desired objective(s). This
442 section could address how feasible it is to implement tools alone or in

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- 443 combination based upon any assessments done of stakeholder support, abilities,
444 or infrastructure.
445
- 446 2. Indicate how the tool(s) would be applied in the program (e.g., frequency, timing,
447 and number of patients and/or health professionals in the targeted populations).
448
 - 449 3. Identify all participants, stakeholders, and key influences (e.g., third party
450 payers) who play a part in the application of the tool(s).
451
 - 452 4. Describe how each tool fits into the overall RMP and its relation to the other
453 tools.
454

455 In the Tools section, an implementation scheme would describe how and when each tool
456 of the RMP is implemented and coordinated. Overall timelines and milestones would be
457 specified.

458 **D. What information would the Evaluation Plan section contain?** 459

460 The Evaluation Plan section would address the success of tools in achieving overall RMP
461 objectives and goals. As such, the evaluation plan would describe the nature and timing
462 of data collection and analyses that would be used to assess the performance of tools vis-
463 à-vis objectives and goals. Like a study protocol, data collection and analytical plans will
464 prespecify the methods, validity, and precision of how the sponsor would measure
465 effectiveness.

466 In the evaluation plan, sources of potential measurement error or bias would be discussed
467 along with the methods to be used (e.g., sensitivity analyses) to account for them. Since
468 RMP evaluations will often rely upon observational data, the analytical plan would
469 appropriately address relevant issues such as the sensitivity and specificity of the
470 measurements for the outcome, power and confidence intervals, as well as potential
471 measurement errors and biases.
472

473 In an RMP submission, the evaluation plan would include an overall schedule for
474 conducting analyses and submitting reports to FDA of individual tool performance, as
475 well as achievement of objectives, and/or program goals. Process and outcome measures
476 both merit inclusion. The tools being used and the outcome under consideration will
477 influence the timing and frequency of analyses and reporting to FDA. FDA may propose
478 that RMP progress reports and evaluations be included in periodic safety update reports
479 (PSURs) or traditional periodic reports, with specific time points for re-evaluation of the
480 overall RMP on a regular basis. To the maximum extent possible, a report of an RMP
481 evaluation would contain the primary data, analyses, statistical estimation, and the
482 sponsor's conclusions on how well the objectives or goals to reduce risk are being met
483 and whether tools are performing as expected.
484