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# Guidance for Industry

## Postmarketing Safety Reporting for Human Drug and Biological Products Including Vaccines

*DRAFT GUIDANCE*

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**U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Drug Evaluation and Research (CDER)  
Center for Biologics Evaluation and Research (CBER)  
March 2001**

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# Guidance for Industry

## Postmarketing Safety Reporting for Human Drug and Biological Products Including Vaccines

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**U.S. Department of Health and Human Services  
Food and Drug Administration  
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March 2001**

## TABLE OF CONTENTS

<b>I</b>	<b>INTRODUCTION.....</b>	<b>1</b>
A.	WHAT DOES THIS GUIDANCE DISCUSS?.....	1
B.	WHAT DOES THIS GUIDANCE <i>Not</i> DISCUSS?.....	2
C.	GOOD GUIDANCE PRACTICES.....	2
<b>II</b>	<b>BACKGROUND.....</b>	<b>3</b>
A.	FINAL RULES.....	3
B.	GUIDANCES.....	3
C.	PROPOSED RULES.....	4
<b>III</b>	<b>WHO MUST REPORT.....</b>	<b>4</b>
<b>IV</b>	<b>WHAT DO I REPORT?.....</b>	<b>5</b>
A.	TYPE OF ADVERSE EXPERIENCES.....	6
B.	DATA ELEMENTS TO INCLUDE IN A POSTMARKETING INDIVIDUAL CASE SAFETY REPORT.....	8
<b>V</b>	<b>TYPE OF REPORTS.....</b>	<b>9</b>
A.	15-DAY REPORTS OF SERIOUS, UNEXPECTED ADVERSE EXPERIENCES.....	9
B.	PERIODIC REPORTS.....	11
C.	FOLLOWUP REPORTS.....	15
D.	DISTRIBUTION REPORTS FOR BIOLOGICAL PRODUCTS INCLUDING VACCINES.....	18
<b>VI</b>	<b>SPECIAL REPORTING SITUATIONS.....</b>	<b>18</b>
A.	SCIENTIFIC LITERATURE REPORTS.....	18
B.	POSTMARKETING, CLINICAL TRIAL, OR SURVEILLANCE STUDIES.....	19
C.	FOREIGN REPORTS.....	20
D.	DEATH REPORTS.....	20
E.	OVERDOSE REPORTS.....	20
F.	LACK OF EFFECT REPORTS.....	21
G.	INFORMATION ON THE INTERNET.....	21
H.	PEDIATRIC PATIENTS.....	21
I.	PRESCRIPTION DRUGS MARKETED FOR HUMAN USE WITHOUT AN APPROVED APPLICATION.....	22
J.	ANOTHER APPLICANT-S PRODUCT.....	22
K.	MULTIPLE SUSPECT PRODUCTS.....	22
L.	SUSPECT DRUGS WITH MULTIPLE NDAs OR ANDAs BY THE SAME APPLICANT.....	23
M.	TWO OR MORE MARKETERS OF A PRODUCT.....	23
N.	UNAPPROVED INDICATIONS.....	23
O.	PRODUCT INTERACTIONS.....	23
P.	REPORTS FROM THE FDA.....	23
Q.	PRODUCT DEFECTS.....	24
R.	REPORTING AMBIGUITIES.....	24
<b>VII</b>	<b>CODING OF ADVERSE EXPERIENCES IN INDIVIDUAL CASE SAFETY REPORTS.....</b>	<b>24</b>
<b>VIII</b>	<b>REPORTING FORMATS.....</b>	<b>25</b>
A.	FDA FORM 3500A.....	25
B.	VAERS FORM FOR VACCINES.....	28
C.	CIOMS I FORM FOR FOREIGN ADVERSE EXPERIENCES.....	29
D.	DISTRIBUTION REPORTS FOR BIOLOGICAL PRODUCTS INCLUDING VACCINES.....	29

E.	ELECTRONIC SUBMISSIONS .....	30
<b>IX.</b>	<b>HOW AND WHERE TO SUBMIT POSTMARKETING SAFETY REPORTS.....</b>	<b>30</b>
A.	HUMAN DRUG PRODUCTS .....	30
B.	HUMAN BIOLOGICAL PRODUCTS AND VACCINES .....	31
<b>X.</b>	<b>WRITTEN PROCEDURES FOR POSTMARKETING SAFETY REPORTING.....</b>	<b>31</b>
<b>XI.</b>	<b>REQUESTS FOR WAIVERS TO POSTMARKETING SAFETY REPORTING REQUIREMENTS .....</b>	<b>32</b>
A.	SUBMISSION OF FDA FORM 3500A FOR NONSERIOUS, EXPECTED ADVERSE EXPERIENCES .....	32
B.	SUBMISSION OF PSUR FORMAT FOR THE PERIODIC REPORT .....	32
C.	SUBMISSION DATE AND FREQUENCY FOR PSUR REPORTS .....	33
D.	HOW AND WHERE TO SUBMIT WAIVER REQUESTS .....	34
<b>XII.</b>	<b>VALIDATION OF ADVERSE EXPERIENCE COMPUTER SYSTEMS .....</b>	<b>34</b>
	<b>APPENDIX A: GLOSSARY .....</b>	<b>35</b>
	<b>APPENDIX B: REPORT CHECKLIST.....</b>	<b>38</b>
	<b>APPENDIX C: FDA FORM 500A.....</b>	<b>41</b>
	<b>APPENDIX D: FORM VAERS-1.....</b>	<b>43</b>
	<b>APPENDIX E: CIOMS 1 FORM.....</b>	<b>45</b>
	<b>APPENDIX F: ONE-PAGE FDA FORM 3500A.....</b>	<b>46</b>

# Guidance for Industry<sup>1</sup>

## Postmarketing Safety Reporting for Human Drug and Biological Products Including Vaccines

This draft guidance, when finalized, represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

### I. INTRODUCTION

This guidance is intended to assist applicants and other responsible parties in fulfilling the FDA's **existing** postmarketing safety reporting requirements for human marketed drug and biological products at 21 CFR 310.305, 314.80, 314.98, 600.80, and 600.81.<sup>2</sup> Under these regulations, postmarketing safety reports must be submitted to the Agency for the following:

1. Serious and unexpected adverse experiences from all sources (domestic and foreign)
2. Spontaneously reported adverse experiences that occur domestically and that are:
  - Serious and expected
  - Nonserious and unexpected
  - Nonserious and expected

#### A. What Does This Guidance Discuss?

This guidance discusses the following postmarketing reports:

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<sup>1</sup> This guidance has been prepared by FDA's Safety Reporting Regulations Working Group, which includes representatives from the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER).

<sup>2</sup> The FDA is planning to propose revisions to these regulations (see section II.C in this guidance). As these proposals are finalized the Agency will revise this guidance to provide industry with assistance in fulfilling the new regulatory requirements.

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- 15-Day Reports of Serious, Unexpected Adverse Experiences
- Periodic Reports
- Followup Reports
- Distribution Reports for Biological Products Including Vaccines

This guidance addresses the following regulations for the following products.<sup>3</sup>

Regulation	Product
21 CFR 310.305	Prescription drugs marketed for human use without an approved application
21 CFR 314.80	Human drugs with approved NDAs
21 CFR 314.98	Human drugs with approved ANDAs
21 CFR 600.80	Human biological products with approved BLAs
21 CFR 600.81	Human biological products with approved BLAs

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47  
48  
49

If you believe the procedures described in this guidance are inapplicable to a particular product or that other procedures are appropriate, you should discuss the matter with the Agency to ensure that your procedures comply with applicable statutes and regulations.

**B. What Does This Guidance Not Discuss?**

50  
51  
52

This guidance does *not* discuss the following:

53  
54  
55  
56  
57

- IND Safety Reports (21 CFR 312.32)<sup>4</sup>
- Safety Update Reports for Drugs (21 CFR 314.50(d)(5)(vi)(b))
- Approved NDA Annual Reports (21 CFR 314.81(b)(2))
- Approved BLA Annual Reports (21 CFR 601.28)

58  
59

This guidance does *not* apply to the following products:

60  
61  
62  
63  
64

- In vitro diagnostic products
- Whole blood or its components
- Product manufacturing defects (unless the defect is associated with an adverse experience in humans)

65  
66

**C. Good Guidance Practices**

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The Agency's good guidance practices (GGPs) regulation<sup>5</sup> does not allow the use of mandatory language in guidances unless it is used to describe regulatory requirements. In

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<sup>3</sup> NDA means new drug application, ANDA means abbreviated new drug application, and BLA means biologics license application

<sup>4</sup> IND means investigational new drug application

70 most guidances, we provide the related cite whenever mandatory language is used to  
71 indicate the basis for the use of such language. This guidance discusses regulatory  
72 requirements in great detail. To avoid including the same regulatory cites repeatedly and  
73 to make the guidance user friendly, we will indicate at the beginning of those sections that  
74 include extensive discussions of regulatory requirements which cites are particularly  
75 relevant. The use of mandatory language (e.g., *must*, *have to*, *required*) will signify a  
76 regulatory requirement while the use of words such as *should* and *recommend* will indicate  
77 Agency policy.

## 80 II. BACKGROUND

81  
82 The FDA has undertaken a major effort to clarify and revise its regulations regarding pre-  
83 and postmarketing safety reporting requirements for human drug and biological products.  
84 To date, the Agency has issued a number of final rules and guidances for industry on this  
85 topic; several proposed rules are under development.

### 87 A. Final Rules

- 89 • Expedited Safety Reports for Human Drug and Biological Products

90  
91 In the *Federal Register* of October 7, 1997 (62 FR 52237), the FDA published a  
92 final rule amending its regulations for expedited safety reporting to implement  
93 certain definitions, reporting periods, and formats recommended by the International  
94 Conference on Harmonisation of Technical Requirements for Registration of  
95 Pharmaceuticals for Human Use (ICH). These recommendations are discussed in  
96 the ICH guidance *E2A Clinical Safety Data Management: Definitions and*  
97 *Standards for Expedited Reporting*; March 1, 1995.

- 99 • Postmarketing Expedited Increased Frequency Reports for Human Drug and  
100 Biological Products

101  
102 In the *Federal Register* of June 25, 1997 (62 FR 34166), the FDA published a final  
103 rule revoking requirements to submit postmarketing increased frequency reports to  
104 the Agency in an expedited manner for human drug and biological products.

### 106 B. Guidances

107  
108 With regard to postmarketing safety reporting for human drug and biological products, the  
109 FDA has made three final guidances available:

- 111 • *Postmarketing Reporting of Adverse Drug Experiences* (March 1992)

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<sup>5</sup> The Agency's regulation on good guidance practices published on September 19, 2000 (21 CFR 10.115; 65 FR 56468).

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- *Guideline for Adverse Experience Reporting for Licensed Biological Products* (October 1993)
- *Postmarketing Adverse Experience Reporting for Human Drug and Licensed Biological Products: Clarification of What to Report* (August 27, 1997).

When finalized, this guidance will replace the three guidances listed above and will reflect the new regulatory requirements in the final rules of June 25, 1997, and October 7, 1997.

### C. Proposed Rules

The Agency currently is in the process of developing proposed rules to further amend its safety reporting requirements for human drug and biological products. Many of the provisions in these proposed rules will be based on recommendations developed by ICH. For instance, the Agency is planning to propose additional amendments to its expedited safety reporting regulations based on the ICH E2A guidance.

In addition, the FDA is planning, as indicated in the final rule of October 7, 1997, to repropose amendments to its postmarketing periodic safety reporting requirements that were initially proposed in the *Federal Register* of October 27, 1994 (59 FR 54046). The new postmarketing periodic safety reporting proposals will be based on recommendations in the ICH guidance *E2C Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs* (May 19, 1997).

The Agency also is planning to issue a proposal requiring the electronic submission of postmarketing safety reports consistent with recommendations developed by ICH.<sup>6</sup>

As these proposed rules are finalized, this postmarketing safety reporting guidance for human drug and biological products will be revised to provide industry with assistance in fulfilling the new regulatory requirements.

### III. WHO MUST REPORT

According to the regulations, the following persons have postmarketing safety reporting responsibilities:

- *Manufacturers* are required to submit postmarketing expedited safety reports to the FDA for prescription drug products marketed for human use without an approved application (§ 310.305).

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<sup>6</sup> See advance notice of proposed rulemaking on electronic reporting of postmarketing adverse drug reactions; request for comments, 63 FR 59746, November 5, 1998.



- 154  
155 • *Applicants* (individual or corporate entity that holds an NDA or ANDA) are required  
156 to submit postmarketing safety reports to the FDA for human drug products with  
157 approved NDAs (§ 314.80) and ANDAs (§ 314.98).  
158  
159 • *Licensed manufacturers* (individual or corporate entity that holds a BLA) are  
160 required to submit postmarketing safety reports to the FDA for human licensed  
161 biological products with approved BLAs (§§ 600.80 and 600.81).  
162  
163 • Any person whose name appears on the label of a marketed drug as its packer or  
164 distributor (§ 310.305(c)(1)(i)) or manufacturer, packer, or distributor  
165 (§ 314.80(c)(1)(iii)) has postmarketing safety reporting responsibilities.  
166  
167 • Any person whose name appears on the label of a licensed biological product as its  
168 manufacturer, packer, distributor, shared manufacturer, joint manufacturer, or any  
169 other participant involved in divided manufacturing has postmarketing safety  
170 reporting responsibilities (§ 600.80(c)(1)(iii)).  
171

172 For the purposes of this guidance, the term *applicant* includes all persons with  
173 postmarketing safety reporting responsibilities under §§ 310.305, 314.80, 314.98, 600.80,  
174 and 600.81.  
175

176 According to the regulations at §§ 310.305(d), 314.80(f), and 600.80(f), if an applicant  
177 becomes aware of a reportable adverse experience, the applicant is responsible for  
178 preparing a postmarketing safety report and submitting it to the FDA. Applicants should  
179 not assume that their responsibilities are fulfilled if they ask the person who pointed out a  
180 reportable adverse experience to submit a safety report to the FDA.  
181

182

#### 183 **IV. WHAT DO I REPORT?**

184

185 The following paragraphs discuss the types of adverse experiences that must be reported  
186 to the FDA under §§ 310.305, 314.80, 314.98, and 600.80. This section also describes  
187 the minimum data elements that should be included in an individual case safety report.  
188

189 An *adverse experience* is any undesirable event that is associated with the use of a drug  
190 or biological product in humans whether or not considered product-related by the  
191 applicant.<sup>7</sup> An *individual case safety report* describes an adverse experience(s) for a  
192 patient or subject. Individual case safety reports of domestic adverse experiences for  
193 marketed human drug and biological products, except vaccines, must be submitted to the  
194 FDA on FDA Form 3500A; a Vaccine Adverse Event Reporting System (VAERS) form  
195 must be used for adverse experiences associated with the use of vaccines. Individual  
196 case safety reports of foreign adverse experiences can be submitted on FDA Form 3500A

---

<sup>7</sup> See Appendix A for definition of *adverse experience*. (See also §§ 310.305(b), 314.80(a) and 600.80(a).)

197 (VAERS form for vaccines) or, if preferred, on a Council for International Organizations for  
198 Medical Sciences (CIOMS) I form. See section VIII in this guidance for discussion of  
199 reporting formats for individual case safety reports.

200

## 201 **A. Type of Adverse Experiences**

202

### 203 1. *Adverse Experiences that are Serious and Unexpected from All Sources* 204 *(Domestic and Foreign)*<sup>8</sup>

205

206 Serious and unexpected adverse experiences from all sources, whether domestic  
207 or foreign, must be submitted to the FDA. Possible sources include, for example,  
208 scientific literature, postmarketing studies, or commercial marketing experience.

209

210 Scientific literature reports include published and unpublished scientific papers that  
211 are known to the applicant (see section VI.A in this guidance for reporting of  
212 adverse experiences from the scientific literature).

213

214 Postmarketing studies include in vitro, animal, clinical, and epidemiological or  
215 surveillance investigations (see section VI.B in this guidance for reporting of  
216 adverse experiences from studies). Adverse experiences from studies must only  
217 be submitted to the FDA if the applicant believes that there is a reasonable  
218 possibility that the drug or biological product caused the adverse experience (see  
219 §§ 310.305(c)(1)(ii), 314.80(e)(1) and 600.80(e)(1)).

220

### 221 2. *Other Spontaneously Reported Adverse Experiences (Domestic Only)*<sup>9</sup>

222

223 Adverse experiences occurring in the United States from commercial marketing  
224 experience must be submitted to the FDA if they are spontaneously reported to  
225 applicants and are:

226

- 227 • serious and expected
- 228 • nonserious and unexpected, or
- 229 • nonserious and expected

230

231 Applicants can request a waiver of the requirement to submit individual case safety  
232 reports of nonserious, expected adverse experiences for drugs and certain  
233 biological products (see section XI.A in this guidance on waiver requests).

234

### 235 3. *Serious Adverse Experiences*<sup>10</sup>

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<sup>8</sup> The requirements for reports of serious, unexpected adverse experiences can be found in §§ 310.305(c), 314.80(c)(1) and 600.80(c)(1).

<sup>9</sup> The requirements for reports describing these adverse experiences can be found in §§ 314.80(c)(2) and 600.80(c)(2).

236  
237 The outcome of an adverse experience must be determined before a report can be  
238 identified as *serious*. A serious report must have one or more of the following  
239 outcomes:

- 240
- 241 • Death
  - 242 • Life-threatening adverse experience
  - 243 • Initial inpatient hospitalization or prolongation of hospitalization
  - 244 • Significant or persistent disability/incapacity
  - 245 • Congenital anomaly/birth defect (including that occurring in a fetus)
  - 246 • Important medical event based upon appropriate medical judgment that may  
247 jeopardize the patient or subject and may require medical or surgical  
248 intervention to prevent one of the other outcomes listed in the definition of  
249 serious.

250

251 A patient admitted to a hospital for 1 or more days as a result of an adverse  
252 experience, even if released on the same day, would qualify for the *initial inpatient*  
253 *hospitalization* outcome. An emergency room visit that results in admission to the  
254 hospital would also qualify for the *initial inpatient hospitalization* outcome.  
255 However, emergency room visits that do not result in admission to the hospital  
256 would not qualify for this outcome and, instead, should be evaluated for one of the  
257 other outcomes in the definition of *serious* (e.g., life-threatening adverse  
258 experience, important medical event).

259

260 Persons incarcerated because of actions allegedly caused by a drug (e.g.,  
261 psychotropic drugs and rage reactions) have sustained a substantial disruption in  
262 their ability to conduct normal life functions. Thus, these adverse experiences would  
263 qualify for the *significant or persistent disability/incapacity* outcome.

264

265 *Important medical events* would include allergic bronchospasm requiring intensive  
266 treatment in an emergency room or at home, blood dyscrasias or convulsions that  
267 do not result in inpatient hospitalization, or the development of drug dependency or  
268 drug abuse. Applicants should mark the "other" box in item B2 of FDA Form 3500A  
269 for adverse experiences identified as *important medical events*.

270

271 Applicants should actively seek the outcome for a suspected serious adverse  
272 experience reported to them. If unable to initially determine the outcome for an  
273 adverse experience, an applicant should continue to actively seek information in an  
274 attempt to determine an outcome. For a serious adverse experience that was not  
275 initially reported to the applicant by a health care professional (e.g., report from a  
276 consumer), the applicant should actively pursue contacting the health care

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<sup>10</sup> See Appendix A for definition of *serious adverse experience*. (See also §§ 310.305(b), 314.80(a) and 600.80(a).)

277 professional associated with the care of the patient to gather further medical  
278 perspective on the case.

279  
280 4. *Unexpected and Expected Adverse Experiences*<sup>11</sup>

281  
282 The current FDA-approved labeling for the human drug or biological product should  
283 be used as the reference document to determine whether an adverse experience is  
284 *unexpected* or *expected*. An adverse experience would be considered *unexpected*  
285 if it is not included in the product's current FDA-approved labeling and *expected* if it  
286 is included in this document.

287  
288 5. *Spontaneous Report*<sup>12</sup>

289  
290 Spontaneous reports are unsolicited communications from individuals (e.g., health  
291 care professional, consumer) to applicants that concern adverse experiences.  
292 Spontaneous reports should not include adverse experiences identified from  
293 information solicited by applicants such as individual cases or findings derived from  
294 a study (e.g., any organized data collection scheme).

295  
296 **B. Data Elements to Include in a Postmarketing Individual Case Safety Report**

297  
298 Before considering any clinical incident for submission to the FDA in an individual case  
299 safety report, applicants should, at a minimum, have knowledge of the following four data  
300 elements:

- 301  
302 1. An identifiable patient  
303 2. An identifiable reporter  
304 3. A suspect drug or biological product  
305 4. An adverse experience or fatal outcome suspected to be due to the suspect  
306 drug or biological product

307  
308 If any one of these basic elements remains unknown after being actively sought by the  
309 applicant, a report on the incident should not be submitted to the FDA because reports  
310 without such information make interpretation of their significance difficult, at best, and  
311 impossible, in most instances. Instead, the applicant should maintain records of its efforts  
312 to obtain the basic elements for an individual case in its corporate drug or biological  
313 product safety files. If an applicant submits a report to the FDA that lacks any of the four  
314 basic elements, it will be returned to the applicant marked *insufficient data for a report*.  
315

---

<sup>11</sup> See Appendix A for definitions of *unexpected and expected adverse experiences*. (See also §§ 310.305(b), 314.80(a) and 600.80(a).)

<sup>12</sup> See Appendix A for definition of *spontaneous report*.

316 An applicant that is actively seeking information on an adverse experience should use  
317 direct verbal contact with the initial reporter of the adverse experience (e.g., in person, by  
318 telephone or other interactive means such as a videoconference). The applicant should not  
319 merely send the initial reporter a letter requesting information concerning the adverse  
320 experience. Applicants should use a health care professional (e.g., physician, physician  
321 assistant, dentist, pharmacist, nurse) for contacts with initial reporters because such  
322 persons should be able to understand the medical consequences of the case and ask  
323 appropriate questions to acquire relevant information rapidly to determine the significance  
324 of the case.

325  
326 With regard to *an identifiable patient*, reports of the type *some patients got anaphylaxis*  
327 should be excluded until further information about the patients is obtained. A report stating  
328 that *an elderly woman had anaphylaxis* or a *young man experienced anaphylaxis* should  
329 be included because there is enough information to suspect that specific patients were  
330 involved. Patients should not be identified by name or address. Instead, the applicant  
331 should assign a unique code (e.g., patient initials) to each report.

332 For spontaneous reports, the applicant should assume that an *adverse experience or fatal*  
333 *outcome* was suspected to be due to the suspect drug or biological product (implied  
334 causality). For clinical studies, an *adverse experience or fatal outcome* need not be  
335 submitted to the FDA unless the applicant concludes that there is a reasonable possibility  
336 that the product caused the adverse experience or fatal outcome (see §§ 310.305(c)(1)(ii),  
337 314.80(e)(1) and 600.80(e)(1)). An *adverse experience* should, at a minimum, consist of  
338 signs (including abnormal laboratory findings, if appropriate), symptoms, or disease  
339 diagnosis (including any colloquial descriptions obtained) for purposes of reporting. Thus,  
340 a report stating that a patient *experienced unspecified injury*, or a patient *suffered*  
341 *irreparable damages* should not be included until more specific information about the  
342 adverse experience can be determined.

343  
344

## 345 **V. TYPE OF REPORTS**

346

347 The following paragraphs discuss the types of postmarketing safety reports that must be  
348 submitted to the FDA based on the regulations as listed.

349

### 350 **A. 15-Day Reports of Serious, Unexpected Adverse Experiences<sup>13</sup>**

351

352 Individual case safety reports of serious, unexpected adverse experiences from all sources  
353 (domestic and foreign) must be reported to the FDA as soon as possible, but in no case  
354 later than 15 calendar days of initial receipt of the information by the applicant. See section  
355 VIII in this guidance for discussion of reporting formats for individual case safety reports.

356

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<sup>13</sup> The requirements for 15-Day Reports can be found in §§ 310.305(a), (c)(1)(i) and (d)(1), 314.80(c)(1)(i) and (f)(1), and 600.80(c)(1)(i) and (f)(1).

357 An applicant should not wait for the initial reporter of a serious, unexpected adverse  
358 experience to send them written information about the experience before submitting a 15-  
359 day report to the FDA. An applicant can and should submit a 15-day report to the FDA  
360 based only on verbal information.

361

362 *1. Determination of 15-Day Reporting Period*

363

364 Serious, unexpected adverse experiences must be submitted to the FDA no later  
365 than 15 calendar days of initial receipt of the information by the applicant. For  
366 reporting purposes, this information should include, at a minimum, the four basic  
367 elements (i.e., an identifiable patient, an identifiable reporter, a suspect drug or  
368 biological product, and a serious, unexpected adverse experience). The date the  
369 company has knowledge of these four basic elements should be entered into item  
370 G4 of FDA Form 3500A or Box 25 of the VAERS form (i.e., this date represents  
371 Day 0 of the 15-day time clock).

372

373 If the 15th calendar day occurs on a weekend or U.S. Federal holiday, the 15-day  
374 report should be submitted the first working day after the weekend or U.S. Federal  
375 holiday.

376

377 The applicant should exercise due diligence to acquire all the information for an  
378 individual case safety report immediately upon receipt of a suspected serious,  
379 unexpected adverse experience (e.g., completion of all the applicable elements on  
380 FDA Form 3500A). The applicant should maintain records of its efforts to obtain  
381 this information and should include in the narrative section of FDA Form 3500A (i.e.,  
382 item B5), a chronological description of these efforts if there is a delay in obtaining  
383 such information.

384

385 When an applicant receives a report of a serious, unexpected adverse experience  
386 but it is not possible to complete all the applicable elements for an individual case  
387 safety report within 15 calendar days, a preliminary report that contains at least the  
388 four basic elements should be submitted. Additional followup information should be  
389 actively sought and submitted within 15 calendar days after obtaining the new  
390 information (see section V.C in this guidance for discussion of followup reports).

391

392 For foreign reports, the 15-day time clock begins when the applicant or its foreign  
393 affiliate has received the four basic elements for a 15-day report. Applicants should  
394 therefore establish effective mechanisms to ensure rapid information transfer from  
395 their foreign affiliates.

396

397 *2. Supporting Documentation*

398

399 For individual case safety reports of serious, unexpected adverse experiences, the  
400 FDA encourages applicants to include relevant hospital discharge summaries and  
401 autopsy reports/death certificates. Applicants should also include in their report a

402 list of other relevant documents (e.g., medical records, relevant laboratory data,  
403 electrocardiograms, and other concise critical clinical data) maintained in their  
404 corporate drug or biological product safety files. The FDA can request that copies  
405 of one or more of these documents be provided to the Agency. Applicants should  
406 submit copies of these documents to the Agency within 5 calendar days after  
407 receipt of the request.

408  
409 **3. Report Identification**

410  
411 Fifteen-day reports must be submitted in duplicate under separate cover  
412 prominently identified as "15-Day Alert Report." For this purpose, the "15-Day Alert  
413 Report" identification should be included on the outside envelope.

414  
415 For prescription drugs marketed for human use without an approved application, a  
416 single copy of the 15-day report and a copy of the U.S. labeling must be submitted.  
417 These reports should be marked on the outside envelope with "15-Day Alert Report  
418 - 310.305."

419  
420 Multiple 15-day reports and 15-day followup reports can be submitted in the same  
421 envelope, but they should not be stapled together (see section V.C for discussion of  
422 followup reports).

423  
424 **B. Periodic Reports<sup>14</sup>**

425  
426 The following paragraphs discuss the reporting frequency for submission of periodic  
427 reports and the content of these reports. See section XI in this guidance for requests for  
428 waivers of the requirement to submit postmarketing periodic safety reports (e.g., waiver to  
429 use periodic safety update report (PSUR) format recommended by ICH for periodic report  
430 instead of format described in the regulations, waiver to submit individual cases of  
431 nonserious, expected adverse experiences in periodic report).

432  
433 **1. Timing of Postmarketing Periodic Reports**

434  
435 Postmarketing periodic reports are required to be submitted to the FDA for each  
436 approved NDA, ANDA, and BLA and are due quarterly for the first 3 years after U.S.  
437 approval of the application and annually thereafter. If marketing is delayed, these  
438 reports should still be submitted quarterly for the first 3 years of marketing. Upon  
439 written notice, the FDA may extend or reestablish the requirement that an applicant  
440 submit quarterly reports or require that the applicant submit periodic reports at  
441 different time intervals.

442  
443 Periodic reports due quarterly must be submitted within 30 calendar days of the last  
444 day of the reporting quarter. Reports due annually must be submitted each year

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<sup>14</sup> The requirements for periodic reports can be found in §§ 314.80(c)(2) and 600.80(c)(2).

445 within 60 calendar days of the anniversary date of U.S. approval of the application  
446 for the drug or biological product (i.e., NDA, ANDA, BLA).  
447

448 Periodic submissions should be clearly marked "Periodic Adverse Experience  
449 Submission" on the front cover of each volume. Each page of the periodic report  
450 should be numbered and include the name and NDA or ANDA number if the  
451 periodic report is for a drug product; the name and submission tracking number  
452 (STN) should be used if the periodic report is for a biological product (a STN for a  
453 biological product can be found on the Internet at [www.fda.gov/cber/stn/stn.htm](http://www.fda.gov/cber/stn/stn.htm)).  
454

## 455 2. *Content of a Postmarketing Periodic Report*

456  
457 The regulations require a postmarketing periodic report to contain:

- 458 • a narrative summary and analysis of the information in the report and an analysis  
459 of the 15-day Alert reports submitted during the reporting interval
- 460 • an FDA Form 3500A for each spontaneously reported adverse experience  
461 occurring in the United States that was not reported in a 15-day Alert report
- 462 • a history of actions taken since the last report because of adverse experiences.  
463

464  
465 The information contained within a postmarketing periodic report should be divided  
466 into four sections in the order described below and should be clearly separated by  
467 an identifying tab. If information for one of these sections is not included, the  
468 applicant should simply explain why the information is not provided.  
469

### 470 a. Section 1: Narrative summary and analysis

471  
472 A narrative summary and analysis of the information in the postmarketing  
473 periodic report and an analysis of the 15-day reports (i.e., serious,  
474 unexpected adverse experiences) submitted during the reporting period  
475 must be provided and should include:

- 476 • The number of non-15-day<sup>15</sup> initial adverse experience reports and  
477 the number of non-15-day followup reports contained in this periodic  
478 report and the time period covered by the periodic report.
- 479 • A line listing of the 15-day reports submitted during the reporting  
480 period. This line listing should include the manufacturer report  
481 number, adverse experience term(s), and the date the 15-day report  
482 was sent to the FDA.  
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484  
485

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<sup>15</sup> These include serious and expected adverse experiences, nonserious and unexpected adverse experiences, and nonserious and expected adverse experiences.



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496
- A summary tabulation by body system (e.g., cardiovascular, central nervous system, endocrine, renal) of all adverse experience terms and counts of occurrences submitted during the reporting period. The information should be taken from :
    - 15-day reports submitted to the FDA;
    - non-15-day reports submitted in the periodic report;
    - reports forwarded to the applicant by the FDA; and
    - any nonserious, expected adverse experiences not submitted to the FDA but maintained on file by the applicant.

497 For the adverse experience term *product interaction*, the interacting  
498 products should be identified in the tabulation.  
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- A summary listing of the adverse experience reports in which the drug or biological product was listed as one of the suspect products, but the report was filed to another NDA, ANDA, or BLA held by the applicant.
  - A narrative discussion of the clinical significance of the 15-day reports submitted during the reporting period and of any increased reporting frequency of serious, expected adverse experiences when, in the judgment of the applicant, it is believed the data reflect a clinically meaningful change in adverse experience occurrence. This narrative should assess clinical significance by type of adverse experience, body system, and overall product safety relating the new information received during this reporting period to what was already known about the product. The narrative should also state what further actions, if any, the applicant plans to undertake based on the information gained during the reporting period and include the time period for completing the actions (i.e., when the applicant plans to start and finish the action and submit the information to the Agency).
  - The narrative discussion should indicate, based on the information learned during the reporting period, whether the applicant believes either that (1) no change in the product's current approved labeling is warranted or (2) there are safety-related issues that need to be addressed in the approved product labeling. If changes in the approved product labeling are under consideration by the FDA, the applicant should state in the narrative the date and number of the supplemental application submitted to address the labeling changes.

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b. Section 2: Narrative discussion of actions taken

A narrative discussion of actions taken must be provided, including any labeling changes and studies initiated since the last periodic report. This section should include:

- A copy of current U.S. product labeling
- A list of any labeling changes made during the reporting period
- A list of studies initiated
- A summary of important foreign regulatory actions (e.g., new warnings, limitations in the indications and use of the product)
- Any communication of new safety information (e.g., a Dear Doctor letter)

c. Section 3: Index line listing

An index line listing of FDA Form 3500As or VAERS forms included in section 4 of the periodic report must be provided. The line listing for each FDA Form 3500A or VAERS form submitted should include:

- Manufacturer report number
- Adverse experience term(s)
- Page number of FDA Form 3500A or VAERS form as located in the periodic report
- Identification of interacting products for any *product interaction* listed as an adverse experience.

d. Section 4: FDA Form 3500As or VAERS forms

FDA Form 3500As or VAERS forms must be provided for the following spontaneously reported adverse experiences that occurred in the United States during the reporting period:

- Serious and expected
- Nonserious and unexpected

- Nonserious and expected

Applicants are encouraged to request a waiver of the requirement to submit individual case safety reports of nonserious, expected adverse experiences for drugs and certain biological products as described below (see section XI.A in this guidance).

Adverse experiences due to a failure to produce the expected pharmacologic action (i.e., *lack of effect*) should be included in this section (see section VI.F in this guidance).

For individual case safety reports of serious, expected adverse experiences, the FDA encourages applicants to include relevant hospital discharge summaries and autopsy reports/death certificates, as well as lists of other relevant documents as described for 15-day reports of serious, unexpected adverse experiences (see section V.A.2 in this guidance).

Initial non-15 day reports should be included in the periodic report in a separate section from non-15 day followup reports (see the following section V.C for discussion of non-15 day followup reports). All initial and followup information obtained for an adverse experience with a given periodic reporting period should be combined and submitted in the periodic report as one initial non-15 day report (i.e., an initial non-15 day report and a non-15 day followup report describing the same adverse experience should not be submitted in the same periodic report).

An FDA Form 3500A or VAERS form for a serious, unexpected adverse experience should not be included in a periodic report because this adverse experience should have been previously submitted to the FDA as a 15-day report.

If no adverse experiences were identified for the human drug or biological product for the time period involved and no regulatory actions concerning safety were taken anywhere in the world where the product is marketed, the periodic report should simply state this and be submitted to the FDA along with a copy of the current U.S. labeling.

### C. Followup Reports<sup>16</sup>

The following paragraphs discuss the content of and reporting considerations for 15-day followup reports that are submitted in an expedited manner and non-15 day followup reports that are submitted as part of a postmarketing periodic report. A followup report provides information about an adverse experience that has been previously reported as an

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<sup>16</sup> The requirements for followup reports can be found in ' ' 310.305(c)(2), 314.80(c) and 600.80(c).

615 initial report with a unique manufacturer report number. The followup report should be  
616 identified with the same unique manufacturer report number as the initial report.

617  
618 A 15-day followup report must be submitted within 15 calendar days of receipt of new  
619 information on a 15-day report. Followup information to adverse experiences submitted  
620 initially in a periodic report can be submitted in the next periodic report.

621  
622 *1. Content of Followup Reports*

623  
624 A followup report should provide a complete picture of the current understanding of  
625 the adverse experience. Relevant information from the initial report should be  
626 combined with the followup information to present an accurate and comprehensive  
627 description of the adverse experience as it is understood at the time of the followup.  
628 Information from the initial report later found to be inaccurate should not be repeated  
629 in the followup report. All new information including correction of previously  
630 submitted inaccurate information that is included in a followup report should be  
631 highlighted (e.g., with an asterisk, underlined).

632  
633 The narrative section of the followup report should be concise (i.e., item B5 of FDA  
634 Form 3500A) because the FDA's adverse event reporting database (AERS) is  
635 limited for this section of the form.

636  
637 For serious adverse experiences, applicants should exercise due diligence in  
638 obtaining followup information for the purposes of completing all the applicable  
639 elements for an individual case safety report (e.g., FDA Form 3500A). For adverse  
640 experiences that are determined to be nonserious and for which the four basic  
641 elements are known (see section IV.B), additional followup is not necessary.

642  
643 Any attachments submitted with an initial report (e.g. scientific journal articles,  
644 hospital discharge summaries) should not be resubmitted with a followup report.

645  
646 *2. Reporting Considerations*

647  
648 A copy of the initial report or a previous followup report should not be sent with the  
649 latest followup report. Fifteen-day followup reports should not be submitted in the  
650 same envelope with periodic reports.

651  
652 If the initial report was submitted as a 15-day report, the followup report should be  
653 submitted as a 15-day followup report even if the followup information shows that the  
654 adverse experience was expected or not serious. All subsequent followup reports  
655 for adverse experiences that are expected or not serious should be submitted in  
656 periodic reports. A 15-day followup report should be submitted if the adverse  
657 experience is found to be serious and unexpected, even if the original report was  
658 not submitted as a 15-day report.

659

660 If a new adverse experience occurs that is associated with the initial adverse  
661 experience, a followup report should be submitted. However, if the new adverse  
662 experience is not associated with the initial adverse experience (e.g., occurs after a  
663 subsequent administration of the product), an initial report with a new manufacturer  
664 report number should be submitted for the new adverse experience. In these cases,  
665 the applicant should consider the clinical relevance of the adverse experiences to  
666 each other when determining whether an initial report or followup report should be  
667 submitted.

668  
669 Followup reports should not be submitted if additional relevant information is not  
670 obtained for the adverse experience. However, as described in the regulations,  
671 applicants should maintain records of their efforts to obtain additional information,  
672 particularly for serious adverse experiences. FDA may request this documentation.  
673

### 674 3. Reporting Forms

675  
676 For followup reports, particular attention should be paid to completing the following  
677 items on FDA Form 3500A:  
678

- 679 • Item G3 - Mark *health professional* if at any time a health professional  
680 provided information for the report.
- 681 • Item G4 - Use the date the followup information was received by the  
682 applicant.
- 683 • Item G7 - Mark *followup*, and indicate whether this is the 1st, 2nd, 3rd,  
684 ... followup report.
- 685 • Item G9 - Use the same unique manufacturer report number assigned  
686 to the initial report. This is essential to prevent duplicate counting of  
687 reports and to ensure that the followup information is coupled with the  
688 correct initial report.

689  
690 For followup reports, particular attention should be paid to completing the following  
691 items on the VAERS form for vaccines:  
692

- 693 • Top right - Indicate the name of the person who provided information  
694 for the report.
- 695 • Box 24 - Use the same manufacturer report number assigned to the  
696 initial report. This is essential to prevent duplicate counting of reports  
697 and to ensure that the followup information is coupled with the correct  
698 initial report.
- 699 • Box 25 - Use the date the followup information was received by the  
700 applicant.
- 701 • Box 27 - Mark *followup*, and indicate whether this is the 1st, 2nd, 3rd,  
702 ... followup report.

703

704 4. *Report Identification*

705  
706 Fifteen-day followup reports must be submitted in duplicate under separate cover  
707 prominently identified as "15-Day Alert Report-Followup." For this purpose, the "15-  
708 Day Alert Report-Followup" identification should be included on the outside  
709 envelope.

710  
711 **D. Distribution Reports for Biological Products Including Vaccines**

712  
713 This section is based primarily on regulations in § 600.81. These regulations only apply to  
714 human biological products with approved BLAs. Unless otherwise notified by the Director,  
715 Center for Biologics Evaluation and Research, an applicant must submit at periodic  
716 intervals two copies of a report containing information about the quantity of the product  
717 distributed domestically (including distributors) under the BLA.

718  
719 Distribution reports are due within the first 6 months after approval of a BLA, and,  
720 subsequently, at 6-month intervals. Upon written notice, the FDA can require that the  
721 applicant submit reports under this section at alternate times.

722  
723 The report must include the bulk lot, fill lot, and label lot numbers for the total number of  
724 dosage units of each strength or potency distributed (e.g., 50,000 per 10-milliliter vials),  
725 labeled date of expiration, and date of distribution of fill lot or label lot. The report must also  
726 include information about any significant amount of a fill lot or label lot that may have been  
727 returned. Disclosure of financial or pricing data is not required. According to the  
728 regulations, the FDA can require submission of more detailed product distribution  
729 information, if needed.

730  
731 See section VIII.E in this guidance for a suggested reporting format for distribution reports.

732  
733  
734 **VI. SPECIAL REPORTING SITUATIONS**

735  
736 **A. Scientific Literature Reports<sup>17</sup>**

737  
738 Serious, unexpected adverse experiences reported in the scientific literature (or in an  
739 unpublished scientific paper) that are known to the applicant must be submitted as 15-day  
740 reports on an FDA Form 3500A or comparable format. Applicants can use literature  
741 search services (e.g., Weekly Reactions) to identify adverse experiences in the scientific  
742 literature. A copy of the article or manuscript must be attached to the completed FDA  
743 Form 3500A; it is not sufficient to submit only abstracts of articles. All reports from the  
744 scientific literature and unpublished scientific papers should be marked *Literature* in item  
745 G3 of FDA Form 3500A.

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<sup>17</sup> The requirements for scientific literature reports can be found in ' ' 314.80(c)(1)(i), 314.80(d), 600.80(c)(1)(i), and 600.80(d).

746  
747 A separate FDA Form 3500A should be completed for each identifiable patient that  
748 experiences a serious, unexpected adverse experience. Thus, if an article describes six  
749 patients that experience a given serious, unexpected adverse experience, six FDA Form  
750 3500As should be completed. In such cases, a copy of the article should be attached only  
751 to one of the FDA Form 3500As. All other FDA Form 3500As submitted for the article  
752 should reference the manufacturer report number of the FDA Form 3500A that has the  
753 copy of the article attached.

754  
755 If multiple products are mentioned in the article, an FDA Form 3500A should be submitted  
756 only by the applicant whose product is the suspect drug. The suspect product is that  
757 identified by the article's author and is usually mentioned in the article's title. If the  
758 applicant believes that the suspect product is different from the one identified by the author  
759 of the article, the applicant should indicate such information in the narrative section of the  
760 FDA Form 3500A.

761  
762 Reports of serious, unexpected adverse experiences described in the scientific literature  
763 should be submitted for products that have the same active moiety as a product marketed  
764 in the United States. This is true even if the excipient, dosage forms, strengths, routes of  
765 administration, and indications vary.

766  
767 When a serious, unexpected adverse experience is based on a foreign language article or  
768 manuscript, the applicant should translate the publication into English promptly. The original  
769 article or unpublished scientific paper and translation should be attached to the submitted  
770 FDA Form 3500A.

771  
772 **B. Postmarketing, Clinical Trial, or Surveillance Studies<sup>18</sup>**  
773

774 For the purposes of this section, a *study* refers to the systematic collection of data involving  
775 solicitation of adverse experience information (e.g., derived from a clinical trial, patient  
776 registry). Adverse experiences incidental to other types of studies not involving monitoring  
777 adverse experiences of products should be treated as spontaneous reports (see Appendix  
778 A in this guidance for definition of *spontaneous report*). For purposes of safety reporting,  
779 reports of suspected adverse experiences obtained from company sponsored patient  
780 support programs and disease management programs should be handled as if they were  
781 study reports and not as spontaneous reports.

782  
783 Serious, unexpected adverse experiences that occur during a study must be submitted as  
784 15-day reports. These adverse experiences are only required to be reported if there is a  
785 reasonable possibility that the drug or biological product caused the adverse experience.  
786

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<sup>18</sup> The requirements for reporting adverse experiences from studies can be found in 310.305(c)(1), 314.80(c)(2)(iii), 314.80(e)(1), 600.80(c)(2)(iii), and 600.80(e)(1).

787 Adverse experiences occurring with marketed drug or biological products during IND trials  
788 must also be submitted, as prescribed under ' 312.32, to the FDA new drug review  
789 division in the Center for Drug Evaluation and Research or the product review office in the  
790 Center for Biologics Evaluation and Research that has responsibility for oversight of the  
791 IND.

792  
793 For each adverse experience, a suspect product should be identified. Reports from  
794 blinded studies should be submitted only after the code is broken. The blind should always  
795 be broken for each patient or subject that experiences a serious, unexpected adverse  
796 experience unless arrangements have been made otherwise with the responsible FDA  
797 review division. Exceptions to breaking the blind usually involve situations in which  
798 mortality or certain serious morbidities are indeed the clinical endpoint. This is consistent  
799 with the ICH E2A guidance.

### 800 801 **C. Foreign Reports**<sup>19</sup>

802  
803 Foreign reports of serious, unexpected adverse experiences must be submitted as 15-day  
804 reports. Other foreign reports, including serious and expected, nonserious and unexpected,  
805 and nonserious and expected adverse experiences are not required to be submitted.

806  
807 Reports of foreign serious, unexpected adverse experiences should be submitted for  
808 products that have the same active moiety as a product marketed in the United States.  
809 This is true even if the excipient, dosage forms, strengths, routes of administration, and  
810 indications vary. When a foreign report is submitted on a product that is not identical to a  
811 product marketed in the United States, item C1 of FDA Form 3500A should contain the  
812 foreign trade name, the generic name, and the NDA number for the product with the same  
813 active moiety that is marketed in the United States.

### 814 815 **D. Death Reports**

816  
817 Death is always a serious outcome (see definition of *serious* in Appendix A of this  
818 guidance and at ' ' 310.305(b), 314.80(a) and 600.80(a)). Thus, if death is associated  
819 with an unexpected adverse experience, or if death is associated with an expected  
820 adverse experience but the labeling does not specifically state that the adverse experience  
821 may be associated with a fatal outcome, a 15-day report should be submitted.

### 822 823 **E. Overdose Reports**

824  
825 Reports of overdose should be submitted *only* when the overdose is associated with an  
826 adverse experience. If the adverse experience associated with the overdose is serious  
827 and unexpected, a 15-day report should be completed. If the adverse experience is serious  
828 and expected, nonserious and unexpected, or nonserious and expected, a non-15 day

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<sup>19</sup> The requirements for reporting of foreign adverse experiences can be found in ' ' 310.305(c)(1)(i), 314.80(c)(2)(iii) and 600.80(c)(2)(iii).



829 report should be submitted in the periodic report for spontaneously reported domestic  
830 cases.

831

832 **F. Lack of Effect Reports**

833

834 The definition of *adverse experience* includes *any failure of expected pharmacological*  
835 *action* that is synonymous with *lack of effect* (see definition of *adverse experience* in  
836 Appendix A of this guidance and at ' ' 310.305(b), 314.80(a) and 600.80(a)). All  
837 spontaneously reported cases of a *lack of effect* that occur in the United States should be  
838 reported on FDA Form 3500A and submitted in the periodic report with other adverse  
839 experiences. The lot number of the suspect product should be included in item C6 of FDA  
840 Form 3500A.

841

842 If the report of *lack of effect* is for an unapproved indication, the event should not be  
843 reported to the FDA as an individual case safety report. Instead, this information should be  
844 included in the narrative summary section of the periodic report.

845

846 **G. Information on the Internet**

847

848 Adverse experience information that is submitted to an applicant via the Internet (e.g., e-  
849 mail) should be reported to the FDA if the applicant has knowledge of the four basic  
850 elements for an individual case safety report (see section IV.B in this guidance).  
851 Applicants should review any Internet sites sponsored by them for adverse experience  
852 information, but are not responsible for reviewing any Internet sites that are not sponsored  
853 by them. However, if an applicant becomes aware of an adverse experience on an Internet  
854 site that it does not sponsor, the applicant should review the adverse experience and  
855 determine if it should be reported to the FDA.

856

857 **H. Pediatric Patients**

858

859 For children under 3 years of age, the child's date of birth and age in days or months (e.g.,  
860 *15 months*) should be included under item A2 of FDA Form 3500A. The word *days* or  
861 *months* should be clearly written. For all pediatric patients, body weight (item A4 of FDA  
862 Form 3500A) and dose (item C2 of FDA Form 3500A) should be included.

863

864 For reports of a congenital anomaly, the age and sex of the infant should be included.  
865 Followup reports for the infant should be considered followup to the initial report; followup  
866 for the mother should be submitted as a new initial individual case safety report on a  
867 separate FDA Form 3500A. The date that the congenital anomaly is detected should be  
868 used as the event onset date (e.g., birth date of the infant, date pregnancy is terminated,  
869 date congenital anomaly is detected by ultrasound or other diagnostic technique). This  
870 date should be used in item B3 of FDA Form 3500A.

871

872 **I. Prescription Drugs Marketed for Human Use Without an Approved**  
873 **Application**<sup>20</sup>  
874

875 For prescription drugs marketed for human use without an approved NDA or ANDA, all  
876 serious, unexpected adverse experiences must be reported to the FDA on an FDA Form  
877 3500A within 15 calendar days. These reports must be submitted in SINGLE copy under  
878 separate cover. The report should be marked on the outside envelope "15-Day Alert  
879 Report - 310.305." A copy of the U.S. product labeling must accompany each report.  
880

881 Postmarketing periodic reports should not be submitted for these drugs.  
882

883 **J. Another Applicant's Product**  
884

885 Reports of adverse experiences in which the initial reporter identifies the suspect product  
886 as one marketed by another applicant should be promptly forwarded to that applicant. An  
887 applicant who receives a report of an adverse experience regarding one of its products  
888 from another applicant must submit the report to the FDA within the same time constraints  
889 applicable to any report received from a third party (see section VI.K in this guidance).  
890

891 An applicant should only submit a report of an adverse experience to the FDA for a  
892 suspect product marketed by another applicant if the applicant of the suspect product is  
893 unknown or the report is for a serious, unexpected adverse experience occurring during the  
894 conduct of a study.  
895

896 **K. Multiple Suspect Products**  
897

898 If a reportable adverse experience involves two or more suspect products from the same  
899 applicant, only one FDA Form 3500A should be completed. The FDA Form 3500A should  
900 reference only one manufacturer report number. The report should be submitted to the  
901 NDA, ANDA, or BLA considered *most suspect* by the initial reporter. If each product is  
902 equally suspect, the report should be submitted to the product first in alphabetical order.  
903 The adverse experience should also be reported in the narrative summary section of the  
904 periodic report for the other product(s).  
905

906 However, if one suspect product is a licensed non-vaccine biologic and the other is a  
907 licensed vaccine, separate reporting forms should be submitted. An FDA Form 3500A  
908 should be used for the licensed non-vaccine biologic and a VAERS form should be used  
909 for the licensed vaccine.  
910

911 If a reportable adverse experience involves two or more suspect products and two or more  
912 applicants, an applicant may choose to submit an FDA Form 3500A to the FDA on the  
913 adverse experience that describes detailed information including the product(s) from the

---

<sup>20</sup> The requirements for prescription drugs marketed for human use without an approved application can be found in ' 310.305.

914 other applicant. In such a case, the other applicant should receive a copy of the FDA Form  
915 3500A including its manufacturer report number so that the other applicant can reference  
916 this report when providing any relevant followup information to the FDA. The other applicant  
917 should not submit to the FDA information originally submitted to the Agency by the first  
918 applicant.

919

920 **L. Suspect Drugs with Multiple NDAs or ANDAs by the Same Applicant**

921

922 A drug substance can be the subject of more than one approved NDA or ANDA. If an  
923 applicant receives a report for a drug and the specific application is identifiable, the report  
924 should be submitted to that application. However, if a drug substance has more than one  
925 application and it cannot be determined which of the approved applications is involved, the  
926 report should be submitted to the application for the drug product that was approved first  
927 and that has the same general route of administration as the suspect drug substance. This  
928 would usually be the application with the lowest number.

929

930 **M. Two or More Marketers of a Product**

931

932 If two or more companies that co-market a specific drug product have an approved NDA  
933 for the product, one of the companies should be identified as having primary responsibility  
934 for reporting adverse experiences for the drug product to the FDA to avoid duplicative  
935 reporting of adverse experiences. This would also be true for two or more companies that  
936 co-market a specific biological product and have an approved BLA for the product.

937

938 **N. Unapproved Indications**

939

940 An adverse experience associated with the use of a product for an unapproved indication  
941 should be reported to the FDA as is required for any other spontaneously reported adverse  
942 experience occurring in the United States (e.g., 15-day report for a serious, unexpected  
943 adverse experience or periodic report for a nonserious, unexpected adverse experience).  
944 However, a *lack of effect* report for an unapproved indication should not be reported on an  
945 FDA Form 3500A. Instead, such information should be included in the narrative summary  
946 section of a periodic report.

947

948 **O. Product Interactions**

949

950 If an applicant receives a report identified as a product interaction, each of the products  
951 should be identified as a suspect product in item C1 of FDA Form 3500A.

952

953 **P. Reports from the FDA<sup>21</sup>**

954

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<sup>21</sup> The requirements for submitting reports received from the FDA can be found in 310.305(c)(5), 314.80(b), and 600.80(b).

955 Sometimes FDA forwards individual case safety reports (i.e., FDA Form 3500As) to  
956 applicants. For example, applicants can participate in the FDA's MedWatch-to-  
957 Manufacturer Program. This program is designed to expedite transmission from the FDA  
958 to applicants participating in the program cases of serious adverse experiences reported  
959 directly to the FDA voluntarily by initial reporters (e.g., health care professionals,  
960 consumers). Details of the program can be found on the Internet at  
961 [www.fda.gov/medwatch/report/mmp.htm](http://www.fda.gov/medwatch/report/mmp.htm).

962  
963 Applicants that receive individual case safety reports from FDA are not required to  
964 resubmit them to the Agency. However, followup information to these initial reports must  
965 be submitted to the FDA (see section V.C in this guidance).

966  
967 **Q. Product Defects**

968  
969 If a product defect results in an adverse experience, the adverse experience should be  
970 reported as any other spontaneously reported adverse experience occurring in the United  
971 States (e.g., 15-day report for a serious, unexpected adverse experience or periodic report  
972 for a nonserious, unexpected adverse experience).

973  
974 **R. Reporting Ambiguities**

975  
976 In some cases, it may be difficult to interpret specific criteria used for reporting. Examples  
977 include determining whether an adverse experience is expected or unexpected or whether  
978 a patient is identifiable or not. For these and any other ambiguities, the applicant should  
979 use a conservative approach and err on the side of reporting the adverse experience to the  
980 FDA. Thus, if there is doubt, consider an adverse experience to be unexpected, consider  
981 a patient to be identifiable, and so on.

982  
983  
984 **VII. CODING OF ADVERSE EXPERIENCES IN INDIVIDUAL CASE SAFETY**  
985 **REPORTS**

986  
987 Companies currently use a variety of medical terminologies to code adverse experiences  
988 in individual case safety reports (e.g., COSTART, WHOART, MedDRA). At this time, the  
989 FDA will accept adverse experiences coded with any of these terminologies. However, as  
990 recommended by ICH, the Agency encourages companies to use MedDRA for this  
991 purpose and as indicated in the FDA's advanced notice of proposed rulemaking on this  
992 topic (63 FR 59746; November 5, 1998), the Agency plans to propose to require use of  
993 MedDRA as the terminology for coding adverse experiences in individual case safety  
994 reports submitted to the FDA.

995  
996 Companies can license MedDRA from an international maintenance and support services  
997 organization (MSSO) (toll free number 877-258-8280 (703-345-7799 in Washington D.C.  
998 area), fax 703-345-7755, e-mail [subscrib@meddramssso.com](mailto:subscrib@meddramssso.com), Internet at  
999 [www.meddramssso.com](http://www.meddramssso.com)).

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**VIII. REPORTING FORMATS<sup>22</sup>**

Individual case safety reports of adverse experiences that occur domestically for marketed human drugs and biological products, except vaccines, must be submitted to the FDA on FDA Form 3500A; a VAERS form must be used for vaccines. Foreign adverse experiences can be submitted either on FDA Form 3500A or, if preferred, on a CIOMS I form. Foreign adverse experiences associated with the use of vaccines can be submitted on either a VAERS form or, if preferred, a CIOMS I form. A separate FDA Form 3500A, VAERS form, or CIOMS I form must be completed for each individual person experiencing an adverse experience.

The following paragraphs describe how to acquire or generate the various reporting forms for individual case safety reports and how to obtain information on FDA’s pilot program for electronic submission of these reports. This section also describes a suggested reporting format for distribution reports for human biological products with approved BLAs.

The following abbreviations should be used when specific information is not available for an individual case safety report or distribution report:

- NA for not applicable
- NI for no information at this time (but may be available later)
- UNK for unknown

**A. FDA Form 3500A**

See Appendix C of this guidance for a copy of the form.<sup>23</sup>

1. Copies of the FDA Form 3500A can be obtained in the following ways:
  - From the Internet at [www.fda.gov/medwatch/report/mfg.htm](http://www.fda.gov/medwatch/report/mfg.htm). Print the form or download it as a PDF file. Form software can also be downloaded and used to complete the forms using a personal computer. Completed forms should be mailed to the FDA because this software does not permit electronic submission of reports. The software is also available on disk. For a copy of the disk, call 1-800-FDA-1088 or send an electronic request via the MedWatch comment page ([www.fda.gov/medwatch/report/mfg.htm](http://www.fda.gov/medwatch/report/mfg.htm)). Note: this software

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<sup>22</sup> The requirements for reporting formats can be found in §§ 310.305(d), 314.80(f) and 600.80(f).

<sup>23</sup> Instructions for completing FDA Form 3500A are available on the Internet at [www.fda.gov/medwatch/report/instruc.htm](http://www.fda.gov/medwatch/report/instruc.htm).

*Draft — Not for Implementation*

1039 contains both FDA Form 3500 for voluntary reporting and FDA Form  
1040 3500A for mandatory reporting.  
1041

1042 • By Fax - Call 1-800-FDA-1088 and make the following selections:  
1043

1044 Press 1 (health professional)  
1045 Press 2 (obtain a copy of a form)  
1046 Press 4 (obtain fax of FDA Form 3500A).  
1047

1048 • By Mail - Up to 10 copies of FDA Form 3500A can be obtained from:  
1049

1050 Office of Post-marketing Drug Risk Assessment  
1051 Center for Drug Evaluation and Research (HFD-400)  
1052 Food and Drug Administration  
1053 5600 Fishers Lane, Room 15B-31  
1054 Rockville, MD 20857  
1055

1056 OR  
1057

1058 Office of Biostatistics and Epidemiology  
1059 Center for Biologics Evaluation and Research (HFM-210)  
1060 Adverse Experience Reporting  
1061 1401 Rockville Pike  
1062 Rockville, MD 20852-1448  
1063

1064 Additional copies can be obtained from:  
1065

1066 Consolidated Forms and Publications Distribution Center  
1067 Washington Commerce Center  
1068 3222 Hubbard Rd.  
1069 Landover, MD 20785  
1070

1071 2. Copies can be created by:  
1072

1073 • Photocopying a blank FDA Form 3500A  
1074  
1075 • Producing a computer-generated facsimile of FDA Form 3500A  
1076

1077 In place of using the preprinted forms, a computer-generated facsimile of  
1078 FDA Form 3500A can be used after approval, in writing, by FDA ( ' '  
1079 310.305(d)(3), 314.80(f)(3) and 600.80(f)(3)). This computer-generated  
1080 facsimile of FDA Form 3500A should:

1081  
1082 a. Contain all the elements (i.e., 2-column format, sections, blocks, titles,  
1083 descriptors within blocks, text for disclaimer) of FDA Form 3500A in

- 1084 the identical enumerated sequence of the form, except as otherwise  
1085 noted. For reports in which no suspect medical device is involved, the  
1086 box Section D. *Suspect Medical Device* on the front page of FDA  
1087 Form 3500A can be replaced with the box Section G. *All*  
1088 *Manufacturers* located on the back page of the form. This would allow  
1089 reporters of adverse experiences for drug and biological products to  
1090 use a one-page form for reporting. See Appendix F of this guidance  
1091 for a sample of a one-page FDA Form 3500A).  
1092
- 1093 b. Have, at least, a 1/4" margin around the entire form so that  
1094 information is not lost during scanning, copying or faxing of the  
1095 document (the left-hand margin may be increased up to 2" to permit  
1096 binding (e.g., hole-punching) of the form) (all other margins have to  
1097 continue to be at least 1/4").  
1098
- 1099 c. Include the name of the company centered on the top of the front  
1100 page.  
1101
- 1102 d. Include in the lower left corner of the front page the phrase *3500A*  
1103 *Facsimile* instead of the phrase *FDA Form 3500A (date of form [e.g.,*  
1104 *6/93])*.  
1105
- 1106 e. Include in the upper right corner of the front page above the *FDA Use*  
1107 *Only* box the phrase *FDA Facsimile Approval: [include date of*  
1108 *approval by FDA]*, instead of the phrase *See OMB statement on*  
1109 *reverse*.  
1110
- 1111 f. Have the data and text contained within the boxes on a computer-  
1112 generated FDA Form 3500A conform to the following specifications:  
1113
- 1114 • The font size should not be less than 10 point.
  - 1115
  - 1116 • A font type should be selected that is easy to read (e.g., CG  
1117 Times, Arial) and not condensed. The form may be copied or  
1118 faxed multiple times. For visual contrast, the font type used for  
1119 the data and text should, if possible, be different from the font  
1120 type used to create the FDA Form 3500A.
  - 1121
  - 1122 • Have all data and text contained within each of the boxes (e.g.,  
1123 a box marked with an *Ax@* should be centered within the box,  
1124 and narratives should include margins so that letters are not  
1125 obscured or made ambiguous by lines defining a box.).  
1126

- 1127 • Have the phrase *continued* included at the end of each field  
1128 that has additional information continued onto another page.  
1129
- 1130 g. Have continuation pages containing additional information for  
1131 narrative entries conform to the following specifications:  
1132
- 1133 • Each page should be identified as Page \_ of \_.
  - 1134
  - 1135 • Each page should include the manufacturer report number in  
1136 the upper right corner.
  - 1137
  - 1138 • Each page should include the name of the company in the  
1139 upper right corner.
  - 1140
  - 1141 • The section and block number (e.g., Block B5) for each  
1142 narrative entry should be included.  
1143

1144 For approval of computer-generated facsimiles of FDA Form 3500As, companies  
1145 should mail their requests along with two copies of the computer-generated  
1146 facsimile, a blank one and one with all the boxes completed with sample data/text,  
1147 to:

1148  
1149 Information Technology Staff  
1150 OPDRA/CDER/FDA Room 15B23  
1151 HFD-420  
1152 5600 Fishers Lane  
1153 Rockville, MD 20857  
1154

1155 Companies can contact the Information Technology Staff at 301-827-3223 to check  
1156 on the status of an approval request. Companies that are using a computer-  
1157 generated facsimile of FDA Form 3500A from a vendor that has already obtained  
1158 approval, in writing, from the FDA for the form do not have to submit another  
1159 approval request to the Agency (the vendor's name and approval date should  
1160 appear in the upper right corner of the form).  
1161

1162 **B. VAERS Form for Vaccines**  
1163

1164 See Appendix D of this guidance for a copy of the form.<sup>24</sup>

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<sup>24</sup> A guidance for industry entitled *How to Complete the Vaccine Adverse Event Reporting System Form (VAERS-1)* (October 1999) is available on the Internet at [www.fda.gov/cber/guidelines.htm](http://www.fda.gov/cber/guidelines.htm) or from the Office of Communication, Training and Manufacturers Assistance (HFM-40), CBER, 1401 Rockville Pike, Rockville, MD 20852-1448, (Fax) 1-888-CBERFAX or 301-827-3844, (Voice Information) 1-800-835-4709 or 301-827-1800.



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1. Copies of the VAERS form can be obtained by calling 1-800-822-7967.
2. In place of using the preprinted forms, a computer-generated facsimile of the VAERS form can be used after approval, in writing, by FDA (‘ 600.80(f)(3)). To request approval of a computer-generated facsimile of a VAERS form, a printed copy with data to illustrate how each data field will be reported should be submitted to:

Office of Biostatistics and Epidemiology (HFM-210)  
 Center for Biologics Evaluation and Research, FDA  
 1401 Rockville Pike  
 Rockville, MD 20852-1448

**C. CIOMS I Form for Foreign Adverse Experiences**

CIOMS, working with several member nations and industry, has developed a format for international adverse experience reporting (CIOMS I form) (see Appendix E of this guidance). Applicants can use an FDA Form 3500A or, if preferred, a CIOMS I form for submission of 15-day reports of foreign adverse experiences to the FDA. Applicants cannot use a CIOMS I form for submissions of adverse experiences that occur within the United States. For these adverse experiences, an FDA Form 3500A must be used.

**D. Distribution Reports for Biological Products Including Vaccines**

This section on distribution reports only applies to human biological products with approved BLAs. Under ‘ 600.81, distribution reports must include the bulk lot, fill lot, and label lot numbers for the total number of dosage units of each strength or potency distributed (e.g., 50,000 per 10-milliliter vials), labeled date of expiration, and date of distribution of fill lot or label lot. The report must also include information about any significant amount of a fill lot or label lot that may have been returned.

The regulations do not specify a reporting form or format for distribution reports. One suggested report format is shown here:

Biologics License No. \_\_\_\_\_ Product name, strength \_\_\_\_\_  
 Product Code \_\_\_\_\_

Bulk Lot No.	Fill Lot No.	Label Lot No.	Expiration Date	Distribution Date	No. of Doses Distributed	No. of Doses Returned

1204

1205  
1206 If there is more than one distribution date for a lot, the report should include each  
1207 distribution date and the number of doses distributed. When reporting returned doses, the  
1208 number of doses distributed should not be repeated.

1209  
1210 For vaccines, if available, distribution of doses can be reported by public, private, or  
1211 military sectors.

## 1212 1213 **E. Electronic Submissions**

1214  
1215 The FDA is in the process of developing a system for electronic submission of  
1216 postmarketing safety reports. At this time, applicants can submit, under a pilot program,  
1217 certain individual case safety reports electronically. Details of this pilot program are  
1218 available on the Internet at [www.fda.gov/cder/aerssub](http://www.fda.gov/cder/aerssub). The Agency also plans to have a  
1219 system for electronic submission of distribution reports for biological products including  
1220 vaccines in the near future.

## 1221 1222 1223 **IX. HOW AND WHERE TO SUBMIT POSTMARKETING SAFETY REPORTS**

1224  
1225 All submissions should be legible and typewritten with a minimum acceptable font size of  
1226 10 point. Legible photostatic copies can be submitted. However, visual contrast should be  
1227 adequate to ensure clear readable archival images. The applicant must submit one or two  
1228 copies of each safety report as specified in this section unless a waiver is granted  
1229 permitting a different number of copies (see section XI in this guidance).

### 1230 1231 **A. Human Drug Products**

- 1232  
1233 1. For prescription drugs marketed for human use **without** an approved NDA  
1234 or ANDA, postmarketing 15-day reports (initial and followup) should be sent  
1235 as *single copies* to:

1236  
1237 Office of Post-marketing Drug Risk Assessment (HFD-400)  
1238 Center for Drug Evaluation and Research  
1239 Food and Drug Administration  
1240 5600 Fishers Lane  
1241 Rockville, MD 20857

- 1242  
1243 2. For drugs with approved **ANDAs**, postmarketing 15-day reports, (initial and  
1244 followup), and periodic reports should be sent as *single copies* to:

1245  
1246 Office of Post-marketing Drug Risk Assessment (HFD-400)  
1247 Center for Drug Evaluation and Research  
1248 Food and Drug Administration  
1249 5600 Fishers Lane

1250 Rockville, MD 20857

1251

1252 3. For drugs with approved **NDAs**, postmarketing 15-day reports (initial and  
1253 followup), and periodic reports should be sent *in duplicate* to:

1254

1255 Food and Drug Administration

1256 Central Document Room

1257 12229 Wilkins Ave.

1258 Rockville, MD 20852

1259

1260 **B. Human Biological Products and Vaccines**

1261

1262 1. For vaccines, postmarketing 15-day reports (initial and followup), and  
1263 periodic reports should be sent *in duplicate* to:

1264

1265 VAERS

1266 P.O. Box 1100

1267 Rockville, MD 20849-1100

1268

1269 2. For biological products other than vaccines, postmarketing 15-day reports  
1270 (initial and followup) and periodic reports should be sent *in duplicate* to:

1271

1272 Office of Biostatistics and Epidemiology (HFM-210)

1273 Center for Biologics Evaluation and Research, FDA

1274 Adverse Experience Reporting

1275 1401 Rockville Pike

1276 Rockville, MD 20852-1448

1277

1278 3. For all biological products and vaccines, distribution reports (' 600.81)  
1279 should be sent *in duplicate* to:

1280

1281 Office of Biostatistics and Epidemiology (HFM-210)

1282 Center for Biologics Evaluation and Research, FDA

1283 Distribution Reports

1284 1401 Rockville Pike

1285 Rockville, MD 20852-1448

1286

1287

1288 **X. WRITTEN PROCEDURES FOR POSTMARKETING SAFETY REPORTING**

1289

1290 Each applicant must develop written standard operating procedures for the surveillance,  
1291 receipt, evaluation, and reporting of adverse experiences to the FDA (' ' 310.305(a),  
1292 314.80(b) and 600.80(b)). The FDA will consider an applicant responsible for information  
1293 known to its employees, affiliates, and contractors. For this purpose, applicants should

1294 develop procedures that allow for expedited handling of adverse experience reports.  
1295 Records of due diligence should be maintained. This applies to surveillance and  
1296 processing for both domestic and foreign reports of adverse experiences.  
1297

1298

1299 **XI. REQUESTS FOR WAIVERS TO POSTMARKETING SAFETY REPORTING**  
1300 **REQUIREMENTS**

1301  
1302 Under §§ 314.90(a) and 600.90(a), applicants may ask the FDA to waive any  
1303 postmarketing safety reporting requirement that applies to the applicant under §§ 314.80  
1304 and 600.80. The following paragraphs discuss certain postmarketing periodic safety  
1305 reporting requirements for which the FDA is currently granting waivers.  
1306

1307

1307 **A. Submission of FDA Form 3500A for Nonserious, Expected Adverse**  
1308 **Experiences**

1309

1310 Applicants are encouraged to request a waiver for submission of FDA Form 3500As for  
1311 individual case safety reports of nonserious, expected adverse experiences that, at a  
1312 minimum, contain the four basic elements (see section IV.B in this guidance). In such  
1313 cases, applicants should maintain records of these nonserious, expected adverse  
1314 experiences in their corporate drug or biological product safety files. The FDA may  
1315 request that an applicant submit to the Agency FDA Form 3500As of one or more of these  
1316 adverse experiences. The agency would expect these forms to be submitted within 5  
1317 calendar days after receipt of the request.  
1318

1319

1319 Applicants who obtain a waiver for the requirement to submit individual case safety reports  
1320 of nonserious, expected adverse experiences would still be expected to submit information  
1321 on these adverse experiences to the FDA in the summary tabulations section of  
1322 postmarketing periodic reports (see section V.B.2.a in this guidance).  
1323

1324

1324 At this time, the FDA does not intend to grant waiver requests for new biological molecular  
1325 entities within one year of licensure or for blood products, plasma derivatives, or vaccines.  
1326 The Agency believes that it is important to continue periodic review of all individual case  
1327 safety reports of adverse experiences for these products to identify safety problems due to  
1328 lot-to-lot variations and also to monitor the safety of newly approved biological products.  
1329

1330

1330 **B. Submission of PSUR format for the Periodic Report**

1331

1332 Applicants can request a waiver of the requirement to submit postmarketing periodic  
1333 safety reports in the format described in the regulations. Instead, applicants can prepare  
1334 these reports using the PSUR (Periodic Safety Update Report) format described in the  
1335 ICH E2C guidance. In addition, the Agency recommends the following:  
1336

1337

- 1337 • If all dosage forms and formulations for the active substance, as well as  
1338 indications, are combined in one PSUR, this information should be

1339 separated into specific sections of the report when such separation is  
1340 appropriate to accurately portray the safety profile of the specific dosage  
1341 forms. For example, one should not combine information from ophthalmic  
1342 drop dosage forms and solid oral dosage forms. One copy of the PSUR  
1343 should be submitted for each approved NDA or ANDA whose product is  
1344 covered in the PSUR as well as an additional copy for review by the  
1345 postmarketing pharmacovigilance office.

- 1346
- 1347 • Copies of the FDA Form 3500A or VAERS form that are required by the  
1348 regulations must be included.<sup>25</sup> These forms should be included with the  
1349 PSUR as an appendix. You can request a waiver for submission of certain  
1350 nonserious, expected adverse experiences on an FDA Form 3500A as  
1351 described in the previous section.
- 1352
- 1353 • A summary tabulation should be included as an appendix listing all  
1354 spontaneously reported U.S. individual case safety reports from consumers if  
1355 such cases are not already included in the PSUR. Summary tabulations  
1356 should be presented by body system of all adverse experience terms and  
1357 counts of occurrences and be segregated by type (i.e., serious/unexpected;  
1358 serious/expected; nonserious/unexpected; and nonserious/expected),  
1359
- 1360 • A narrative should be included as an appendix that references the changes,  
1361 if any, to the approved U.S. labeling for the dosage forms covered by the  
1362 PSUR based on new information in the PSUR. A copy of the most recently  
1363 approved U.S. labeling for the product(s) covered by the PSUR should be  
1364 included.
- 1365

### 1366 **C. Submission Date and Frequency for PSUR Reports**

1367

1368 Applicants can request a waiver to submit PSURs to the FDA based on the month and day  
1369 of the international birth date of the product instead of the month and day of the anniversary  
1370 date of U.S. approval of the product.<sup>26</sup> The waiver request should specify that these  
1371 PSURs would be submitted to the FDA within 60 calendar days of the data lock point (i.e.,  
1372 month and day of the international birth date of the product or any other day agreed on by  
1373 the applicant and the FDA).<sup>27</sup>

1374

1375 Applicants can also request a waiver to submit PSURs to the FDA at a frequency other  
1376 than those required under § § 314.80(c)(2)(i) and 600.80(c)(2)(i).

1377

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<sup>25</sup> See §§ 314.80(c)(2)(ii)(b) and 600.80(c)(2)(ii)(B).

<sup>26</sup> The international birth date for a product is the date the first regulatory authority in the world approved the first marketing application for a human drug product containing the drug substance or a human biological product.

<sup>27</sup> The data lock point is the date designated as the cut-off date for data to be included in a PSUR.

1378 **D. How and Where to Submit Waiver Requests**

1379

1380 1. *Marketed human drug products*

1381

1382 For waivers under ' 314.90(a), applicants should submit a written waiver request  
1383 (include the product's name(s), date(s) of U.S. approval, and the application  
1384 number(s)) to:

1385

1386

Director

1387

Office of Post-Marketing Drug Risk Assessment

1388

Center for Drug Evaluation and Research

1389

Food and Drug Administration

1390

5600 Fishers Lane, HFD-400

1391

Rockville, MD 20857

1392

1393 2. *Licensed biological products*

1394

1395 For waivers under ' 600.90(a), applicants should submit a written waiver request  
1396 (include the product name(s), date(s) of U.S. approval, and the application  
1397 number(s)) to:

1398

1399

Director

1400

Office of Biostatistics & Epidemiology

1401

Center for Biologics Evaluation and Research

1402

Food and Drug Administration

1403

140I Rockville Pike, HFM-220

1404

Rockville, MD 20852-1448

1405

1406

1407 **XII. VALIDATION OF ADVERSE EXPERIENCE COMPUTER SYSTEMS**

1408

1409 If an electronic record of an adverse experience is created, modified, maintained,  
1410 archived, retrieved, or transmitted, the applicant is required, among other things, to employ  
1411 procedures to ensure that records are trustworthy, reliable, and consistent with FDA's  
1412 ability to promote and protect public health (21 CFR part 11). Those procedures must  
1413 include validation of systems to ensure accuracy, reliability, consistent intended  
1414 performance, and the ability to discern invalid or altered records.

## APPENDIX A: GLOSSARY

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**Adverse Experience** - Any adverse event associated with the use of a drug or biological product in humans, whether or not considered product-related, including the following: An adverse event occurring in the course of the use of a drug product in professional practice; an adverse event occurring from drug overdose whether accidental or intentional; an adverse event occurring from drug abuse; an adverse event occurring from drug withdrawal; and any failure of expected pharmacological action. Reporting an adverse experience does not necessarily reflect a conclusion by the applicant or the FDA that the product caused or contributed to the adverse experience. Adverse experience is synonymous with *adverse drug experience*, *adverse biological experience*, *adverse product experience*, and *adverse event*.

**Affiliate** - Any individual or entity related by employment or organizational structure to the applicant, including all subsidiaries, whether domestic or foreign.

**Applicant** - An individual or entity who holds the new drug application (NDA), abbreviated new drug application (ANDA), or the biologics license application (BLA). For purposes of this guidance, this term includes any person whose name appears on the label of a marketed drug or licensed biological product as its manufacturer, packer, distributor, shared manufacturer, joint manufacturer, or any participant involved in divided manufacturing.

**Causality Assessment** - Determination of whether there is a reasonable possibility that the product is etiologically related to the adverse experience. Causality assessment includes, for example, assessment of temporal relationships, dechallenge/rechallenge information, association with (or lack of association with) underlying disease, presence (or absence) of a more likely cause, and physiologic plausibility.

**Challenge** - Administration of a suspect product by any route.

**Dechallenge** - Withdrawal of a suspect product from a patient's therapeutic regimen.

**Negative Dechallenge** - Continued presence of an adverse experience after withdrawal of the suspect product.

**Positive Dechallenge** - Partial or complete disappearance of an adverse experience after withdrawal of the suspect product.

**Rechallenge** - Reintroduction of a suspect product suspected of having caused an adverse experience following a positive dechallenge.

1458           **Negative Rechallenge** - Failure of the product, when reintroduced, to produce  
1459 signs or symptoms similar to those observed when the suspect product was  
1460 previously introduced.

1461  
1462           **Positive Rechallenge** - Reoccurrence of similar signs and symptoms upon  
1463 reintroduction of the suspect product.

1464  
1465           **Disability** - A substantial disruption in one's ability to conduct normal life functions.

1466  
1467           **Expected Adverse Experience** - Adverse experience listed in the current FDA-approved  
1468 labeling for the drug or licensed biological product. This would include any section of the  
1469 labeling that refers to adverse experience information.

1470  
1471           **Initial Reporter** - The original source of information concerning an adverse experience  
1472 (e.g., consumer, healthcare professional).

1473  
1474           **Life-threatening Adverse Experience** - An adverse experience that, in the view of the  
1475 initial reporter, places the patient at immediate risk of death from the adverse experience  
1476 as it occurred. It does not include an adverse experience that, had it occurred in a more  
1477 severe form, might have caused death.

1478  
1479           **Serious Adverse Experience** - An adverse experience occurring at any dose that results  
1480 in any of the following outcomes:

- 1481
- 1482           • Death
  - 1483
  - 1484           • Life-threatening adverse experience
  - 1485
  - 1486           • Initial inpatient hospitalization
  - 1487
  - 1488           • Prolongation of hospitalization
  - 1489
  - 1490           • Significant or persistent disability/incapacity
  - 1491
  - 1492           • Congenital anomaly/birth defect (including that occurring in a fetus);
  - 1493
  - 1494           • Important medical events, based upon appropriate medical judgment, that may  
1495           jeopardize the patient or subject and may require medical or surgical intervention to  
1496           prevent one of the outcomes listed above.

1497  
1498           **Spontaneous Report** - A communication from an individual (e.g. health care  
1499 professional, consumer) to a company or regulatory authority that describes a suspected  
1500 adverse experience. It does not include cases identified from information solicited by the  
1501 applicant such as individual cases or findings derived from a study.

1502



1503 **Study** - Any organized data collection system (e.g., adverse experience information  
1504 derived from a clinical trial, patient registry including pregnancy registries). Reports from  
1505 company sponsored patient support programs and disease management programs should  
1506 be handled as if they were study reports and not as spontaneous reports.

1507

1508 **Suspect Product** - Drug or biological product associated with an adverse experience as  
1509 determined by the initial reporter, regardless of the opinion of the applicant.

1510

1511 **Unexpected Adverse Experience** - Adverse experience not included in any section of  
1512 the current FDA-approved labeling for the drug or licensed biological product. This  
1513 includes an adverse experience that may differ from a labeled adverse experience  
1514 because of greater severity or specificity (e.g., abnormal liver function versus hepatic  
1515 necrosis). Adverse experiences listed as occurring with a class of drugs or biological  
1516 products but not specifically mentioned with a particular drug or biological product are  
1517 considered unexpected (e.g., rash with antibiotic X would be unexpected if the labeling  
1518 said "rash may be associated with antibiotics"). This is because the labeling does not  
1519 specifically state "rash is associated with antibiotic X." Reports of death from an adverse  
1520 experience are considered unexpected unless the possibility of a fatal outcome from that  
1521 adverse experience is stated in the labeling.

1522

## APPENDIX B: REPORT CHECKLIST

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Before mailing your postmarketing safety reports to the FDA, you should make sure that the following questions have been addressed:

### A. For All FDA Form 3500A Reports

1. Have you completed a separate FDA Form 3500A for each patient?
2. Have you included the manufacturer report number in item G9 on FDA Form 3500A? (Note: For followup reports, this number should be identical to the manufacturer report number on the initial report.)
3. Have you clearly marked the report "Periodic" or "15-Day" as appropriate in item G7 on FDA Form 3500A?
4. Have you clearly marked the report "Initial" or "Followup" as appropriate in item G7 on FDA Form 3500A? Do not package and send a 15-day followup report with a non-15 day followup report.
5. Have you included the name, address, and telephone number of the initial reporter in item E1 on FDA Form 3500A?
6. Have you left all the boxes in item B2 of the FDA Form 3500A blank for a nonserious adverse experience? A box should only be checked in item B2 if the outcome for the adverse experience is serious.
7. Have you included all relevant attachments and eliminated unnecessary attachments?

Attachments can include copies of:

- hospital discharge summaries
- autopsy/biopsy reports
- death certificates
- relevant office visit notes
- summaries of relevant laboratory tests and other diagnostic procedures, particularly pre- and post-drug values.

Each page of an attachment should identify the manufacturer report number (i.e., reported in item G9 on FDA Form 3500A) for that case.

In general, attachments should not include:

- lengthy legal records

- 1568 • complete medical records  
1569  
1570  
1571 8. If two or more products produced by your company were suspected by the  
1572 initial reporter:  
1573  
1574 • Have you completed only one FDA Form 3500A? (You should not  
1575 prepare more than one FDA Form 3500A even if more than one of  
1576 the suspect products was produced by your company.)  
1577  
1578 • Have you identified all the suspect products in item C1 on FDA Form  
1579 3500A?  
1580  
1581 • Have you indicated on FDA Form 3500A the product considered  
1582 most suspect by the initial reporter and prepared the report  
1583 accordingly? (If the initial reporter ranked them equally, you should  
1584 submit an FDA Form 3500A to the file of the first suspect product in  
1585 alphabetical order. You should list the adverse experience(s) for each  
1586 of the other suspected product(s) in the narrative summary section of  
1587 the periodic report.)  
1588  
1589 9. Have you completed an FDA Form 3500A for another applicant's drug?  
1590 (You should send the report to the FDA if the applicant of the suspect product  
1591 is unknown or the report is for a serious, unexpected adverse experience  
1592 occurring during the conduct of a study. For all other cases, you should send  
1593 the report to the applicant holder of the suspect drug and not to the FDA.)  
1594

1595 **B. For 15-Day Reports**  
1596

- 1597 1. Have you clearly marked "15-Day Report" in item G7 on the FDA Form  
1598 3500A?  
1599  
1600 2. Have you packaged the 15-day report (FDA Form 3500A initial or followup)  
1601 separately? (Do not package and send an initial 15-day report with a 15-day  
1602 followup report. You should not submit copies of 15-day reports with a  
1603 periodic report.)  
1604  
1605 3. Have you submitted the report in duplicate? (Exceptions: for prescription  
1606 drugs marketed for human use without an approved application and for drugs  
1607 with approved ANDAs, only a single copy should be sent.)  
1608  
1609 4. Have you clearly marked the outside mailing envelope "15-Day Report"?

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**C. For Periodic Reports**

1. Have you included the four types of information required for a periodic report and clearly separated the four sections with marked tabs?
2. Have you submitted the report in duplicate? (Exception: For drugs with approved ANDAs, only a single copy should be sent).
3. Have you eliminated all unnecessary attachments to FDA Form 3500As?

**D. For Followup Reports**

- I. Have you included the manufacturer report number in item G9 on FDA Form 3500A? (Note: this number should be identical to the manufacturer report number on the initial report).
2. Have you marked *ifollowup@* in item G7 on FDA Form 3500A and indicated what number followup report it is?

# APPENDIX C

For use by user-facilities,  
distributors and manufacturers for  
**MANDATORY** reporting

Form Approved: OMB No. 0910-0291 Expires: 12/31/00  
See OMB statement on reverse

Mfr report #
UF/Dial report #
FDA Use Only

# MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

Page \_\_\_\_ of \_\_\_\_

## A. Patient information

1. Patient identifier	2. Age at time of event: or _____ Date of birth: _____	3. Sex <input type="checkbox"/> female <input type="checkbox"/> male	4. Weight _____ lbs or _____ kgs
-----------------------	--	--	---

## B. Adverse event or product problem

1.  Adverse event and/or  Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

<input type="checkbox"/> death _____ (m/d/yyyy)	<input type="checkbox"/> disability
<input type="checkbox"/> life-threatening	<input type="checkbox"/> congenital anomaly
<input type="checkbox"/> hospitalization – initial or prolonged	<input type="checkbox"/> required intervention to prevent permanent impairment/damage
	<input type="checkbox"/> other: _____

3. Date of event (m/d/yyyy)

4. Date of this report (m/d/yyyy)

## 5. Describe event or problem

6. Relevant tests/laboratory data, including dates

## 7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

## C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)

#1 \_\_\_\_\_

#2 \_\_\_\_\_

2. Dose, frequency & route used

#1 \_\_\_\_\_

#2 \_\_\_\_\_

3. Therapy dates (if unknown, give duration) from/to (or best estimate)

#1 \_\_\_\_\_

#2 \_\_\_\_\_

4. Diagnosis for use (indication)

#1 \_\_\_\_\_

#2 \_\_\_\_\_

5. Event abated after use stopped or dose reduced

#1  yes  no  doesn't apply

#2  yes  no  doesn't apply

6. Lot # (if known)

#1 \_\_\_\_\_

#2 \_\_\_\_\_

7. Exp. date (if known)

#1 \_\_\_\_\_

#2 \_\_\_\_\_

8. Event reappeared after reintroduction

#1  yes  no  doesn't apply

#2  yes  no  doesn't apply

9. NDC # – for product problems only (if known)

#1 \_\_\_\_\_

#2 \_\_\_\_\_

10. Concomitant medical products and therapy dates (exclude treatment of event)

## D. Suspect medical device

1. Brand name

2. Type of device

3. Manufacturer name & address

4. Operator of device

health professional

lay user/patient

other: \_\_\_\_\_

5. Expiration date (m/d/yyyy)

6. model # \_\_\_\_\_

7. If implanted, give date (m/d/yyyy)

8. If explanted, give date (m/d/yyyy)

9. Device available for evaluation? (Do not send to FDA)

yes  no  returned to manufacturer on \_\_\_\_\_ (m/d/yyyy)

10. Concomitant medical products and therapy dates (exclude treatment of event)

## E. Initial reporter

1. Name & address

phone # \_\_\_\_\_

2. Health professional?

yes  no

3. Occupation

4. Initial reporter also sent report to FDA

yes  no  unk

PLEASE TYPE OR USE BLACK INK



Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

# Medication and Device Experience Report

(continued)

Refer to guidelines for specific instructions

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Public Health Service • Food and Drug Administration

Page \_\_\_\_ of \_\_\_\_

FDA Use Only

F. For use by user facility/distributor—devices only		
1. Check one <input type="checkbox"/> user facility <input type="checkbox"/> distributor		2. UF/Dist report number
3. User facility or distributor name/address		
4. Contact person		5. Phone Number
6. Date user facility or distributor became aware of event (m/d/yyyy)	7. Type of report <input type="checkbox"/> initial <input type="checkbox"/> follow-up # _____	8. Date of this report (m/d/yyyy)
9. Approximate age of device	10. Event problem codes (refer to coding manual) patient code: [ ] - [ ] - [ ] device code: [ ] - [ ] - [ ]	
11. Report sent to FDA? <input type="checkbox"/> yes _____ (m/d/yyyy) <input type="checkbox"/> no	12. Location where event occurred <input type="checkbox"/> hospital <input type="checkbox"/> outpatient diagnostic facility <input type="checkbox"/> home <input type="checkbox"/> ambulatory surgical facility <input type="checkbox"/> nursing home <input type="checkbox"/> outpatient treatment facility <input type="checkbox"/> other: _____ specify	
13. Report sent to manufacturer? <input type="checkbox"/> yes _____ (m/d/yyyy) <input type="checkbox"/> no	14. Manufacturer name/address	

G. All manufacturers	
1. Contact office - name/address (& mailing site for devices)	
2. Phone number	
3. Report source (check all that apply) <input type="checkbox"/> foreign <input type="checkbox"/> study <input type="checkbox"/> literature <input type="checkbox"/> consumer <input type="checkbox"/> health professional <input type="checkbox"/> user facility <input type="checkbox"/> company representative <input type="checkbox"/> distributor <input type="checkbox"/> other: _____	
4. Date received by manufacturer (m/d/yyyy)	5. (A)NDA # _____ IND # _____ PLA # _____ pre-1938 <input type="checkbox"/> yes OTC product <input type="checkbox"/> yes
6. If IND, protocol #	8. Adverse event term(s)
7. Type of report (check all that apply) <input type="checkbox"/> 5-day <input type="checkbox"/> 15-day <input type="checkbox"/> 10-day <input type="checkbox"/> periodic <input type="checkbox"/> initial <input type="checkbox"/> follow-up # _____	
9. Mfr. report number	

H. Device manufacturers only	
1. Type of reportable event <input type="checkbox"/> death <input type="checkbox"/> serious injury <input type="checkbox"/> malfunction (see guidelines) <input type="checkbox"/> other: _____	
2. If follow-up, what type? <input type="checkbox"/> correction <input type="checkbox"/> additional information <input type="checkbox"/> response to FDA request <input type="checkbox"/> device evaluation	
3. Device evaluated by mfr? <input type="checkbox"/> not returned to mfr. <input type="checkbox"/> yes <input type="checkbox"/> evaluation summary attached <input type="checkbox"/> no (attach page to explain why not) or provide code: _____	
4. Device manufacture date (m/yy)	
5. Labeled for single use? <input type="checkbox"/> yes <input type="checkbox"/> no	
6. Evaluation codes (refer to coding manual) method: [ ] - [ ] - [ ] - [ ] results: [ ] [ ] [ ] - [ ] conclusions: [ ] - [ ] - [ ] - [ ]	
7. If remedial action initiated, check type <input type="checkbox"/> recall <input type="checkbox"/> notification <input type="checkbox"/> repair <input type="checkbox"/> inspection <input type="checkbox"/> replace <input type="checkbox"/> patient monitoring <input type="checkbox"/> relabeling <input type="checkbox"/> modification/adjustment <input type="checkbox"/> other: _____	
8. Usage of device <input type="checkbox"/> initial use of device <input type="checkbox"/> reuse <input type="checkbox"/> unknown	
9. If action reported to FDA under 21 USC 360(i)(f), list correction/removal reporting number:	

10. <input type="checkbox"/> Additional manufacturer narrative	and/or	11. <input type="checkbox"/> Corrected data
--	--------	---


The public reporting burden for this collection of information has been estimated to average one-hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS Reports Clearance Office  
Paperwork Reduction Project (0910-0291)  
Hubert H. Humphrey Building, Room 531-H  
200 Independence Avenue, S.W.  
Washington, D.C. 20201

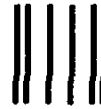
"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."

Please DO NOT RETURN this form to this address.

**APPENDIX D**

 <p><b>VACCINE ADVERSE EVENT REPORTING SYSTEM</b>                  24 Hour Toll-free information line 1-800-822-7967                  P.O. Box 1100, Rockville, MD 20849-1100  <b>PATIENT IDENTITY KEPT CONFIDENTIAL</b></p>			<i>For CDC/FDA Use Only</i> VAERS Number _____ Date Received _____					
<b>Patient Name:</b> Last _____ First _____ MI _____ Address _____ _____ City _____ State _____ Zip _____ Telephone no. (____) _____			<b>Vaccine administered by (Name):</b> Responsible Physician _____ Facility Name/Address _____ _____ City _____ State _____ Zip _____ Telephone no. (____) _____			<b>Form completed by (Name):</b> Relation <input type="checkbox"/> Vaccine Provider <input type="checkbox"/> Patient/Parent to Patient <input type="checkbox"/> Manufacturer <input type="checkbox"/> Other Address (if different from patient or provider) _____ _____ City _____ State _____ Zip _____ Telephone no. (____) _____		
1. State	2. County where administered	3. Date of birth mm / dd / yy	4. Patient age	5. Sex M F	6. Date form completed mm / dd / yy			
7. Describe adverse event(s) (symptoms, signs, time course) and treatment, if any				8. Check all appropriate: <input type="checkbox"/> Patient died (date ____ / ____ / ____) <input type="checkbox"/> Life threatening illness mm dd yy <input type="checkbox"/> Required emergency room/doctor visit <input type="checkbox"/> Required hospitalization (____ days) <input type="checkbox"/> Resulted in prolongation of hospitalization <input type="checkbox"/> Resulted in permanent disability <input type="checkbox"/> None of the above				
9. Patient recovered <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> UNKNOWN				10. Date of vaccination mm / dd / yy AM PM	11. Adverse event onset mm / dd / yy AM PM			
12. Relevant diagnostic tests/laboratory data								
13. Enter all vaccines given on date listed in no. 10								
Vaccine (type)		Manufacturer	Lot number	Route/Site	No. Previous doses			
a. _____		_____	_____	_____	_____			
b. _____		_____	_____	_____	_____			
c. _____		_____	_____	_____	_____			
d. _____		_____	_____	_____	_____			
14. Any other vaccinations within 4 weeks of date listed in no. 10								
Vaccine (type)		Manufacturer	Lot number	Route/Site	No. Previous doses			
a. _____		_____	_____	_____	_____			
b. _____		_____	_____	_____	_____			
15. Vaccinated at: <input type="checkbox"/> Private doctor's office/hospital <input type="checkbox"/> Public health clinic/hospital		16. Vaccine purchased with: <input type="checkbox"/> Military clinic/hospital <input type="checkbox"/> Other/unknown <input type="checkbox"/> Private funds <input type="checkbox"/> Public funds <input type="checkbox"/> Military funds <input type="checkbox"/> Other/unknown		17. Other medications				
18. Illness at time of vaccination (specify)			19. Pre-existing physician-diagnosed allergies, birth defects, medical conditions (specify)					
20. Have you reported this adverse event previously? <input type="checkbox"/> No <input type="checkbox"/> To health department <input type="checkbox"/> To doctor <input type="checkbox"/> To manufacturer			<i>Only for children 5 and under</i>					
			22. Birth weight _____ lb. _____ oz.	23. No. of brothers and sisters				
21. Adverse event following prior vaccination (check all applicable, specify) Adverse Event Onset Age Type Vaccine Dose no. in series <input type="checkbox"/> In patient <input type="checkbox"/> In brother or sister			<i>Only for reports submitted by manufacturer/immunization project</i>					
			24. Mfr. / imm. proj. report no.	25. Date received by mfr. / imm. proj.				
			26. 15 day report? <input type="checkbox"/> Yes <input type="checkbox"/> No	27. Report type <input type="checkbox"/> Initial <input type="checkbox"/> Follow-Up				
Health care providers and manufacturers are required by law (42 USC 300aa-25) to report reactions to vaccines listed in the Vaccine Injury Table. Reports for reactions to other vaccines are voluntary except when required as a condition of immunization grant awards.								

**"Fold in thirds, tape & mail - DO NOT STAPLE FORM"**



**NO POSTAGE  
NECESSARY  
IF MAILED  
IN THE  
UNITED STATES  
OR APO/FPO**

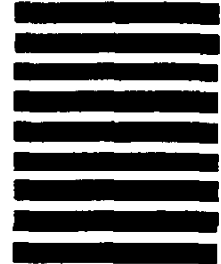
**BUSINESS REPLY MAIL**  
FIRST CLASS MAIL PERMIT NO. 1005 ROCKVILLE, MD

POSTAGE WILL BE PAID BY ADDRESSEE



**VAERS**

c/o Ogden BioServices Corporation  
P.O. Box 1100  
Rockville MD 20849-1100



**DIRECTIONS FOR COMPLETING FORM**

(Additional pages may be attached if more space is needed.)

**GENERAL**

- Use a separate form for each patient. Complete the form to the best of your abilities. Items 3, 4, 7, 8, 10, 11, and 13 are considered essential and should be completed whenever possible. Parents/Guardians may need to consult the facility where the vaccine was administered for some of the information (such as manufacturer, lot number or laboratory data.)
- Refer to the Vaccine Injury Table (VIT) for events mandated for reporting by law. Reporting for other serious events felt to be related but not on the VIT is encouraged.
- Health care providers other than the vaccine administrator (VA) treating a patient for a suspected adverse event should notify the VA and provide the information about the adverse event to allow the VA to complete the form to meet the VA's legal responsibility.
- These data will be used to increase understanding of adverse events following vaccination and will become part of CDC Privacy Act System 09-20-0136, "Epidemiologic Studies and Surveillance of Disease Problems". Information identifying the person who received the vaccine or that person's legal representative will not be made available to the public, but may be available to the vaccinee or legal representative.
- Postage will be paid by addressee. Forms may be photocopied (must be front & back on same sheet).

**SPECIFIC INSTRUCTIONS**

Form Completed By: To be used by parents/guardians, vaccine manufacturers/distributors, vaccine administrators, and/or the person completing the form on behalf of the patient or the health professional who administered the vaccine.

- Item 7: Describe the suspected adverse event. Such things as temperature, local and general signs and symptoms, time course, duration of symptoms diagnosis, treatment and recovery should be noted.
- Item 9: Check "YES" if the patient's health condition is the same as it was prior to the vaccine, "NO" if the patient has not returned to the pre-vaccination state of health, or "UNKNOWN" if the patient's condition is not known.
- Item 10: Give dates and times as specifically as you can remember. If you do not know the exact time, please
- and 11: indicate "AM" or "PM" when possible if this information is known. If more than one adverse event, give the onset date and time for the most serious event.
- Item 12: Include "negative" or "normal" results of any relevant tests performed as well as abnormal findings.
- Item 13: List ONLY those vaccines given on the day listed in Item 10.
- Item 14: List ANY OTHER vaccines the patient received within four weeks of the date listed in Item 10.
- Item 16: This section refers to how the person who gave the vaccine purchased it, not to the patient's insurance.
- Item 17: List any prescription or non-prescription medications the patient was taking when the vaccine(s) was given.
- Item 18: List any short term illnesses the patient had on the date the vaccine(s) was given (i.e., cold, flu, ear infection).
- Item 19: List any pre-existing physician-diagnosed allergies, birth defects, medical conditions (including developmental and/or neurologic disorders) the patient has.
- Item 21: List any suspected adverse events the patient, or the patient's brothers or sisters, may have had to previous vaccinations. If more than one brother or sister, or if the patient has reacted to more than one prior vaccine, use additional pages to explain completely. For the onset age of a patient, provide the age in months if less than two years old.
- Item 26: This space is for manufacturers' use only.



# APPENDIX E

CIOMS FORM

<p><b>SUSPECT ADVERSE REACTION REPORT</b></p>	

## I. REACTION INFORMATION

1. PATIENT INITIALS <small>(first, last)</small>	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION  <input type="checkbox"/> PATIENT DIED  <input type="checkbox"/> INVOLVED OR PROLONGED INPATIENT HOSPITALISATION  <input type="checkbox"/> INVOLVED PERSISTENCE OR SIGNIFICANT DISABILITY OR INCAPACITY  <input type="checkbox"/> LIFE THREATENING
		Day	Month	Year	Years		Day	Month	Year	
7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)										

## II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)		20 DID REACTION ABATE AFTER STOPPING DRUG? <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> NA
15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION	21. DID REACTION REAPPEAR AFTER REINTRODUCTION? <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> NA
17. INDICATION(S) FOR USE		
18. THERAPY DATES (from/to)		19. THERAPY DURATION

## III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

## IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER	
	24b. MFR CONTROL NO.
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE <input type="checkbox"/> STUDY <input type="checkbox"/> LITERATURE <input type="checkbox"/> HEALTH PROFESSIONAL
DATE OF THIS REPORT	25a. REPORT TYPE <input type="checkbox"/> INITIAL <input type="checkbox"/> FOLLOWUP

APPENDIX F

Form Approved: OMB No. 0910-0291 Expires: 01/31/81  
See OMB statement on reverse

# MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

For use by user-facilities,  
distributors and manufacturers for  
**MANDATORY** reporting

Page \_\_\_ of \_\_\_

Mfr report #
UD/Dist report #
FDA Use Only

A. Patient information			
1. Patient Identifier	2. Age at time of event: or Date of birth:	3. Sex <input type="checkbox"/> female <input type="checkbox"/> male	4. Weight ____ lbs or ____ kgs
In confidence			
B. Adverse event or product problem			
1. <input type="checkbox"/> Adverse event and/or <input type="checkbox"/> Product problem (e.g., defects/malfunctions)			
2. Outcomes attributed to adverse event (check all that apply)			
<input type="checkbox"/> death (m/d/yyyy)	<input type="checkbox"/> life-threatening	<input type="checkbox"/> hospitalization - initial or prolonged	<input type="checkbox"/> disability <input type="checkbox"/> congenital anomaly <input type="checkbox"/> required intervention to prevent permanent impairment/damage <input type="checkbox"/> other: _____
3. Date of event (m/d/yyyy)	4. Date of this report (m/d/yyyy)		
5. Describe event or problem			
6. Relevant tests/laboratory data, including dates			
7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)			

C. Suspect medication(s)			
1. Name (give labeled strength & mfr/labeler, if known)			
#1 _____			
#2 _____			
2. Dose, frequency & route used		3. Therapy dates (if unknown, give duration) (m/d/yyyy or best estimate)	
#1 _____		#1 _____	
#2 _____		#2 _____	
4. Diagnosis for use (indication)		5. Event abated after use stopped or dose reduced	
#1 _____		#1 <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> doesn't apply	
#2 _____		#2 <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> doesn't apply	
6. Lot # (if known)		7. Exp. date (if known)	
#1 _____		#1 _____	
#2 _____		#2 _____	
8. Event reappeared after reintroduction			
#1 <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> doesn't apply			
#2 <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> doesn't apply			
9. NDC # - for product problems only (if known)			
- - - - -			
10. Concomitant medical products and therapy dates (exclude treatment of event)			

G. All manufacturers	
1. Contact office - name/address (& mfring site for devices)	2. Phone number
3. Report source (check all that apply)	
<input type="checkbox"/> foreign	
<input type="checkbox"/> study	
<input type="checkbox"/> literature	
<input type="checkbox"/> consumer	
<input type="checkbox"/> health professional	
<input type="checkbox"/> user facility	
<input type="checkbox"/> company representative	
<input type="checkbox"/> distributor	
<input type="checkbox"/> other: _____	
4. Date received by manufacturer (m/d/yyyy)	5. (A)NDA # _____
6. If IND, protocol #	IND # _____
7. Type of report (check all that apply)	PLA # _____
<input type="checkbox"/> 5-day <input type="checkbox"/> 15-day	pre-1938 <input type="checkbox"/> yes
<input type="checkbox"/> 10-day <input type="checkbox"/> periodic	OTC product <input type="checkbox"/> yes
<input type="checkbox"/> initial <input type="checkbox"/> follow-up # _____	8. Adverse event term(s)
9. Mfr. report number	

E. Initial reporter			
1. Name & address		phone #	
2. Health professional? <input type="checkbox"/> yes <input type="checkbox"/> no			
3. Occupation			
4. Initial reporter also sent report to FDA <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unk			

PLEASE TYPE OR USE BLACK INK



Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.