

**CORPORATE INTEGRITY AGREEMENT  
BETWEEN THE  
OFFICE OF INSPECTOR GENERAL  
OF THE  
DEPARTMENT OF HEALTH AND HUMAN SERVICES  
AND  
SHIRE NORTH AMERICAN GROUP, INC.**

**I. PREAMBLE**

Shire North American Group, Inc., on behalf of itself and its operating subsidiaries, including but not limited to Shire Pharmaceuticals, LLC (SP, LLC) (collectively, “Shire”), and pursuant to authority granted by the Board of Directors of Shire plc, hereby enters into this Corporate Integrity Agreement (CIA) with the Office of Inspector General (OIG) of the United States Department of Health and Human Services (HHS) to promote compliance with the statutes, regulations, and written directives of Medicare, Medicaid, and all other Federal health care programs (as defined in 42 U.S.C. § 1320a-7b(f)) (Federal health care program requirements) and with the statutes, regulations, and written directives of the Food and Drug Administration (FDA requirements).

Contemporaneously with this CIA, SP, LLC is entering into a Settlement Agreement with the United States. SP, LLC will also enter into settlement agreements with various States (State Settlement Agreements) and Shire’s agreement to this CIA is a condition precedent to those agreements.

Prior to the Effective Date of this CIA (as defined below), Shire established a U.S. Compliance Program. Shire’s U.S. Compliance Program includes a Senior Vice President and Chief Compliance and Risk Officer, a Compliance Department, and a U.S. Compliance Committee. The U.S. Compliance Program also includes a Code of Ethics, written policies and procedures, educational and training initiatives, a disclosure program, procedures for investigating potential compliance violations, disciplinary procedures, and regular internal monitoring and auditing procedures.

Shire shall continue its U.S. Compliance Program throughout the term of this CIA and shall do so in accordance with the terms set forth below. Shire may modify its U.S. Compliance Program as appropriate, but, at a minimum, Shire shall ensure that during the

term of this CIA, it shall comply with the obligations set forth herein.

## **II. TERM AND SCOPE OF THE CIA**

A. The period of the compliance obligations assumed by Shire under this CIA shall be five years from the Effective Date of this CIA. The “Effective Date” shall be the date on which the final signatory of this CIA executes this CIA. Each one-year period, beginning with the one-year period following the Effective Date, shall be referred to as a “Reporting Period.”

B. Sections VII, X, and XI shall expire no later than 120 days after OIG’s receipt of: (1) Shire’s final Annual Report (as defined below in Section V); or (2) any additional materials submitted by Shire pursuant to OIG’s request, whichever is later.

C. The scope of this CIA shall be governed by the following definitions:

1. “Covered Persons” includes:

- a. all owners of Shire plc or Shire (as defined above) who are natural persons (other than shareholders who: (i) have an ownership interest of less than 5% and (ii) acquired the ownership interest through public trading);
- b. all officers, directors, and employees of Shire plc or Shire who are engaged in or have job responsibilities relating to any of the Covered Functions (as defined below in Section II.C.7); and
- c. all contractors, subcontractors, agents, and other persons who perform any of the Covered Functions on behalf of Shire plc, or Shire and in that capacity either: (i) interact directly with health care professionals (HCPs), health care institutions (HCIs), Payors (as defined below in Section II.C.6), or consumers; or (ii) perform activities, provide services, or create materials relating to the Covered Functions and those activities, services, or materials are not reviewed or supervised by a Shire plc or Shire employee who is a Covered Person prior to execution or dissemination.

Notwithstanding the above, the term Covered Persons does not include part-time or per diem employees, contractors, subcontractors, agents, and other persons who are not reasonably expected to work more than 160 hours per year, except that any such individuals shall become “Covered Persons” at the point when they work more than 160 hours during the calendar year.

2. “Relevant Covered Persons” includes all Covered Persons who engage in any of the Covered Functions and all individuals who supervise Covered Persons who engage in any of the Covered Functions.

3. “Government Reimbursed Products” refers to all Shire products that are: (a) marketed or sold by Shire in the United States (or pursuant to contracts with the United States) and (b) reimbursed by Federal health care programs.

4. The term “Promotional Functions” includes: (a) the selling, detailing, marketing, advertising, promoting, or branding of Government Reimbursed Products; and (b) the preparation or external dissemination of promotional materials or information about, or the provision of promotional services relating to, Government Reimbursed Products, including those functions relating to Shire’s review process for materials and any applicable review committee for promotional materials.

5. The term “Product Related Functions” includes: (a) the preparation or external dissemination of non-promotional materials that are governed by Federal health care program and/or FDA requirements and distributed to HCPs, HCIs, and Payors about Government Reimbursed Products, including those functions relating to any applicable review committees and those functions involved in scientific exchange (such as medical affairs); (b) contracting with HCPs licensed in the United States to conduct post-marketing clinical trials, Investigator-Sponsored Studies, Investigator Initiated Trials, or Investigator Initiated Research (Investigator-Sponsored Studies, Investigator Initiated Trials, and Investigator Initiated Research referred to hereafter as “ISSs”), and any other types of post-marketing studies relating to Government Reimbursed Products; (c) authorship, publication, and disclosure of articles or study results relating to Government Reimbursed Products; and (d) activities related to the submission of information about Government Reimbursed Products to compendia (such as Drugdex or other compendia of information about Government Reimbursed Products).

6. The term “Payor Related Functions” refers to Promotional Functions and Product Related Functions as they relate to interactions (including contracting functions) between Shire and entities that provide a drug health benefit program for Government Reimbursed Products, including but not limited to government payors (*e.g.*, Medicaid and Medicare) or individuals or entities under contract with or acting on behalf of government payors and commercial health plans (collectively referred to as “Payors”). Payor Related Functions also includes interactions with Payors related to formulary placement, supplemental rebate agreements, and other types of rebate agreements.

7. The term “Covered Functions” refers to “Promotional Functions,” “Product Related Functions,” and “Payor Related Functions” collectively.

8. The term “Independent Medical Education Activity” shall mean any professional program, meeting, or event, including but not limited to, continuing medical education (CME) or symposia, conducted by a third party, such as an accredited medical education provider, and supported by Shire to educate individuals such as HCPs about pharmaceutical therapies, disease states, and other topics.

9. The term “Third Party Personnel” shall mean personnel, if any, who perform Promotional Functions or Product Related Functions and are employees of entities with whom Shire has or may in the future (during the term of this CIA) enter into agreements to promote or co-promote a Government Reimbursed Product in the United States or to engage in joint promotional activities in the United States relating to such a product. Shire has represented that: (a) Third Party Personnel are employed by entities other than Shire; (b) Shire does not control the Third Party Personnel; and (c) it would be commercially impracticable to compel the compliance of Third Party Personnel with the requirements set forth in this CIA. Shire agrees that Shire shall promote compliance by Third Party Personnel with Federal health care program requirements and FDA requirements by complying with the provisions set forth below in Sections III.B.2, V.A.7, and V.B.5. Provided that Shire complies with the requirements of Sections III.B.2, V.A.7, and V.B.5, Shire shall not be required to fulfill the other CIA obligations that would otherwise apply to Third Party Personnel who meet the definition of Covered Persons.

10. The term “Shire Affiliate(s)” shall include any entity, other than Shire North American Group, Inc. or its operating subsidiaries, that is owned or controlled, directly or indirectly, by Shire plc and whose employees or contractors perform any Covered Functions. All obligations set forth in Section III below apply to

the Covered Functions performed by Shire Affiliates, all references to “Shire” in the defined terms set forth in this Section II shall mean Shire and Shire Affiliate(s), and qualified Shire personnel shall supervise any Shire Affiliate employee or contractor who performs Covered Functions. In addition, the notice requirements in Section IV and the certification obligations set forth in Section V.C. below shall apply to Shire and any Shire Affiliate(s).

### **III. CORPORATE INTEGRITY OBLIGATIONS**

Shire shall establish and maintain a U.S. Compliance Program that includes the following elements:

#### **A. Compliance Officer, Compliance Committee, Board of Directors, and Management and Accountability Certifications**

1. *Compliance Officer.* Since prior to the Effective Date, Shire has had in place an individual to serve as its chief compliance officer (known as its Senior Vice President and Chief Compliance and Risk Officer or CCRO). Shire shall maintain a CCRO for the term of the CIA who fulfills, at a minimum, the obligations set forth in this CIA. The CCRO is and shall continue to be responsible for developing and implementing policies, procedures, and practices designed to ensure compliance with the requirements set forth in this CIA and with Federal health care program requirements and FDA requirements. The CCRO is and shall continue to be a member of senior management of Shire plc, shall report directly to the Chief Executive Officer of Shire plc, shall make periodic (at least quarterly) reports regarding compliance matters directly to the Board of Directors of Shire plc, or a subcommittee thereof, and is and shall continue to be authorized to report on such matters to the Board of Directors of Shire plc at any time. The CCRO is not and shall not be or be subordinate to the General Counsel or Chief Financial Officer of Shire plc or Shire. The CCRO is and shall continue to be responsible for monitoring the day-to-day compliance activities that are required by this CIA and engaged in by Shire, as well as for any reporting obligations created under this CIA. Any job responsibilities of the CCRO unrelated to compliance shall be limited and must not interfere with the CCRO’s ability to perform the duties outlined in this CIA.

Shire shall report to OIG, in writing, any change in the identity of the CCRO, or any actions or changes that would affect the CCRO’s ability to perform the duties necessary to meet the obligations in this CIA, within five days after such a change.

2. *Compliance Committee.* Since prior to the Effective Date, Shire has had in place a U.S. Compliance Committee specifically focused on its U.S. business which, in conjunction with the CCRO assists in the implementation and enhancement of the U.S. Compliance Program. Shire shall maintain a U.S. Compliance Committee during the term of this CIA that, at a minimum, meets the obligations set forth in this Section III.A.2. The U.S. Compliance Committee shall, at a minimum, include the CCRO and other members of senior management necessary to meet the requirements of this CIA (*e.g.*, senior executives of relevant departments and functional areas), such as sales and marketing, human resources, and finance. The CCRO, or the individual who serves as Head of Americas Compliance as of the Effective Date of this CIA, shall chair the U.S. Compliance Committee, and the U.S. Compliance Committee shall support the CCRO in fulfilling his/her responsibilities (*e.g.*, shall assist in the analysis of Shire's risk areas and shall oversee monitoring of internal and external audits and investigations). The U.S. Compliance Committee shall meet at least quarterly.

Shire shall report to OIG, in writing, any changes in the composition of the U.S. Compliance Committee, or any actions or changes that would affect the U.S. Compliance Committee's ability to perform the duties necessary to meet the obligations in this CIA, within 15 days after such a change.

3. *Board of Directors Compliance Obligations.* The Board of Directors (or a Committee of the Board) of Shire plc (Board) shall be responsible for the review and oversight of matters related to compliance with Federal health care program requirements and FDA requirements and the obligations of this CIA. The Board must include independent (*i.e.*, non-executive) members.

The Board (or a Committee of the Board) shall, at a minimum, be responsible for the following:

- a. meeting at least quarterly to review and oversee Shire's U.S. Compliance Program, including but not limited to the performance of the CCRO and U.S. Compliance Committee;
- b. evaluating the effectiveness of the U.S. Compliance Program, including at a minimum, by receiving updates about the activities of the CCRO and other compliance personnel and updates about the adoption and implementation of policies, procedures, and practices designed to ensure compliance with

the requirements set forth in this CIA and with applicable Federal health care program requirements and FDA requirements; and

- c. for each Reporting Period of the CIA, adopting a resolution, signed by each member of the Board or Committee of the Board summarizing its review and oversight of Shire's compliance with Federal health care program requirements and FDA requirements, and the obligations of this CIA.

At minimum, the resolution shall include the following language:

“The Board of Directors [or a Committee of the Board] has made a reasonable inquiry into the operations of Shire's U.S. Compliance Program including the performance of the CCRO and the U.S. Compliance Committee. Based on its inquiry and review, the Board has concluded that, to the best of its knowledge, Shire has implemented an effective Compliance Program to meet Federal health care program requirements and FDA requirements and the obligations of the CIA.”

If the Board, or a Committee of the Board, is unable to provide such a conclusion in the resolution, the Board shall include in the resolution a written explanation of the reasons why it is unable to provide the conclusion and the steps it is taking to implement an effective U.S. Compliance Program at Shire.

Shire shall report to OIG, in writing, any changes in the composition of the Board, or any actions or changes that would affect the Board's ability to perform the duties necessary to meet the obligations in this CIA, within 15 days after such a change.

4. *Management Accountability and Certifications.* In addition to the responsibilities set forth in this CIA for all Covered Persons, certain Shire officers or employees (Certifying Employees) are specifically expected to monitor and oversee activities within their areas of authority and shall annually certify that the applicable Shire business unit is compliant with applicable Federal health care program requirements and FDA requirements and with the obligations of this CIA. These Certifying Employees shall include, at a minimum, Chief Executive Officer, Senior Vice President and Head of the Rare Diseases Business Unit, Senior Vice President and Head of the Internal Medicine Business Unit, Senior Vice President and Head of the Gastrointestinal Disease Business Unit, Senior Vice President and Head of the

Neuroscience Business Unit, Executive Vice President and Head of Research and Development, Senior Vice President and Head of Global Commercial Operations, and Senior Vice President and Head of Global Market Access; and, to the extent that a Shire business unit performs Covered Functions and is not covered by the certifications of one of the above-listed individuals, such other Shire executives, vice-presidents, or leaders of business units as would be necessary to ensure that there is a Certifying Employee from each such business unit or functional area engaged in Covered Functions.

For each Reporting Period, each Certifying Employee shall sign a certification that states:

“I have been trained on and understand the compliance requirements and responsibilities as they relate to [insert name of department or functional area], an area under my supervision. My job responsibilities include ensuring compliance with regard to the \_\_\_\_\_ [insert name of the department or functional area] with all applicable Federal health care program requirements, FDA requirements, obligations of the Corporate Integrity Agreement, and Shire policies, and I have taken steps to promote such compliance. To the best of my knowledge, except as otherwise described herein, the \_\_\_\_\_ [insert name of department or functional area] of [insert applicable Shire entity name] is in compliance with all applicable Federal health care program requirements, FDA requirements, and the obligations of the Corporate Integrity Agreement. I understand that this certification is being provided to and relied upon by the United States.”

If any Certifying Employee is unable to provide such a conclusion in the certification, the Certifying Employee shall provide a written explanation of the reasons why he or she is unable to provide the certification outlined above and the steps being taken to address the issue(s) identified in the certification.

## B. Written Standards

1. *Code of Ethics.* Prior to the Effective Date, Shire developed, implemented, and distributed to all Covered Persons a written Code of Ethics that, at a minimum, met the requirements of this Section III.B. Shire shall make the promotion of, and adherence to, the Code of Ethics an element in evaluating the performance of all employees who are Covered Persons. The Code of Ethics shall, at a minimum, set forth:



- a. Shire's commitment to full compliance with all Federal health care program requirements and FDA requirements, including its commitment to comply with all requirements relating to the Covered Functions;
- b. Shire's requirement that all Covered Persons shall be expected to comply with all Federal health care program requirements, FDA requirements, and with Shire's own Policies and Procedures;
- c. Shire's requirement that all Covered Persons shall be expected to report to the CCRO, or other appropriate individual designated by Shire, suspected violations of any Federal health care program requirements, FDA requirements, or of Shire's Policies and Procedures;
- d. the personal obligations of each Covered Person to comply with Federal health care program requirements, FDA requirements, and Shire's Policies and Procedures; and
- e. the right of all individuals to use the Disclosure Program described in Section III.F, and Shire's commitment to nonretaliation and to maintain, as appropriate, confidentiality and anonymity with respect to such disclosures.

To the extent not already accomplished within 90 days prior to the Effective Date, within 120 days after the Effective Date, each Covered Person shall certify, in writing or in electronic form, that he or she has received, read, understood, and shall abide by Shire's Code of Ethics. New Covered Persons shall receive the Code of Ethics and shall complete the required certification within 30 days after becoming a Covered Person or within 120 days after the Effective Date, whichever is later.

Shire shall periodically review the Code of Ethics to determine if revisions are appropriate and shall make any necessary revisions based on such review. The Code of Ethics shall be distributed at least annually to all Covered Persons.

2. *Third Party Personnel.* Within 120 days after the Effective Date, and annually thereafter by the anniversary of the Effective Date, Shire shall send,

electronically or in hard copy format, a letter to each entity employing Third Party Personnel. The letter shall outline Shire's obligations under the CIA and their commitment to full compliance with all Federal health care program requirements and FDA requirements. The letter shall include a description of Shire's U.S. Compliance Program. Shire shall include with the letter a copy of Shire's Code of Ethics and shall request the entity employing Third Party Personnel to either: (a) make a copy of Shire's Code of Ethics and a description of Shire's Compliance Program available to its Third Party Personnel; or (b) represent to Shire that it has and enforces a substantively comparable code of conduct and compliance program for its Third Party Personnel.

3. *Policies and Procedures.* To the extent not already accomplished and within 120 days after the Effective Date, Shire shall implement written Policies and Procedures regarding the operation of its U.S. Compliance Program and compliance with Federal health care program requirements and FDA requirements (Policies and Procedures). The Policies and Procedures shall address, at a minimum, the following:

- a. the subjects relating to the Code of Ethics identified in Section III.B.1;
- b. appropriate ways to conduct Promotional Functions in compliance with all applicable Federal health care program requirements, including, but not limited to the Federal Anti-Kickback Statute (codified at 42 U.S.C. § 1320a-7b(b)) and the False Claims Act (codified at 31 U.S.C. §§ 3729-3733), and in compliance with all applicable FDA requirements, including but not limited to requirements relating to the dissemination of information that is fair, accurate, and supported by clinically significant data;
- c. appropriate ways to conduct Product Related Functions in compliance with all applicable Federal health care program requirements, including, but not limited to the Federal Anti-Kickback Statute (codified at 42 U.S.C. § 1320a-7b(b)) and the False Claims Act (codified at 31 U.S.C. §§ 3729-3733), and in compliance with all applicable FDA requirements;
- d. appropriate ways to conduct Payor Related Functions in compliance with all: (i) applicable Federal health care program,

requirements, including but not limited to the Federal Anti-Kickback Statute (codified at 42 U.S.C. § 1320a-7b(b)) and the False Claims Act (codified at 31 U.S.C. §§ 3729-3733); (ii) applicable FDA requirements; and (iii) applicable state laws;

- e. the materials and information that may be distributed by sales representatives about Government Reimbursed Products, including a requirement that such materials and information be fair, accurate and supported by clinically significant data as required by law; and the manner in which sales representatives respond to requests for information about non-FDA approved (or “off-label”) uses of Government Reimbursed Products. These Policies and Procedures shall require that sales representatives: (i) not engage in off-label promotion of Government Reimbursed Products (*i.e.*, sales representatives shall not promote the products for usages, dosages, length of treatment, or patient populations other than those in, or consistent with, the FDA-approved label); and (ii) refer all requests for information about off-label uses of Government Reimbursed Products to the medical affairs function;
- f. the materials and information that may be distributed by medical affairs personnel, including the requirement that such materials and information be fair, accurate and supported by clinically significant data as required by law; and the mechanisms through, and manner in which, medical affairs personnel receive and respond to requests for information from an HCP or another individual or entity about off-label uses of Government Reimbursed Products; the form and content of information disseminated by Shire in response to such requests; and the internal review process for the information disseminated.

The Policies and Procedures shall include a requirement that Shire develop databases for use by medical affairs personnel (Inquiries Databases) to track all requests for information about Government Reimbursed Products made to medical affairs personnel. The Inquiries Databases shall include the following items of information for each unique inquiry (Inquiry) received

for information about Government Reimbursed Products: (i) date of Inquiry; (ii) form of Inquiry (*e.g.*, fax, phone, etc.); (iii) name of the requesting HCP, HCI, or other individual or entity; (iv) nature and topic of request (including exact language of the Inquiry if made in writing); (v) an evaluation of whether the Inquiry relates to information about an off-label use for the product; (vi) nature/form of the response from Shire (including a record of the materials provided to the HCP or HCI in response to the request); and (vii) the name of the Shire representative who called on or interacted with the HCP, customer, or HCI, if known;

- g. the manner and circumstances under which Medical Science Liaisons (MSLs) interact with or participate in meetings or events with HCPs, HCIs, or Payors (either alone or with sales representatives or account executives) and the role of the MSLs at such meetings or events, as well as how they handle responses to requests for information about off-label uses of Government Reimbursed Products. These Policies and Procedures shall require that MSLs not engage in the off-label promotion of Government Reimbursed Products and provide information about Government Reimbursed Products that is fair, accurate, and supported by clinically significant data, as required by law;
- h. the development, implementation, and review of call plans for sales representatives and other Shire representatives who promote and sell Government Reimbursed Products. For each Government Reimbursed Product, the Policies and Procedures shall require that Shire review the call plans for the product and the bases upon, and circumstances under which HCPs and HCIs belonging to specified medical specialties or types of clinical practice are included in, or excluded from, the call plans. The Policies and Procedures shall also require that Shire design, and modify the call plans, as necessary, in a manner to ensure that Shire is promoting Government Reimbursed Products in a manner that complies with all applicable Federal health care program requirements and FDA requirements. The call plan reviews shall occur at least annually and shall also occur each

time when the FDA approves a new or additional indication for a Government Reimbursed Product;

- i. if Shire distributes samples of, or coupons or vouchers for any Government Reimbursed Product, the development, implementation, and review of policies, procedures, and plans for the distribution of samples of, or coupons or vouchers for such products. This shall include a review of the bases upon, and circumstances under, which HCPs and HCIs belonging to specified medical specialties or types of clinical practice may receive samples from Shire. The Policies and Procedures shall also require that Shire modify plans for the distribution of samples of, or coupons or vouchers for Government Reimbursed Product, as necessary, in a manner designed to ensure that Government Reimbursed Products are promoted in a manner that complies with all applicable Federal health care program requirements and FDA requirements;
- j. consultant or other fee-for-service arrangements relating to Covered Functions and entered into with HCPs or HCIs (including but not limited to speaker programs, speaker training programs, presentations, consultant meetings, advisory boards, and ad hoc advisory activities, and any other financial engagement or arrangement with an HCP or HCI) and all events and expenses relating to such engagements or arrangements. These Policies and Procedures shall be designed to ensure that the arrangements and related events are used for legitimate and lawful purposes in accordance with applicable Federal health care program requirements and FDA requirements. The Policies and Procedures shall include requirements about the content and circumstances of such arrangements and events;
- k. programs to educate sales representatives, including but not limited to presentations by HCPs at sales meetings, and experience-based learning activities, if any. These Policies and Procedures shall be designed to ensure that the programs are used for legitimate and lawful purposes in accordance with applicable Federal health care program requirements and FDA

requirements. The Policies shall include requirements about the content and circumstances of such arrangements and events;

- l. sponsorship or funding of grants (including support for educational programs for non-HCP audiences) to health care related organizations or charitable contributions to health care related organizations. These Policies and Procedures shall be designed to ensure that Shire's funding, sponsorship, or charitable contribution complies with all applicable Federal health care program requirements and FDA requirements;
- m. funding of, or participation in, any Independent Medical Education Activity as defined in Section II.C.8 above. These Policies and Procedures shall be designed to ensure that Shire's funding and/or sponsorship of such programs satisfies all applicable Federal health care program requirements and FDA requirements;

The Policies and Procedures shall require that: (i) Shire or the provider of the Independent Medical Education Activity disclose Shire's financial support of the Independent Medical Education Activity and, to the extent feasible consistent with subsection III.B.3.m.iv below, any financial relationships with faculty, speakers, or organizers at such Activity; (ii) as a condition of funding, the third party provider of the Independent Medical Education Activity shall agree to disclose Shire's financial support of the Independent Medical Education Activity and to require faculty, speakers, or organizers at such Activity to disclose any financial relationship with Shire; (iii) the Independent Medical Education Activity have an educational focus; (iv) the content, organization, and operation of the Independent Medical Education Activity (including the faculty, educational methods, materials, and venue) be independent of Shire's control; (v) Shire support only Independent Medical Education Activity that is non-promotional in tone/nature; (vi) Shire's support of an Independent Medical Education Activity shall be contingent on the provider's commitment to provide information at the Independent Medical Education Activity that

is fair, balanced, accurate and not misleading; (vii) Independent Medical Education Activity funding requests are reviewed and evaluated by the medical affairs function to ensure that the request meets compliance criteria; (viii) funding decisions are based on objective criteria such as the qualifications of the requestor, the quality of the Independent Medical Education Activity program, and pre-established educational goals; (ix) Independent Medical Education Activity funding is provided only pursuant to a written agreement with the funding recipient, and payments to the Independent Medical Education Activity are consistent with the written agreement; and (x) Independent Medical Education Activity programs funded by Shire are developed and implemented independently of Shire staff involvement;

- n. review of promotional, reimbursement, and disease state materials and information intended to be disseminated outside Shire by appropriate qualified personnel (such as regulatory, medical, and/or legal personnel) in a manner designed to ensure that legal, regulatory, and/or medical concerns are properly addressed during Shire's review and approval process and are elevated when appropriate. The Policies and Procedures shall be designed to ensure that such materials and information comply with all applicable Federal health care program requirements and FDA requirements. Among other things, the Policies and Procedures shall require that: (i) applicable review committees review all promotional materials prior to the distribution or use of such materials; and (ii) deviations from the standard review committee practices and protocols (including timetables for the submission of materials for review) shall be documented and referred for appropriate follow-up;
- o. compensation (including through salaries, bonuses, contests, or other means) for Relevant Covered Persons who are sales representatives and their managers. These Policies and Procedures shall: (i) be designed to ensure that financial incentives do not inappropriately motivate such individuals to engage in improper promotion, sales, and marketing of

Government Reimbursed Products; and (ii) include mechanisms, where appropriate, that are designed to exclude from incentive compensation sales that Shire knows or should reasonably be aware were the result of the promotion of non-FDA-approved uses of Government Reimbursed Products or other improper promotion;

- p. the submission of information, if any, about any Government Reimbursed Product to any CMS-recognized compendia, such as Drugdex or other published source of information used in connection with the determination of coverage by a Federal health care program for the product (hereafter “Compendia”). This includes any initial submission of information to any Compendia and the submission of any additional, updated, supplemental, or changed information (including any changes based on Shire’s discovery of erroneous or scientifically unsound information or data associated with the information in the Compendia and the publication of new study results). The Policies and Procedures shall include a requirement that Shire conduct: (i) a review at the time of submission of information to Compendia, to verify that the information submitted to the Compendia (including information about clinical studies and other Research) is complete and accurate; (ii) an annual review of Government Reimbursed Product listings and monographs within the Compendia designed to identify errors or inaccuracies; and (iii) an annual review of all arrangements, processing fees, or other payments or financial support (if any) provided by Shire to any Compendia. Shire’s legal or compliance personnel shall be involved in this review;
  
- q. sponsorship or support by Shire of post-marketing research involving human subjects and Government Reimbursed Products. This includes post-marketing clinical trials and other post-marketing studies sponsored by Shire involving human subjects and Government Reimbursed Products (Shire-Sponsored Research) and support by Shire of ISSs (Shire-Sponsored Research and ISSs supported by Shire are collectively referred to as “Research” for purposes of this CIA), including the decision to



provide financial or other support for such Research; the manner in which Research support is provided; the publication of information about the Research, including the publication of information about the Research results and trial outcomes; and uses made of publications relating to Research;

Policies/Procedures regarding Research:

Shire represents that it requires that all Research sponsored or funded by Shire address a legitimate scientific question or need, and be reviewed and approved by the relevant governance body within its research and development organization. Research and Development personnel are responsible for all steps of the design, conduct, and/or publication of Research. Commercial personnel do not participate in the decision to fund Research or in the approval of the publication of Research results.

Registration of Studies and Publication of Study Results:

Shire represents that it registers Shire-Sponsored Research that involves clinical trials and reports results of such clinical trials on the National Institutes of Health (NIH) sponsored website ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)) in accordance with Shire's Policies and Procedures governing clinical trial disclosure, which shall at minimum require registration consistent with all Federal requirements. Shire shall continue to comply with Federal requirements or other applicable requirements relating to the registration and results reporting of such Shire-Sponsored Research throughout the term of this CIA. In addition, if there is a change in Federal requirements or other applicable requirements relating to registration and results reporting of information about Shire-Sponsored Research, Shire shall fully comply with such requirements.

Shire represents that it has established policies, procedures and practices with respect to prematurely discontinued Shire - Sponsored Research, which require timely notification of the relevant institutional review board or ethics committee about the

decision and reasons for premature discontinuation. As specified in Shire's Policies and Procedures governing clinical trial disclosure, Shire posts status updates with respect to Shire-Sponsored Research (including discontinued studies) to the NIH sponsored website ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)).

Shire represents that it has established policies, systems and practices to ensure that adverse event information regarding its products is collected, processed, analyzed, communicated and reported to the FDA.

While recognizing the decision-making role of the authors and journals, respectively, Shire represents that it makes good faith efforts to publish Shire-Sponsored Research results in peer-reviewed journals and includes specified timeframes for the submission of manuscripts following completion of a Shire-Sponsored Research study in the global publication plan for each Government Reimbursed Product. Shire's Policies and Procedures govern the publication of results from Shire-Sponsored Research. Shire further represents that its written agreements pertaining to ISSs require the investigator to exercise best efforts to publish the results of the ISS.

The standards, policies, and practices described above shall hereafter be referred to collectively as the "Research and Publication Practices." Shire shall maintain its Research and Publication Practices (or standards and practices substantively equivalent to those set forth above) for Research initiated, supported, or completed after the Effective Date for the term of the CIA;

- r. authorship of journal articles or other publications about Government Reimbursed Products or about therapeutic areas or disease states that may be treated with Government Reimbursed Products, including, but not limited to, the disclosure of any and all financial relationships between the author and Shire, or other potential conflicts of interest that might bias the author's work, the identification of all authors or contributors (including

professional writers) associated with a given publication, and the scope and breadth of research results made available to each author or contributor.

Authorship Requirements: Shire represents that it requires all authors of journal articles about Shire-Sponsored Research to adhere to International Committee of Medical Journal Editors (ICMJE) requirements regarding authorship. In addition, Shire requires all authors of articles about Research to disclose any Shire financial support for the study and any financial relationship with Shire (including any financial interest the author may have in Shire, or a Shire product). In addition, Shire represents that individuals may be considered an “author” on a publication about Shire-Sponsored Research only if the individual has made substantial contributions to the study and has given final approval to the version of the publication ultimately published. Shire’s policies and procedures strictly prohibit guest/honorary/gift authorship, ghostwriting, and plagiarism.

The standards, policies and practices described above shall be referred to collectively as “Authorship-Related Practices”; and

- s. disciplinary policies and procedures for violations of the Policies and Procedures, including policies relating to Federal health care program requirements and FDA requirements.

To the extent not already accomplished, within 120 days after the Effective Date, the Policies and Procedures shall be made available to all Covered Persons. Appropriate and knowledgeable staff shall be available to explain the Policies and Procedures.

At least annually (and more frequently, if appropriate), Shire shall assess and update, as necessary, the Policies and Procedures. Within 30 days after the effective date of any revisions, any such revised Policies and Procedures shall be made available to all Covered Persons.

C. Training and Education

1. *General Training.* Within 120 days after the Effective Date, Shire shall provide at least one hour of General Training to each Covered Person. This training, at a minimum, shall explain Shire's:

- a. CIA requirements; and
- b. U.S. Compliance Program, including the Code of Ethics.

New Covered Persons shall receive the General Training described above within 30 days after becoming a Covered Person or within 120 days after the Effective Date, whichever is later. After receiving the initial General Training described above, each Covered Person shall receive at least one hour of General Training in each subsequent Reporting Period.

2. *Specific Training.* Within 120 days after the Effective Date, each Relevant Covered Person shall receive at least three hours of Specific Training in addition to the General Training required above. This Specific Training shall include a discussion of:

- a. all applicable Federal health care program requirements relating to Covered Functions;
- b. all applicable FDA requirements relating to Covered Functions;
- c. all Shire Policies and Procedures and other requirements applicable to Covered Functions;
- d. Shire's systems and processes applicable to Payor Related Functions;
- e. the personal obligation of each individual involved in Covered Functions to comply with all applicable Federal health care program requirements and FDA requirements and all other applicable legal requirements;

- f. the personal obligation of each individual involved in Payor Related Functions to ensure that all information provided or reported to Payors is complete, accurate, and not misleading;
- g. the legal sanctions for violations of the applicable Federal health care program requirements and FDA requirements; and
- h. examples of proper and improper practices related to Covered Functions.

New Relevant Covered Persons shall receive this training within 30 days after the beginning of their employment or becoming Relevant Covered Persons, or within 120 days after the Effective Date, whichever is later.

After receiving the initial Specific Training described in this section, each Relevant Covered Person shall receive at least three hours of Specific Training, in addition to the General Training, in each subsequent Reporting Period.

3. *Board Member Training.* To the extent not already accomplished between July 14, 2014 and the Effective Date, within 120 days after the Effective Date, Shire shall provide at least two hours of training to each member of the Board, in addition to the General Training. This training shall address the responsibilities of board members and corporate governance.

New members of the Board shall receive the Board Member Training described above within 30 days after becoming a member or within 120 days after the Effective Date, whichever is later.

4. *Certification.* Each Covered Person who is required to attend training shall certify, in writing or in electronic form, that he or she has received the required training. The certification shall specify the type of training received and the date received. The CCRO (or designee) shall retain the certifications, along with all course materials. These shall be made available to OIG, upon request.

5. *Qualifications of Trainer.* Persons providing the training shall be knowledgeable about the subject area, including about applicable Federal health care program requirements and FDA requirements.

6. *Update of Training.* Shire shall review the training annually, and, where appropriate, shall update the training to reflect changes in Federal health care program requirements, FDA requirements, any issues discovered during internal audits or the IRO Reviews, and any other relevant information.

7. *Computer-based Training.* Shire may provide the training required under this CIA through appropriate computer-based training approaches. If Shire chooses to provide computer-based training, it shall make available appropriately qualified and knowledgeable staff or trainers to answer questions or provide additional information to the individuals receiving such training. In addition, if Shire chooses to provide computer-based training to meet the requirements of Section III.C., all applicable requirements to provide a number of “hours” of training may be met by providing the required number of “normative” hours of computer-based training, as that term is used in the computer-based training industry.

D. Risk Assessment and Mitigation Process.

Shire shall implement a standardized, centralized annual risk assessment and mitigation process (RAMP), as further described in this Section III.D and Appendix B. The RAMP shall require compliance, legal and other relevant representatives, including personnel from the applicable business unit(s), to assess and identify risks associated with Government Reimbursed Products that have one or more sales representatives assigned in the United States during the Reporting Period, are marketed in the United States, and are subject to FDA requirements governing the marketing of such Government Reimbursed Products. The RAMP shall involve an evaluation, at least annually, of the risks associated with Government Reimbursed Products marketed in the United States. Based on the outcomes of the risk-identification component of the RAMP Program, Shire legal, compliance and other personnel shall centrally develop and implement specific plans designed to mitigate or reduce the identified risks. The risk mitigation plans shall be developed annually and a plan shall be developed for each Government Reimbursed Product. Shire shall mitigate risks associated with marketing the Government Reimbursed Products in the United States, taking into account each risk assessment and applicable Federal health care program and FDA requirements.

E. Review Procedures

1. *General Description*

- a. *Engagement of Independent Review Organization.* Within 90 days after the Effective Date, Shire shall engage an entity (or entities), such as an accounting, auditing, or consulting firm (hereafter “Independent Review Organization” or “IRO”), to perform reviews to assist Shire in assessing and evaluating its Covered Functions and its Risk Assessment and Mitigation Process. More specifically, the IRO(s) shall conduct reviews that assess Shire’s systems, processes, policies, procedures, and practices relating to the Covered Functions and to Shire’s RAMP.

The applicable requirements relating to the IRO are outlined in Appendix A to this CIA, which is incorporated by reference. Each IRO engaged by Shire shall have expertise in applicable Federal health care program requirements and FDA requirements as may be appropriate to the IRO Review for which the IRO is retained. Each IRO shall assess, along with Shire, whether it can perform the engagement in a professionally independent and objective fashion, as appropriate to the nature of the IRO Review, taking into account any other business relationships or other engagements that may exist.

- b. *Frequency and Brief Description of Reviews.*

Systems, Transactions, and Additional Items Reviews. As set forth more fully in Appendix B, the IRO Reviews shall consist of two components: Systems Reviews and Transactions Reviews. Systems Reviews shall assess Shire’s systems, processes, policies and procedures relating to the Covered Functions and to the RAMP. If there are no material changes in Shire’s relevant systems, processes, policies, and procedures, the Systems Reviews shall be performed the second and fourth Reporting Periods. If Shire materially

changes its relevant systems, processes, policies, and procedures, the IRO shall perform a Systems Review for the Reporting Period in which such changes were made, in addition to conducting the Systems Review for the second and fourth Reporting Periods, as set forth more fully in Appendix B.

The Transactions Reviews shall be performed annually and shall cover each of the five Reporting Periods. The IRO(s) shall perform all components of each annual Transaction Review. As set forth more fully in Appendix B, the Transactions Review shall include several components.

In addition, as set forth in Appendix B, each Transactions Review shall also include a review of up to three additional areas or practices of Shire identified by OIG in its discretion (hereafter “Additional Items”). For purposes of identifying the Additional Items to be included in the Transactions Review for a particular Reporting Period, OIG will consult with Shire and may consider internal audit and monitoring work conducted by Shire, the Government Reimbursed Product portfolio, the nature and scope of Shire’s promotional practices and arrangements with HCPs and HCIs, and other information known to it.

As set forth more fully in Appendix B, Shire may propose to OIG that its internal audit(s) be partially substituted for one or more of the Additional Items that would otherwise be reviewed by the IRO as part of the Transactions Review. OIG retains sole discretion over whether, and in what manner, to allow Shire’s internal audit work to be substituted for a portion of the Additional Items review conducted by IRO.

OIG shall notify Shire of the nature and scope of IRO review for each of the Additional Items not later than 150 days prior to the end of each Reporting Period. Prior to undertaking the review of the Additional Items, the IRO and/or Shire shall submit an audit work plan to OIG for approval and the IRO



shall conduct the review of the Additional Items based on a work plan approved by OIG.

- c. *Retention of Records.* The IRO and Shire shall retain and make available to OIG, upon request, all work papers, supporting documentation, correspondence, and draft reports (those exchanged between the IRO and Shire) related to the IRO Reviews.

2. **IRO Review Reports.** The IRO shall prepare a report based upon each IRO Review performed (IRO Review Report). Information to be included in the IRO Review Report is described in Appendices A and B.

3. *Validation Review.* In the event OIG has reason to believe that: (a) any Shire IRO Review fails to conform to the requirements of this CIA; or (b) the IRO's findings or IRO Review results are inaccurate, OIG may, at its sole discretion, conduct its own review to determine whether the IRO Review complied with the requirements of the CIA and/or the findings or IRO Review results are inaccurate (Validation Review). Shire shall pay for the reasonable cost of any such review performed by OIG or any of its designated agents. Any Validation Review of Reports submitted as part of Shire's final Annual Report shall be initiated no later than one year after Shire's final submission (as described in Section II) is received by OIG.

Prior to initiating a Validation Review, OIG shall notify Shire of its intent to do so and provide a written explanation of why OIG believes such a review is necessary. To resolve any concerns raised by OIG, Shire may request a meeting with OIG to: (a) discuss the results of the IRO Review submissions or findings; (b) present any additional information to clarify the results of the IRO Review or to correct the inaccuracy of the IRO Review; and/or (c) propose alternatives to the proposed Validation Review. Shire agrees to provide any additional information as may be requested by OIG under this Section III.E.3 in an expedited manner. OIG will attempt in good faith to resolve any IRO Review issues with Shire prior to conducting a Validation Review. However, the final determination as to whether or not to proceed with a Validation Review shall be made at the sole discretion of OIG.

4. *Independence and Objectivity Certification.* The IRO shall include in its report(s) to Shire a certification that the IRO has (a) evaluated its professional independence and objectivity with respect to the reviews conducted under this Section

III.E; and (b) concluded that it is, in fact, independent and objective, in accordance with the requirements specified in Appendix A to this CIA.

F. Disclosure Program

Prior to the Effective Date, Shire established a Disclosure Program that meets the requirements of this Section III.F and shall maintain the Disclosure Program throughout the term of this CIA. The Disclosure Program includes a mechanism (the Compliance Helpline) to enable individuals to disclose, to the CCRO or some other person who is not in the disclosing individual's chain of command, any identified issues or questions associated with Shire's policies, conduct, practices, or procedures with respect to a Federal health care program requirement or an FDA requirement believed by the individual to be a potential violation of criminal, civil, or administrative law. Shire publicizes, and shall continue to appropriately publicize the existence of the Disclosure Program and the Compliance Helpline (*e.g.*, via periodic e-mails to employees or by posting the information in prominent common areas, or through references in the Code of Ethics and during training).

The Disclosure Program shall emphasize a nonretribution, nonretaliation policy, and shall include a reporting mechanism for anonymous communications for which appropriate confidentiality shall be maintained. Upon receipt of a disclosure, the CCRO (or designee) shall gather all relevant information from the disclosing individual. The CCRO (or designee) shall make a preliminary, good faith inquiry into the allegations set forth in every disclosure to ensure that he or she has obtained all of the information necessary to determine whether a further review should be conducted. For any disclosure that is sufficiently specific so that it reasonably: (1) permits a determination of the appropriateness of the alleged improper practice; and (2) provides an opportunity for taking corrective action, Shire shall conduct an internal review of the allegations set forth in the disclosure and ensure that proper follow-up is conducted.

The CCRO (or designee) shall maintain a disclosure log, which shall include a record and summary of each disclosure received (whether anonymous or not), the status of the respective internal reviews, and any corrective action taken in response to the internal reviews. This disclosure log shall be made available to OIG upon request.

G. Ineligible Persons

1. *Definitions.* For purposes of this CIA:

- a. an “Ineligible Person” shall include an individual or entity who:
  - i. is currently excluded, debarred, suspended, or otherwise ineligible to participate in the Federal health care programs or in Federal procurement or nonprocurement programs; or
  - ii. has been convicted of a criminal offense that falls within the scope of 42 U.S.C. § 1320a-7(a), but has not yet been excluded, debarred, suspended, or otherwise declared ineligible.
- b. “Exclusion Lists” include:
  - i. the HHS/OIG List of Excluded Individuals/Entities (available through the Internet at <http://www.oig.hhs.gov>); and
  - ii. the General Services Administration’s System for Award Management (available through the Internet at <http://www.sam.gov>).

2. *Screening Requirements.* Shire shall ensure that all prospective and current Covered Persons are not Ineligible Persons, by implementing the following screening requirements.

- a. As part of the hiring or contracting process, Shire shall screen all prospective Covered Persons against the Exclusion Lists prior to engaging their services and, shall require such Covered Persons to disclose whether they are Ineligible Persons.
- b. Shire shall screen all Covered Persons against the Exclusion Lists within 120 days after the Effective Date and on an annual basis thereafter. Shire represents that it conducted comprehensive annual screening that meets the requirements

of this Paragraph III.G.2.b during the time period that commenced on May 15, 2014 through the Effective Date (the “Pre-Effective Date Screening Period”). Consequently, Shire shall not be required to re-screen Covered Persons screened during the Pre-Effective Date Screening Period again within 120 days after the Effective Date.

- c. Shire has implemented a policy requiring all Covered Persons to disclose immediately any debarment, exclusion, suspension, or other event that makes that person an Ineligible Person.

Nothing in Section III.G affects Shire’s responsibility to refrain from (and liability for) billing Federal health care programs for items or services furnished, ordered, or prescribed by excluded persons. Shire understands that items or services furnished, ordered or prescribed by excluded persons are not payable by Federal health care programs and that Shire may be liable for overpayments and/or criminal, civil, and administrative sanctions for employing or contracting with an excluded person regardless of whether Shire meets the requirements of Section III.G.

3. *Removal Requirement.* If Shire has actual notice that a Covered Person has become an Ineligible Person, Shire shall remove such Covered Person from responsibility for, or involvement with, Shire’s business operations related to the Federal health care programs and shall remove such Covered Person from any position for which the Covered Person’s compensation or the items or services furnished, ordered, or prescribed by the Covered Person are paid in whole or part, directly or indirectly, by Federal health care programs or otherwise with Federal funds at least until such time as the Covered Person is reinstated into participation in the Federal health care programs.

4. *Pending Charges and Proposed Exclusions.* If Shire has actual notice that a Covered Person is charged with a criminal offense that falls within the scope of 42 U.S.C. §§ 1320a-7(a), 1320a-7(b)(1)-(3), or is proposed for exclusion during the Covered Person’s employment or contract term, Shire shall take all appropriate actions to ensure that the responsibilities of that Covered Person have not and shall not adversely affect the quality of care rendered to any beneficiary, patient, or resident, or any claims submitted to any Federal health care program.

## H. Notification of Government Investigation or Legal Proceedings

Within 30 days after discovery, Shire shall notify OIG, in writing, of any ongoing investigation or legal proceeding known to Shire conducted or brought by a U.S.-based governmental entity or its agents involving an allegation that Shire has committed a crime or has engaged in fraudulent activities. This notification shall include a description of the allegation, the identity of the investigating or prosecuting agency, and the status of such investigation or legal proceeding. Shire shall also provide written notice to OIG within 30 days after the resolution of the matter, and shall provide OIG with a description of the findings and/or results of the investigation or proceedings, if any.

## I. Reportable Events

1. *Definition of Reportable Event.* For purposes of this CIA, a “Reportable Event” means anything that involves:

- a. a matter that a reasonable person would consider a probable violation of criminal, civil, or administrative laws applicable to any Federal health care program for which penalties or exclusion may be authorized;
- b. a matter that a reasonable person would consider a probable violation of criminal, civil, or administrative laws applicable to any FDA requirements relating to the promotion of Government Reimbursed Products;
- c. any FDA Warning Letter issued to Shire;
- d. the employment of or contracting with a Covered Person who is an Ineligible Person as defined by Section III.G.1.a; or
- e. the filing of a bankruptcy petition by Shire.

A Reportable Event may be the result of an isolated event or a series of occurrences.

2. *Reporting of Reportable Events.* If Shire determines (after a reasonable opportunity to conduct an appropriate review or investigation of the allegations) through any means that there is a Reportable Event, Shire shall notify OIG,

in writing, within 30 days after making the determination that the Reportable Event exists.

3. *Reportable Events under Section III.I.1.a. through III.I.1.d.* For Reportable Events under Section III.I.1.a through III.I.1.d, the report to OIG shall include:

- a. a complete description of the Reportable Event, including the relevant facts, persons involved, and legal and Federal health care program or FDA authorities implicated;
- b. a description of Shire's actions taken to correct the Reportable Event; and
- c. any further steps Shire plans to take to address the Reportable Event and prevent it from recurring.

Shire shall not be required to report as a Reportable Event a matter which is the subject of an ongoing investigation or legal proceeding by a government entity or its agents previously disclosed under Section III.H above.

4. *Reportable Events under Section III.I.1.e.* For Reportable Events under Section III.I.1.e, the report to OIG shall include documentation of the bankruptcy filing and a description of any Federal health care program and/or FDA authorities implicated.

J. Notification of Communications with FDA. Within 30 days after the date of any written report, correspondence, or communication between Shire and the FDA that materially discusses Shire's or a Covered Person's actual or potential unlawful or improper promotion of Shire's Government Reimbursed Products (including any improper dissemination of information about off-label indications), Shire shall provide a copy of the report, correspondence, or communication to OIG. Shire shall also provide written notice to OIG within 30 days after the resolution of any such disclosed off-label matter, and shall provide OIG with a description of the findings and/or results of the matter, if any.

K. Sales and Marketing Monitoring and Review Efforts. Shire has established a comprehensive Sales and Marketing Monitoring Program (SMMP) that meets the

requirements of this Section III.K to evaluate and monitor its sales representatives' interactions with HCPs and HCIs. Shire shall maintain the SMMP throughout the term of this CIA. The SMMP is a formalized process designed to directly and indirectly observe the appropriateness of sales representatives' interactions with HCPs and HCIs and to identify potential off-label promotional activities or other improper conduct, including but not limited to promotional activities that involve misrepresentations or inaccurate statements about abuseability of Government Reimbursed Products. As described in more detail below, the SMMP shall include: (1) monitoring of speaker program activities (Speaker Monitoring Program); (2) direct field observations (Observations) of sales representatives; and (3) the monitoring and review of other records relating to sales representatives' interactions with HCPs and HCIs (Records Reviews).

1. *Speaker Program Activities.* As a component of the SMMP, Shire requires that all speakers be qualified, complete training, and enter into written agreements that describe the scope of work to be performed, the speaker fees to be paid, and compliance obligations for the speakers (including requirements that the speaker may only use Shire approved materials and may not directly or indirectly promote the product for off-label uses). Shire shall maintain processes designed to ensure that there is a legitimate need for each speaker program and, by or before December 31, 2014, shall establish a centralized system through which all speaker programs are, and shall be, administered throughout the term of the CIA. Shire has instituted controls regarding eligibility and qualifications of speakers and venues for the programs and requires that speakers are paid according to a centrally managed, pre-set rate structure determined based on a fair market value analysis conducted by Shire. Shire shall maintain a comprehensive list of speaker program attendees through its centralized system. In addition, Shire tracks and reviews, and shall continue to track and review, the aggregate amount (including speaker fees, travel, and other expenses) paid to each speaker in connection with speaker programs conducted during each Reporting Period. Shire requires, and shall continue to require, certified evaluations by sales representatives or other Shire personnel regarding whether a speaker program complied with Shire requirements, and in the event of non-compliance, Shire requires, and shall continue to require, the identification of the policy violation and ensure appropriate follow up activity to address the violation.

As a component of the SMMP, Shire compliance or other appropriately trained personnel who are independent from the functional area being monitored (Monitoring Personnel) attend speaker programs during each Reporting Period. Shire will conduct live monitoring of 50 such programs (Speaker Program Monitoring). The programs subject to the Speaker Monitoring Program shall be selected based on both a risk-based

targeting approach and on a sampling approach. For each program reviewed, Monitoring Personnel shall review slide materials and other materials used as part of the speaker program, speaker statements made during the program, and Shire representative activities during the program to assess whether the programs were conducted in a manner consistent with Shire's Policies and Procedures. Shire shall maintain the controls around speaker programs as described above and shall conduct its Speaker Monitoring Program as described above throughout the term of the CIA.

2. *Observations.* As a component of the SMMP, Shire Monitoring Personnel shall conduct observations of sales representatives, as described below, to assess whether the messages delivered and materials distributed to HCPs are consistent with applicable legal requirements and with Shire's Policies and Procedures. These observations are full day ride-alongs with sales representatives (Observations), and each Observation consists of directly observing all meetings between a sales representative and HCPs during the workday. The Observations are scheduled throughout the year and selected by Shire Monitoring Personnel both on a risk-based targeting approach and on a sampling approach. They include each therapeutic area and actively promoted Government Reimbursed Product, and are conducted across the United States. At the completion of each Observation, Shire Monitoring Personnel shall prepare a report which includes:

- a. the identity of the sales representative;
- b. the identity of the Shire Monitoring Personnel;
- c. the date and duration of the Observation;
- d. the product(s) promoted during the Observation;
- e. an overall assessment of compliance with Shire policy; and
- f. the identification of any potential off-label or other potentially illegal promotional activity by the sales representative.

Shire Monitoring Personnel shall conduct at least 30 Observations during each Reporting Period.

3. *Records Reviews.* As a component of the SMMP, Shire also reviews various types of records to assess sales representatives' interactions with HCPs and HCIs in order to identify potential or actual compliance violations. For each Reporting Period, Shire shall develop and implement a plan for conducting Records Reviews associated with at least three Government Reimbursed Products and a sampling of the representatives promoting those products in every separate region of the United States. OIG shall have the discretion to identify the three Government Reimbursed Products to



be reviewed for each Reporting Period. OIG will select the products based on information about Shire's products provided by Shire no later than 60 days prior to the beginning of the Reporting Period and other information known to OIG. If OIG does not identify the Government Reimbursed Products to be reviewed during a given Reporting Period, Shire shall select the three products to be reviewed.

These Records Reviews shall include the monitoring and review of: a) records and systems relating to sales representatives' interactions with HCPs and HCIs (including records from any available electronic detailing system(s) for the particular sales representatives, sales communications from managers, sample distribution records, and expense reports); b) requests for, or inquiries relating to, medical information about Government Reimbursed Products; c) message recall studies or similar records (such as Verbatims) purporting to reflect the details of sales representatives' interactions with HCPs and HCIs; d) sales representative call notes; e) sales representatives' e-mails and other electronic records; f) records of promotional materials provided by sales personnel to HCPs and HCIs; and g) recorded results of the Observations of sales representatives and applicable notes or information from the sales representatives' managers.

4. *Reporting and Follow-Up.* Personnel conducting the Speaker Program Monitoring, Observations and Records Reviews shall have access to all relevant records and information necessary to assess field representatives' interactions with HCPs and HCIs and to identify potential or actual compliance violations. Results from the SMMP monitoring shall be compiled and reported to the Compliance Department for review and remediation, as appropriate. In the event that a compliance issue, including but not limited to a potential improper promotion or noncompliance with Shire's legal requirements, compliance program requirements or Policies and Procedures, is identified during any Speaker Program Monitoring, Observation, or Records Review, Shire shall investigate the incident consistent with established Policies and Procedures for the handling of investigations. As part of the investigation procedures, findings shall be made and all necessary and appropriate responsive action (including disciplinary action) and corrective action shall be taken, including the disclosure of Reportable Events pursuant to Section III.I above, as applicable. Any compliance issues identified during a Speaker Program Monitoring, Observation and/or report from Records Review, and any corrective action shall be recorded in the files of the Compliance Department.

Shire shall include a summary of the SMMP and the results of the SMMP as part of each Annual Report. As part of each Annual Report, Shire also shall provide OIG with copies of the Observation Report for any instances in which it was determined that

improper promotion occurred and a description of the action(s) that Shire took as a result of such determinations. Shire shall make the Observation reports for all other Observations available to OIG upon request.

L. Monitoring of Non-Promotional Activities. To the extent not already accomplished, within 120 days after the Effective Date, Shire shall develop and implement a monitoring program, that comports with the requirements of this Section III.L, for the following types of activities: 1) consultant arrangement activities; and 2) Independent Medical Education Activity grants. This program shall be referred to as the Non-Promotional Monitoring Program (NPMP) and shall be maintained throughout the term of this CIA.

1. *Consultant Arrangement Activities.* To the extent that Shire engages U.S.-based U.S.-licensed HCPs or HCIs for services other than for speaker programs, research-related functions, or publication activities that relate to one or more Covered Functions (*e.g.*, as a member of an advisory board or to attend consultant meetings), such HCPs or HCIs shall be referred to herein as Consultants. Shire shall require all Consultants to enter into written agreements describing the scope of work to be performed, the fees to be paid, and compliance obligations for the Consultants. Consultants shall be paid according to a centrally managed, pre-set rate structure that is determined based on a fair-market value analysis conducted by Shire.

To the extent not already accomplished, within 120 days after the Effective Date, Shire shall establish a process to develop periodic budgeting plans (at least annual budgeting plans) that identify the business needs for, and the estimated numbers of, various Consultant engagements and activities to occur during the following year (or period, if more frequent than annual). The Consultant budgeting plans shall also identify the budgeted amounts to be spent on Consultant-related activities. Shire's compliance personnel shall be involved in the review and approval of such budgeting plans, including any subsequent modification of an approved plan. The purpose of this review shall be designed to ensure that Consultant arrangements and related events are used for legitimate purposes in

accordance with applicable Shire Policies and Procedures and with applicable Federal health care program and FDA requirements.

To the extent not already accomplished, within 120 days after the Effective Date, Shire shall establish a process designed to ensure that a documented needs assessment has been completed to justify the retention of a Consultant prior to the retention of the Consultant. The needs assessment shall identify the business need for the retention of the Consultant and provide specific details about the consulting arrangement (*e.g.*, information about the numbers and qualifications of the HCPs or HCIs to be engaged, the agenda for the proposed meeting, and a description of the proposed work to be done and type of work product to be generated.) Any deviations from the Consultant budgeting plans shall be documented in the needs assessment and shall be subject to review and approval by Shire compliance personnel.

To the extent not already accomplished, within 120 days after the Effective Date, Shire shall amend its policies and procedures in a manner designed to ensure that each Consultant performed the work for which the Consultant was engaged and that, as applicable, Shire received the work product generated by the Consultant.

Within 120 days after the Effective Date, Shire shall establish a Consultant Monitoring Program through which it shall conduct audits for each Reporting Period (Consultant Program Audits) of at least 40 Consultant arrangements with HCPs. The Consultant Program Audits shall include at least 30 advisory board programs and 10 professional services agreements with HCPs. In connection with the Consultant Monitoring Program, Shire Monitoring Personnel shall review Consultant arrangements both on a risk-based targeting approach and on a sampling approach. Shire Monitoring Personnel shall conduct the Consultant Program Audits by reviewing needs assessment documents, consultant contracts, and materials relating to the program or work of the Consultant (including work product resulting from any program or event), in order to assess whether the programs and arrangements were conducted in a manner consistent with Shire's Policies and Procedures. Results from the

Consultant Program Audits, including the identification of potential violations of policies, shall be compiled and reported to the CCRO (or designee) for review and follow-up as appropriate.

2. *Independent Medical Education Activity Grants.* Shire has established grants management processes, which comport with the requirements of this Section III.L.2, and are the exclusive mechanisms through which requestors may seek or be awarded grants for Independent Medical Education Activities supported by Shire. The grants management processes ensure that the Shire sales and marketing departments have no involvement in, or influence over, the review and approval of Independent Medical Education Activity grants. These grant requests shall be submitted through the grants management processes, and processed in accordance with standardized criteria developed by Shire. Shire has developed processes for grants submission and processing which are not operated by the sales or marketing division. Shire shall continue the Independent Medical Education Activity grant processes described above (or equivalent processes) throughout the term of the CIA, and shall notify OIG in writing at least 30 days prior to the implementation of any new process(es) subsequent to the Effective Date.

Shire has established a Grants Monitoring Program, which comports with the requirements of this Section III.L.2, through which it shall conduct audits for each Reporting Period of at least 20 Independent Medical Education Activity grants. The Grants Monitoring Program shall select grants for review both on a risk-based targeting approach and on a sampling approach. Shire Monitoring Personnel conducting the Grants Monitoring Program shall review proposal documents (including grant requests), approval documents, contracts, payments, and materials relating to Shire's review of the requests and any events or activities funded through the grants in order to assess whether the activities were conducted in a manner consistent with Shire's Policies and Procedures. Results from the Grants Monitoring Program, including the identification of potential violations of policies, are compiled and reported to the Compliance Department for review and follow-up as appropriate. Shire shall

maintain the Grants Monitoring Program described above throughout the term of this CIA.

3. *Follow-Up Reviews and Reporting.* In the event that a potential violation of Shire's Policies and Procedures or of legal or compliance requirements, including but not limited to potential improper promotion, are identified during any aspect of the NPMP monitoring, Shire shall investigate the incident consistent with established Policies and Procedures for the handling of investigations and shall take all necessary and appropriate responsive action (including disciplinary action) and corrective action, including the disclosure of Reportable Events pursuant to Section III.I above, if applicable. Any compliance issues identified during any aspect of the NPMP referenced above, and any corrective action, shall be recorded in the files of the Compliance Department. Shire shall include a summary of the NPMP and the results of the NPMP as part of each Annual Report. As part of each Annual Report, Shire also shall provide OIG with descriptions of any instances identified through the NPMP in which it was determined that improper promotion of Government Reimbursed Products occurred or the activities violated Shire's requirements or Policies and Procedures, and a description of the action(s) that Shire took as a result of such determinations. Shire shall make the documents relating to the NPMP available to OIG upon request.

M. Reporting of Physician Payments.

1. *Reporting of Payment Information.* Within 30 days after the Effective Date, Shire shall post on its website a report of the cumulative value of the Payments provided to all Physician Covered Recipients from Shire from August 1, 2013 through December 31, 2013 (the "partial 2013 report"). In addition, on or before March 31, 2015 and on or before March 31 of each subsequent calendar year during the term of the CIA, Shire shall post on its website a report of the cumulative value of the Payments provided to all Physician Covered Recipients from Shire during the prior applicable calendar year (each, an "annual report"). The partial 2013 report and each annual report shall be easily accessible and readily searchable.

The partial 2013 report posted pursuant to this Section III.M shall include a complete list of all Physician Covered Recipients to whom Shire made Payments from August 1, 2013 through December 31, 2013. Each annual report posted pursuant to this Section III.M shall include a complete list of all Physician Covered Recipients to whom Shire made Payments in the preceding calendar year. Each report made pursuant to this Section III.M shall be arranged alphabetically according to the Physician Covered Recipient's last name. The Payment amounts in the reports shall be reported in the actual amount paid for all Physician Covered Recipients on the report. For each Physician Covered Recipient, the applicable report shall include the following information: (i) physician's full name; (ii) city and state that the physician has provided to Shire for contact purposes; and (iii) the aggregate value of the Payments from August 1, 2013 through December 31, 2013, for the partial 2013 report; or (iv) the aggregate value of the Payment(s) in the preceding calendar year, for each annual report.

2. *Definitions and Miscellaneous Provisions.*

a. Shire shall make each report of Payments required by this Section III.M available on its website during the term of the CIA. Shire shall retain and make available to OIG, upon request, all supporting documentation, correspondence, and records related to all applicable Payments and to the reports of Payments. Nothing in this Section III.M affects the responsibility of Shire to comply with (or liability for noncompliance with) all applicable Federal health care program requirements and state laws as they relate to all applicable Payments made to Physician Covered Recipients.

b. For purposes of Section III.M.1, "Payments" is defined to include all "direct or indirect payments or other transfers of value" as that term is defined in 42 U.S.C. § 1320a-7h and applicable regulations and guidance (including FAQs) published by CMS. The term Payments includes the types of payments or other transfers of value enumerated in 42 U.S.C. § 1320a-7h(a)(1)(A)(vi) and applicable regulations. The term includes all indirect payments or other transfers of value made to a Physician Covered Recipient through a third party where Shire requires, instructs, directs, or otherwise causes the third party to provide the Payment to the Physician Covered Recipient. The term also includes direct and indirect payments or other transfers of value provided to a third party at the request of or designated by the Shire on behalf of a Physician Covered Recipient.

c. For purposes of its website postings required by this Section III.M, and only with regard to Payments made pursuant to product research or development agreements and clinical investigations as set forth in 42 U.S.C. § 1320a-7h(c)(1)(E), Shire may delay the inclusion of such Payments on its website listings consistent with 42 U.S.C. § 1320a-7h(c)(1)(E) and any regulations promulgated thereunder.

d. The term “Payments” does not include direct or indirect payments or other transfers of value or other items that are not included in or are excluded from the definition of “payment” or otherwise excluded from reporting under 42 U.S.C. § 1320a-7h and applicable regulations and guidance (including FAQs) published by CMS.

e. For purposes of this Section III.M, the term “Physician Covered Recipient” is defined to include any physician, except for a physician who is a bona fide employee of Shire, as that term is defined in 42 U.S.C. §1320a-7h(e)(6) and applicable regulations.

N. Other Transparency/Disclosure Initiatives.

1. Independent Medical Education Activity Grants and Health Care Related Charitable Contributions.

Shire represents that, on a quarterly basis, it posts on its company website the following information with respect to all Independent Medical Education Activity grants and health care related charitable contributions. The information posted on the company website includes: (i) the name of the recipient; (ii) the program name; and (iii) the amount of the grant or donation. Shire shall continue to post (and provide updates to) the above-described information about Independent Medical Education Activity grants and health care related charitable contributions throughout the term of this CIA. Shire shall notify OIG in writing at least 60 days prior to any change in the substance of its policies regarding the funding of Independent Medical Education Activity grants and health care related charitable contributions or posting of the above-referenced information relating to such funding.

## 2. Consultant Disclosure Obligations.

Shire shall require all Consultants to fully comply with all applicable disclosure obligations relating to their relationship with Shire that may be externally imposed on the Consultants based on their affiliation with formulary or Pharmacy & Therapeutics (P&T) committees or committees associated with the development of treatment protocols or standards or that are required by any HCI, medical committee, or other medical or scientific organization with which the Consultants are affiliated. Within 120 days after the Effective Date, to the extent not already accomplished, Shire shall amend its policies relating to Consultants to explicitly state that Shire requires all Consultants to fully comply with all applicable disclosure obligations relating to their relationship with Shire that may be externally imposed on the Consultants based on their affiliation with formulary, P&T committees, or committees associated with the development of treatment protocols or standards or that are required by any HCI, medical committee, or other medical or scientific organization with which the Consultants are affiliated. In addition, for any amendment to its contracts with Consultants and in any new contracts with Consultants entered into after 120 days following the Effective Date, Shire shall include an explicit requirement that the Consultants fully comply with all applicable disclosure requirements, as referenced above in this paragraph. Shire shall continue these disclosure requirements throughout the term of this CIA.

## 3. Authors.

Shire represents that it expects all authors of biomedical manuscripts to fully comply with the International Committee of Medical Journal Editors (ICMJE) criteria regarding authorship and disclosure of their relationship with Shire and to disclose any potential conflicts of interest, including any financial or personal relationships that might be perceived to bias their work. Within 120 days following the Effective Date, to the extent not already accomplished, Shire shall implement a requirement that all authors of biomedical manuscripts must fully comply with the International Committee of Medical Journal Editors (ICMJE) criteria regarding authorship and disclosure of their relationship with Shire and disclose any potential conflicts of interest, including any financial or personal relationships that might be perceived to bias their work. Within 120 days after the Effective Date, to the extent not already accomplished, Shire shall amend its policies to explicitly state Shire's requirement about full disclosure by authors consistent with ICMJE criteria and the requirements of any HCI, medical committee or other medical or scientific organization with which the authors are affiliated. In addition, for any amendments to its contracts and/or engagement letters with authors and in any contracts



and/or engagement letters with authors entered into after 120 days following the Effective Date, Shire shall include an explicit requirement that authors disclose in their manuscripts, journal submissions, and elsewhere as appropriate or required, any potential conflicts of interest, including their financial or personal relationship with Shire, the names of any individuals who have provided editorial support for any manuscript or other publication, and all funding sources for the study or publication.

4. Post-Marketing Commitments.

Within 30 days after the first date when Shire engages in any FDA post-marketing commitment (PMC), Shire shall post or make available information on its company website about PMCs. The Shire website or links included therein shall provide access to general information about the PMC process, descriptions of ongoing Shire studies, and information about the nature and status of FDA post-marketing commitments. Shire shall continue to post or make available the above-described information about PMCs on its website or links included therein throughout the term of this CIA.

**IV. CHANGES TO BUSINESS UNITS OR LOCATIONS**

A. Sale of Business, Business Unit or Location.

In the event that, after the Effective Date, Shire proposes to sell any or all of its business, business units or locations (whether through a sale of assets, sale of stock, or other type of transaction) that are subject to this CIA, Shire shall notify OIG of the proposed sale no later than five business days after the date on which the sale is publicly disclosed by Shire. This notification shall include a description of the business, business unit or location to be sold, a brief description of the terms of the sale, and the name and contact information of the prospective purchaser. This CIA shall be binding on the purchaser of the business, business unit or location, unless otherwise determined and agreed to in writing by OIG.

B. Change or Closure of Business, Business Unit or Location

In the event that, after the Effective Date, Shire changes locations or closes a business, business unit or location related to or engaged in any of the Covered Functions, Shire shall notify OIG of this fact as soon as possible, but no later than within 30 days after the date of change or closure of the business, business unit or location.

C. Purchase or Establishment of New Business, Business Unit or Location

In the event that, after the Effective Date, Shire purchases or establishes a new business, business unit or location related to or engaged in any of the Covered Functions, Shire shall notify OIG no later than five business days after the date of such purchase or the date on which the operation of the new business, business unit or location is publicly disclosed by Shire. This notification shall include the address of the new business, business unit or location, phone number, fax number, the location's Federal health care program provider number and/or supplier number(s), if applicable; and the name and address of Federal health care program contractor to which Shire currently submits claims (if applicable). Each new business, business unit or location and all Covered Persons at each new business, business unit or location shall be subject to the applicable requirements of this CIA, unless otherwise agreed to in writing by OIG.

V. IMPLEMENTATION AND ANNUAL REPORTS

A. Implementation Report

Within 150 days after the Effective Date, Shire shall submit a written report to OIG summarizing the status of its implementation of the requirements of this CIA (Implementation Report). The Implementation Report shall, at a minimum, include:

1. the name, address, phone number, and position description of the CCRO required by Section III.A.1, and a summary of other noncompliance job responsibilities the CCRO may have;
2. the names and positions of the members of the U.S. Compliance Committee required by Section III.A.2;
3. the names of the Board members who are responsible for satisfying the Board of Directors compliance obligations described in Section III.A.3;
4. the names and positions of the Certifying Employees required by Section III.A.4;
5. a copy of Shire's Code of Ethics required by Section III.B.1;

6. the number of individuals required to complete the Code of Ethics certification required by Section III.B.1, the percentage of individuals who have completed such certification, and an explanation of any exceptions (the documentation supporting this information shall be available to OIG upon request);

7. (a) a copy of the letter (including all attachments) required by Sections II.C.9 and III.B.2 sent to each party employing Third Party Personnel; (b) a list of all such existing co-promotions and other applicable agreements with the party employing the Third Party Personnel; and (c) a description of the entities' responses to Shire's letter;

8. a summary of all Policies and Procedures required by Section III.B.3 (copies of the Policies and Procedures shall be made available to OIG upon request);

9. the following information regarding each type of training required by Section III.C:

- a. a description of such training, including a summary of the topics covered, the length of sessions, and a schedule of training sessions; and
- b. the number of individuals required to be trained, percentage of individuals actually trained, and an explanation of any exceptions.

A copy of all training materials and the documentation supporting this information shall be made available to OIG upon request.

10. the following information regarding the IRO(s): (a) identity, address, and phone number; (b) a copy of the engagement letter; (c) information to demonstrate that the IRO has the qualifications outlined in Appendix A to this CIA; (d) a summary and description of any and all current and prior engagements and agreements between Shire and the IRO; and (e) a certification from the IRO regarding its professional independence and objectivity with respect to Shire;

11. a description of the Disclosure Program required by Section III.F;

12. a description of the process by which Shire fulfills the requirements of Section III.G regarding Ineligible Persons;

13. a certification from the CCRO that, if required under Section III.M and to the best of his/her knowledge, information regarding Payments has been posted on Shire's website as required by Section III.M;

14. a list of all of Shire's locations (including locations and mailing addresses) engaged in Covered Functions; the corresponding name under which each location is doing business; the corresponding phone numbers and fax numbers; each location's Federal health care program provider number and/or supplier number(s) (if applicable); and the name and address of each Federal health care program contractor to which Shire currently submits claims (if applicable);

15. a description of Shire's corporate structure, including identification of any parent and sister companies or subsidiaries, and their respective lines of business; and

16. the certifications required by Section V.C.

#### B. Annual Reports

Shire shall submit to OIG annually a report with respect to the status of, and findings regarding, Shire's compliance activities for each of the five Reporting Periods (Annual Report). Each Annual Report shall include, at a minimum:

1. any change in the identity, position description, or other noncompliance job responsibilities of the CCRO and any change in the membership of the U.S. Compliance Committee, the Board of Directors, or the group of Certifying Employees described in Sections III.A.2-III.A.4;

2. a copy of the resolution by the Board or a Committee of the Board, required by Section III.A.3;

3. a summary of any changes or amendments to Shire's Code of Ethics required by Section III.B.1 and the reason for such changes, along with a copy of the revised Code of Ethics;

4. the number of individuals required to complete the Code of Ethics certification required by Section III.B.1, the percentage of individuals who have completed such certification, and an explanation of any exceptions (the documentation supporting this information shall be made available to OIG upon request);

5. (a) a copy of the letter (including all attachments) required by Section II.C.9 and III.B.2 sent to each party employing Third Party Personnel; (b) a list of all such existing co-promotion and other applicable agreements; and (c) a description of the entities' response to Shire's letter;

6. a summary of any significant changes or amendments to the Policies and Procedures required by Section III.B and the reasons for such changes (*e.g.*, change in contractor policy);

7. the following information regarding each type of training required by Section III.C:

a. a description of the initial and annual training, including a summary of the topics covered, the length of sessions, and a schedule of training sessions; and

b. the number of individuals required to complete the initial and annual training, the percentage of individuals who actually completed the initial and annual training, and an explanation of any exceptions.

A copy of all training materials and the documentation to support this information shall be made available to OIG upon request.

8. a complete copy of all reports prepared pursuant to Section III.E and Appendix B, along with a copy of the IRO's engagement letter;

9. Shire's response to the reports prepared pursuant to Section III.E and Appendix B, along with corrective action plan(s) related to any issues raised by the reports;

10. a summary and description of any and all current and prior engagements and agreements between Shire and the IRO (if different from what was submitted as part of the Implementation Report);
11. a certification from the IRO regarding its professional independence and objectivity with respect to Shire;
12. a summary of the disclosures in the disclosure log required by Section III.F that relate to Federal health care programs, FDA requirements, or Government Reimbursed Products (the complete disclosure log shall be made available to OIG upon request);
13. any changes to the process by which Shire fulfills the requirements of Section III.G regarding Ineligible Persons;
14. a summary describing any ongoing investigation or legal proceeding required to have been reported pursuant to Section III.H. The summary shall include a description of the allegation, the identity of the investigating or prosecuting agency, and the status of such investigation or legal proceeding;
15. a summary of Reportable Events (as defined in Section III.I) identified during the Reporting Period and the status of any corrective and preventative action relating to all such Reportable Events;
16. a summary describing any written communication with the FDA required to have been reported pursuant to Section III.J. This summary shall include a description of the matter and the status of the matter;
17. a summary of the SMMP and the results of the SMMP required by Section III.K, including copies of the Observation report for any instances in which it was determined that improper promotion occurred and a description of the action(s) that Shire took as a result of such determinations;
18. a summary of the NPMP and the results of the program described in Section III.L, including detailed description of any identified instances in which it was determined that the activities violated Shire's policies or that improper promotion of Government Reimbursed Products occurred and a description of the action(s) Shire took

as a result of such determinations;

19. a certification from the CCRO that, if required under Section III.M and to the best of his/her knowledge, information regarding Payments has been posted on Shire's website as required by Section III.M.

20. a certification from the CCRO that, to the best of his/her knowledge, information required to be posted under Section III.N has been posted to Shire's website as required by Section III.N.

21. a description of all changes to the most recently provided list of locations (including addresses) required by Section V.A.14; the corresponding name under which each location is doing business; and the corresponding phone and fax numbers; and

22. a description of: (i) any additional, updated, supplemental or changed information submitted to any Compendia in accordance with Section III.B.3.p; (ii) Shire's review of information submitted to the Compendia and Shire's conclusion as to whether information submitted to the Compendia and product listings and monographs contained in the Compendia about Government Reimbursed Products are accurate and complete and do not contain any errors; and (iii) all arrangements, processing fees, and other payments or financial support (if any) with or made to any Compendia evaluated during the annual review described in Section III.B.3.p; and

23. the certifications required by Section V.C.

The first Annual Report shall be received by OIG no later than 120 days after the end of the first Reporting Period. Subsequent Annual Reports shall be received by OIG no later than the anniversary date of the due date of the first Annual Report.

### C. Certifications

The following certifications shall be included in the Implementation Report and Annual Reports (as specified below):

1. Certifying Employees. In each Annual Report, Shire shall include the certifications of Certifying Employees as required by Section III.A.4; and

2. Senior Vice President and Chief Compliance and Risk Officer. In the Implementation Report and Annual Reports, Shire shall include the following individual certification by the CCRO:

a. to the best of his or her knowledge, except as otherwise described in the applicable report, Shire is in compliance with all of the requirements of this CIA;

b. he or she has reviewed the report and has made reasonable inquiry regarding its content and believes that the information in the report is accurate and truthful; and

c. Shire's Policies and Procedures as referenced in Section III.B.3 above; 2) templates for standardized contracts and other similar documents; and 3) the training materials used for purposes of Section III.C all have been reviewed by competent legal counsel and have been found to be in compliance with all applicable Federal health care program requirements and FDA requirements. In addition, all promotional materials containing claims or information about Government Reimbursed Products and other materials and information intended to be disseminated outside Shire have been reviewed by competent regulatory, medical, and/or legal personnel in accordance with applicable Policies and Procedures to ensure that legal, medical, and regulatory concerns are properly addressed and are brought to the attention of the appropriate individuals, when required, and that the materials and information when finally approved are in compliance with all applicable Federal health care program requirements and FDA requirements. If the applicable legal requirements have not changed, after the initial review of the documents listed above, only material changes to the documents must be reviewed by competent regulatory, medical, and/or legal personnel. The certification shall include a description of the document(s) reviewed and approximately when the review was completed. The documentation supporting this certification shall be available to OIG, upon request; and

d. all call plans for Government Reimbursed Products were reviewed at least once during the Reporting Period (consistent with Section III.B.3.h) and, for each product the call plans were found to be consistent with Shire's policy objectives as referenced above in Section III.B.3.h.



D. Designation of Information

Shire shall clearly identify any portions of its submissions that it believes are trade secrets, or information that is commercial or financial and privileged or confidential, and therefore potentially exempt from disclosure under the Freedom of Information Act (FOIA), 5 U.S.C. § 552. Shire shall refrain from identifying any information as exempt from disclosure if that information does not meet the criteria for exemption from disclosure under FOIA.

**VI. NOTIFICATIONS AND SUBMISSION OF REPORTS**

Unless otherwise stated in writing after the Effective Date, all notifications and reports required under this CIA shall be submitted to the following entities:

OIG:

Administrative and Civil Remedies Branch  
Office of Counsel to the Inspector General  
Office of Inspector General  
U.S. Department of Health and Human Services  
Cohen Building, Room 5527  
330 Independence Avenue, S.W.  
Washington, DC 20201  
Telephone: 202.619.2078  
Facsimile: 202.205.0604

Shire:

Caroline H. West  
Senior Vice President and Chief Compliance and Risk Officer  
Shire Pharmaceuticals LLC  
725 Chesterbrook Blvd.  
Wayne, PA 19087  
Telephone: (484) 595-8808  
Facsimile: (484) 595-8667

Unless otherwise specified, all notifications and reports required by this CIA may be made by certified mail, overnight mail, hand delivery, or other means, provided that there is proof that such notification was received. For purposes of this requirement,

internal facsimile confirmation sheets do not constitute proof of receipt. Upon request by OIG, Shire may be required to provide OIG with an electronic copy of each notification or report required by this CIA in searchable portable document format (pdf), in addition to a paper copy.

## **VII. OIG INSPECTION, AUDIT, AND REVIEW RIGHTS**

In addition to any other rights OIG may have by statute, regulation, or contract, OIG or its duly authorized representative(s) may examine or request copies of Shire's books, records, and other documents and supporting materials and/or conduct on-site reviews of any of Shire's locations for the purpose of verifying and evaluating: (a) Shire's compliance with the terms of this CIA; and (b) Shire's compliance with the requirements of the Federal health care programs in which it participates and with applicable FDA requirements. The documentation described above shall be made available by Shire to OIG or its duly authorized representative(s) at all reasonable times for inspection, audit, or reproduction. Furthermore, for purposes of this provision, OIG or its duly authorized representative(s) may interview any of Shire's employees, contractors, or agents who consent to be interviewed at the individual's place of business during normal business hours or at such other place and time as may be mutually agreed upon between the individual and OIG. Shire shall assist OIG or its duly authorized representative(s) in contacting and arranging interviews with such individuals upon OIG's request. Shire's employees may elect to be interviewed with or without a representative of Shire present.

## **VIII. DOCUMENT AND RECORD RETENTION**

Shire shall maintain for inspection all documents and records relating to reimbursement from the Federal health care programs and to compliance with this CIA for six years (or longer if otherwise required by law) from the Effective Date.

## **IX. DISCLOSURES**

Consistent with HHS's FOIA procedures, set forth in 45 C.F.R. Part 5, OIG shall make a reasonable effort to notify Shire prior to any release by OIG of information submitted by Shire pursuant to its obligations under this CIA and identified upon submission by Shire as trade secrets, or information that is commercial or financial and privileged or confidential, under the FOIA rules. With respect to such releases, Shire shall have the rights set forth at 45 C.F.R. § 5.65(d).

## **X. BREACH AND DEFAULT PROVISIONS**

Shire is expected to fully and timely comply with all of its CIA obligations.

### **A. Stipulated Penalties for Failure to Comply with Certain Obligations**

As a contractual remedy, Shire and OIG hereby agree that failure to comply with certain obligations as set forth in this CIA may lead to the imposition of the following monetary penalties (hereafter referred to as “Stipulated Penalties”) in accordance with the following provisions.

1. A Stipulated Penalty of \$2,500 (which shall begin to accrue on the day after the date the obligation became due) for each day Shire fails to establish and implement any of the following obligations as described in Section III:

- a. a Chief Compliance and Risk Officer;
- b. a U.S. Compliance Committee;
- c. the Board of Directors compliance obligations, including the resolution of the Board;
- d. the management accountability and certification obligations;
- e. a written Code of Ethics;
- f. written Policies and Procedures;
- g. the training of Covered Persons, Relevant Covered Persons, and Board Members;
- h. a Risk Assessment and Mitigation Process;
- i. a Disclosure Program;
- j. Ineligible Persons screening and removal requirements;

- k. notification of Government investigations or legal proceedings; and
- l. reporting of Reportable Events;
- m. notification of written communications with FDA as required by Section III.J;
- n. a program for SMMP as required by Section III.K;
- o. a program for NPMP as required by Section III.L;
- p. posting of any Payments as required by Section III.M; and
- q. the Other Transparency/Disclosure Initiatives as required by Section III.N.

2. A Stipulated Penalty of \$2,500 (which shall begin to accrue on the day after the date the obligation became due) for each day Shire fails to engage and use an IRO, as required in Section III.E, Appendix A, and Appendix B.

3. A Stipulated Penalty of \$2,500 (which shall begin to accrue on the day after the date the obligation became due) for each day Shire fails to submit the Implementation Report or any Annual Reports to OIG in accordance with the requirements of Section V by the deadlines for submission.

4. A Stipulated Penalty of \$2,500 (which shall begin to accrue on the day after the date the obligation became due) for each day Shire fails to submit any IRO Review Report(s) in accordance with the requirements of Section III.E and Appendices A through B.

5. A Stipulated Penalty of \$1,500 for each day Shire fails to grant access as required in Section VII. (This Stipulated Penalty shall begin to accrue on the date Shire fails to grant access.)

6. A Stipulated Penalty of \$50,000 for each false certification submitted by or on behalf of Shire as part of its Implementation Report, Annual Report,

additional documentation to a report (as requested by OIG), or otherwise required by this CIA.

7. A Stipulated Penalty of \$1,000 for each day Shire fails to comply fully and adequately with any obligation of this CIA. OIG shall provide notice to Shire stating the specific grounds for its determination that Shire has failed to comply fully and adequately with the CIA obligation(s) at issue and steps Shire shall take to comply with the CIA. (This Stipulated Penalty shall begin to accrue 10 days after Shire receives this notice from OIG of the failure to comply.) A Stipulated Penalty as described in this Subsection shall not be demanded for any violation for which OIG has sought a Stipulated Penalty under Subsections 1-6 of this Section.

B. Timely Written Requests for Extensions

Shire may, in advance of the due date, submit a timely written request for an extension of time to perform any act or file any notification or report required by this CIA. Notwithstanding any other provision in this Section, if OIG grants the timely written request with respect to an act, notification, or report, Stipulated Penalties for failure to perform the act or file the notification or report shall not begin to accrue until one day after Shire fails to meet the revised deadline set by OIG. Notwithstanding any other provision in this Section, if OIG denies such a timely written request, Stipulated Penalties for failure to perform the act or file the notification or report shall not begin to accrue until three business days after Shire receives OIG's written denial of such request or the original due date, whichever is later. A "timely written request" is defined as a request in writing received by OIG at least five business days prior to the date by which any act is due to be performed or any notification or report is due to be filed.

C. Payment of Stipulated Penalties

1. *Demand Letter.* Upon a finding that Shire has failed to comply with any of the obligations described in Section X.A and after determining that Stipulated Penalties are appropriate, OIG shall notify Shire of: (a) Shire's failure to comply; and (b) OIG's exercise of its contractual right to demand payment of the Stipulated Penalties. (This notification shall be referred to as the "Demand Letter.")

2. *Response to Demand Letter.* Within 10 days after the receipt of the Demand Letter, Shire shall either: (a) cure the breach to OIG's satisfaction and pay the applicable Stipulated Penalties or (b) request a hearing before an HHS administrative law

judge (ALJ) to dispute OIG's determination of noncompliance, pursuant to the agreed upon provisions set forth below in Section X.E. In the event Shire elects to request an ALJ hearing, the Stipulated Penalties shall continue to accrue until Shire cures, to OIG's satisfaction, the alleged breach in dispute. Failure to respond to the Demand Letter in one of these two manners within the allowed time period shall be considered a material breach of this CIA and shall be grounds for exclusion under Section X.D.

3. *Form of Payment.* Payment of the Stipulated Penalties shall be made by electronic funds transfer to an account specified by OIG in the Demand Letter.

4. *Independence from Material Breach Determination.* Except as set forth in Section X.D.1.c, these provisions for payment of Stipulated Penalties shall not affect or otherwise set a standard for OIG's decision that Shire has materially breached this CIA, which decision shall be made at OIG's discretion and shall be governed by the provisions in Section X.D, below.

D. Exclusion for Material Breach of this CIA

1. *Definition of Material Breach.* A material breach of this CIA means:

- a. a repeated or flagrant violation of the obligations under this CIA, including, but not limited to, the obligations addressed in Section X.A;
- b. a failure by Shire to report a Reportable Event and take corrective action as required in Section III.I.
- c. a failure by Shire to respond to a Demand Letter concerning the payment of Stipulated Penalties in accordance with Section X.C;
- d. a failure to engage and use an IRO in accordance with Section III.E, Appendix A, and Appendix B; or
- e. a failure of the Board (or a Committee thereof) to issue a resolution in accordance with Section III.A.3.

2. *Notice of Material Breach and Intent to Exclude.* The parties agree that a material breach of this CIA by Shire constitutes an independent basis for Shire's exclusion from participation in the Federal health care programs. Upon a determination by OIG that Shire has materially breached this CIA and that exclusion is the appropriate remedy, OIG shall notify Shire of: (a) Shire's material breach; and (b) OIG's intent to exercise its contractual right to impose exclusion. (This notification shall be referred to as the "Notice of Material Breach and Intent to Exclude.")

3. *Opportunity to Cure.* Shire shall have 30 days from the date of receipt of the Notice of Material Breach and Intent to Exclude to demonstrate to OIG's satisfaction that:

- a. Shire is in compliance with the obligations of the CIA cited by OIG as being the basis for the material breach;
- b. the alleged material breach has been cured; or
- c. the alleged material breach cannot be cured within the 30 day period, but that: (i) Shire has begun to take action to cure the material breach; (ii) Shire is pursuing such action with due diligence; and (iii) Shire has provided to OIG a reasonable timetable for curing the material breach.

4. *Exclusion Letter.* If, at the conclusion of the 30 day period, Shire fails to satisfy the requirements of Section X.D.3, OIG may exclude Shire from participation in the Federal health care programs. OIG shall notify Shire in writing of its determination to exclude Shire. (This letter shall be referred to as the "Exclusion Letter.") Subject to the Dispute Resolution provisions in Section X.E, below, the exclusion shall go into effect 30 days after the date of Shire's receipt of the Exclusion Letter. The exclusion shall have national effect. Reinstatement to program participation is not automatic. After the end of the period of exclusion, Shire may apply for reinstatement by submitting a written request for reinstatement in accordance with the provisions at 42 C.F.R. §§ 1001.3001-.3004.

#### E. Dispute Resolution

1. *Review Rights.* Upon OIG's delivery to Shire of its Demand Letter or of its Exclusion Letter, and as an agreed-upon contractual remedy for the resolution of

disputes arising under this CIA, Shire shall be afforded certain review rights comparable to the ones that are provided in 42 U.S.C. § 1320a-7(f) and 42 C.F.R. Part 1005 as if they applied to the Stipulated Penalties or exclusion sought pursuant to this CIA. Specifically, OIG's determination to demand payment of Stipulated Penalties or to seek exclusion shall be subject to review by an HHS ALJ and, in the event of an appeal, the HHS Departmental Appeals Board (DAB), in a manner consistent with the provisions in 42 C.F.R. § 1005.2-1005.21. Notwithstanding the language in 42 C.F.R. § 1005.2(c), the request for a hearing involving Stipulated Penalties shall be made within 10 days after receipt of the Demand Letter and the request for a hearing involving exclusion shall be made within 25 days after receipt of the Exclusion Letter.

2. *Stipulated Penalties Review.* Notwithstanding any provision of Title 42 of the United States Code or Title 42 of the Code of Federal Regulations, the only issues in a proceeding for Stipulated Penalties under this CIA shall be: (a) whether Shire was in full and timely compliance with the obligations of this CIA for which OIG demands payment; and (b) the period of noncompliance. Shire shall have the burden of proving its full and timely compliance and the steps taken to cure the noncompliance, if any. OIG shall not have the right to appeal to the DAB an adverse ALJ decision related to Stipulated Penalties. If the ALJ agrees with OIG with regard to a finding of a breach of this CIA and orders Shire to pay Stipulated Penalties, such Stipulated Penalties shall become due and payable 20 days after the ALJ issues such a decision unless Shire requests review of the ALJ decision by the DAB. If the ALJ decision is properly appealed to the DAB and the DAB upholds the determination of OIG, the Stipulated Penalties shall become due and payable 20 days after the DAB issues its decision.

3. *Exclusion Review.* Notwithstanding any provision of Title 42 of the United States Code or Title 42 of the Code of Federal Regulations, the only issues in a proceeding for exclusion based on a material breach of this CIA shall be:

- a. whether Shire was in material breach of this CIA;
- b. whether such breach was continuing on the date of the Exclusion Letter; and
- c. whether the alleged material breach could not have been cured within the 30-day period, but that: (i) Shire had begun to take action to cure the material breach within that period; (ii) Shire has pursued and is pursuing such action with due



diligence; and (iii) Shire provided to OIG within that period a reasonable timetable for curing the material breach and Shire has followed the timetable.

For purposes of the exclusion herein, exclusion shall take effect only after an ALJ decision favorable to OIG, or, if the ALJ rules for Shire, only after a DAB decision in favor of OIG. Shire's election of its contractual right to appeal to the DAB shall not abrogate OIG's authority to exclude Shire upon the issuance of an ALJ's decision in favor of OIG. If the ALJ sustains the determination of OIG and determines that exclusion is authorized, such exclusion shall take effect 20 days after the ALJ issues such a decision, notwithstanding that Shire may request review of the ALJ decision by the DAB. If the DAB finds in favor of OIG after an ALJ decision adverse to OIG, the exclusion shall take effect 20 days after the DAB decision. Shire shall waive its right to any notice of such an exclusion if a decision upholding the exclusion is rendered by the ALJ or DAB. If the DAB finds in favor of Shire, Shire shall be reinstated effective on the date of the original exclusion.

4. *Finality of Decision.* The review by an ALJ or DAB provided for above shall not be considered to be an appeal right arising under any statutes or regulations. Consequently, the parties to this CIA agree that the DAB's decision (or the ALJ's decision if not appealed) shall be considered final for all purposes under this CIA.

## **XI. EFFECTIVE AND BINDING AGREEMENT**

Shire and OIG agree as follows:

A. This CIA shall become final and binding on the date the final signature is obtained on the CIA.

B. This CIA constitutes the complete agreement between the parties and may not be amended except by written consent of the parties to this CIA.

C. The undersigned Shire signatories represent and warrant that they are authorized to execute this CIA. The undersigned OIG signatories represent that they are signing this CIA in their official capacities and that they are authorized to execute this CIA.

D. This CIA may be executed in counterparts, each of which constitutes an original and all of which constitute one and the same CIA. Facsimiles of signatures shall constitute acceptable, binding signatures for purposes of this CIA.

**ON BEHALF OF SHIRE**

/Ellen Rosenberg/  
\_\_\_\_\_

9-12-14  
\_\_\_\_\_

Ellen Rosenberg, Secretary  
Shire North American Group, Inc.

DATE

/Caroline H. West/  
\_\_\_\_\_

9-12-14  
\_\_\_\_\_

Caroline H. West  
Senior Vice President and  
Chief Compliance and Risk Officer

DATE

/Melissa B. Tearney/  
\_\_\_\_\_

9-12-14  
\_\_\_\_\_

Melissa B. Tearney  
Choate, Hall & Stewart, LLP  
Counsel for Shire

DATE

/Christine G. Savage/  
\_\_\_\_\_

9-12-14  
\_\_\_\_\_

Christine G. Savage  
Choate, Hall & Stewart, LLP  
Counsel for Shire

DATE

**ON BEHALF OF THE OFFICE OF INSPECTOR GENERAL  
OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES**

/Robert K. DeConti/

9/12/14

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ROBERT K. DECONTI  
Assistant Inspector General for Legal Affairs  
Office of Inspector General  
U. S. Department of Health and Human Services

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DATE

/Keshia B. Thompson/

9/15/14

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KESHIA B. THOMPSON  
Senior Counsel  
Office of Inspector General  
U. S. Department of Health and Human Services

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DATE

**APPENDIX A**

**TO CIA FOR**

**SHIRE NORTH AMERICAN GROUP, INC.**

**INDEPENDENT REVIEW ORGANIZATION**

This Appendix contains the requirements relating to the Independent Review Organization (IRO) required by Section III.E of the CIA.

A. IRO Engagement

1. Shire shall engage an IRO that possesses the qualifications set forth in Paragraph B, below, to perform the responsibilities in Paragraph C, below. The IRO shall conduct the review in a professionally independent and objective fashion, as set forth in Paragraph D. Within 30 days after OIG receives the information identified in Section V.A.10 of the CIA or any additional information submitted by Shire in response to a request by OIG, whichever is later, OIG will notify Shire if the IRO is unacceptable. Absent notification from OIG that the IRO is unacceptable, Shire may continue to engage the IRO.

2. If Shire engages a new IRO during the term of the CIA, this IRO shall also meet the requirements of this Appendix. If a new IRO is engaged, Shire shall submit the information identified in Section V.A.10 of the CIA to OIG within 30 days of engagement of the IRO. Within 30 days after OIG receives this information or any additional information submitted by Shire at the request of OIG, whichever is later, OIG will notify Shire if the IRO is unacceptable. Absent notification from OIG that the IRO is unacceptable, Shire may continue to engage the IRO.

B. IRO Qualifications

The IRO shall:

1. assign individuals to conduct the IRO Reviews who have expertise in the pharmaceutical industry and have expertise in all applicable Federal health care program requirements and FDA requirements relating to Covered Functions and the RAMP, including but not limited to expertise relating to marketing and promotional activities associated with pharmaceutical products. The assigned individuals shall also be experienced in risk identification and mitigation in relation to pharmaceutical product marketing and promotion. The assigned individuals shall also be knowledgeable about the general requirements of the Federal health care program(s) under which Government Reimbursed Products are reimbursed;

2. assign individuals to design and select the sample for the Transaction Reviews who are knowledgeable about the appropriate statistical sampling techniques; and

3. have sufficient staff and resources to conduct the reviews required by the CIA on a timely basis.

C. IRO Responsibilities

The IRO shall:

1. perform each IRO Review in accordance with the specific requirements of the CIA;

2. follow all applicable Federal health care program requirements and FDA requirements in making assessments in each IRO Review;

3. if in doubt of the application of a particular Federal health care program or FDA requirement, policy or regulation, request clarification from the appropriate authority (*e.g.*, CMS or FDA);

4. respond to all OIG inquiries in a prompt, objective, and factual manner; and

5. prepare timely, clear, well-written reports that include all the information required by Appendix B to the CIA.

D. IRO Independence and Objectivity

The IRO must perform each IRO Review in a professionally independent and objective fashion, as appropriate to the nature of the engagement, taking into account any other business relationships or engagements that may exist between the IRO and Shire.

E. IRO Removal/Termination

1. *Shire Termination of IRO.* If Shire terminates its IRO during the course of the engagement, Shire must submit a notice explaining its reasons to OIG no later than 30 days after termination. Shire must engage a new IRO in accordance with Paragraph A of this Appendix and within 60 days of termination of the IRO.

2. *OIG Removal of IRO.* In the event OIG has reason to believe the IRO does not possess the qualifications described in Paragraph B, is not independent and

objective as set forth in Paragraph D, or has failed to carry out its responsibilities as described in Paragraph C, OIG may, at its sole discretion, require Shire to engage a new IRO in accordance with Paragraph A of this Appendix. Shire must engage a new IRO within 60 days of termination of the IRO.

Prior to requiring Shire to engage a new IRO, OIG shall notify Shire of its intent to do so and provide a written explanation of why OIG believes such a step is necessary. To resolve any concerns raised by OIG, Shire may present additional information regarding the IRO's qualifications, independence or performance of its responsibilities. Shire shall provide any additional information as may be required by OIG under this Paragraph in an expedited manner. OIG will attempt in good faith to resolve any differences regarding the IRO with Shire prior to requiring Shire to terminate the IRO. However, the final determination as to whether or not to require Shire to engage a new IRO shall be made at the sole discretion of OIG.

**APPENDIX B**  
**TO CIA FOR**  
**SHIRE NORTH AMERICAN GROUP, INC.**  
**IRO REVIEWS**

**I. IRO Engagement, General Description**

As specified more fully below, Shire shall retain an Independent Review Organization(s) (IRO) to perform engagements to assist Shire in assessing and evaluating certain of its systems, processes, policies, and procedures related to Shire's Covered Functions and Risk Assessment and Mitigation Process (RAMP) (IRO Review). The IRO Review shall consist of two components - a Systems Review (the Covered Functions and RAMP Systems Review) and a transactions review (the Transactions Review), as described more fully below. Shire may engage, at its discretion, a single entity to perform both components of the IRO Review, provided that the entity has the necessary expertise and capabilities to perform both.

If there are no material changes in Shire's systems, processes, policies, and procedures relating to the Covered Functions or its RAMP, the IRO shall perform the Systems Review for the second and fourth Reporting Periods. If Shire materially changes its systems, processes, policies, and procedures relating to Covered Functions or its RAMP, the IRO shall perform a Systems Review for the Reporting Period(s) in which such changes were made in addition to conducting the Review for the second and fourth Reporting Periods. The additional Systems Review(s) shall consist of: 1) an identification of the material changes; 2) an assessment of whether other systems, processes, policies, and procedures previously reported did not materially change; and 3) a review of the systems, processes, policies, and procedures that materially changed. The IRO shall conduct the Transactions Review for each Reporting Period of the CIA.

**II. IRO Systems Review**

The Covered Functions and RAMP Systems Review shall be a review of Shire's systems, processes, policies, and procedures (including the controls on those systems, processes, policies, and procedures) relating to certain Covered Functions and its RAMP. Where practical, Shire personnel may compile documentation, schedule and organize interviews, and undertake other efforts to assist the IRO in performing the Systems Review. The IRO is not required to undertake a de novo review of the information gathered or activities undertaken by Shire pursuant to the preceding sentence. Specifically, the IRO shall review Shire's systems, processes, policies, and procedures associated with the following (hereafter "Reviewed Policies and Procedures"):



1) Shire’s systems, policies, processes, and procedures applicable to the manner in which sales representatives handle requests or inquiries relating to information about the uses of Government Reimbursed Products (including non-FDA-approved (*i.e.*, off-label) uses) and the dissemination of materials relating to off-label uses of Government Reimbursed Products. This review includes:

- a) the manner in which sales representatives handle requests for information about off-label uses of Government Reimbursed Products (*i.e.*, by referring all requests to medical affairs), including any electronic system(s) that Shire uses to collect, process, and/or store such information;
- b) the manner in which medical affairs personnel handle and respond to requests for information about off-label uses of Government Reimbursed Products (including tracking the requests and using the materials provided in response to the request);
- c) the form and content of information and materials related to Government Reimbursed Products disseminated to physicians, pharmacists, or other health care professionals (collectively “HCPs”) or health care institutions (“HCIs”) by Shire;
- d) Shire’s systems, processes, and procedures (including the Inquiries Databases) used to track requests for information about off-label uses of Government Reimbursed Products and responses to those requests;
- e) the manner in which Shire collects and supports information reported in any systems used to track and respond to requests for Government Reimbursed Product information, including the Inquiries Databases;
- f) the processes and procedures by which medical affairs personnel and Shire’s Compliance Department or their designees monitor and identify situations in which it appears that improper promotion may have occurred; and
- g) Shire's processes and procedures for investigating, documenting, resolving, and taking appropriate disciplinary action for potential situations involving improper promotion;

2) Shire’s systems, processes, policies and procedures applicable to the manner and circumstances under which Medical Science Liaisons (MSLs) interact with or participate in meetings or events with HCPs or HCIs (either alone or with sales representatives) and the role of the MSLs at such meetings or events, including the manner in which they handle responses to unsolicited requests about off-label indications of Government Reimbursed Products;

- 3) Shire's systems, policies, processes, and procedures relating to Shire's internal review and approval of information and materials that are disseminated to HCPs or HCIs and relate to Government Reimbursed Products;
- 4) Shire's systems, processes, policies, and procedures relating to incentive compensation for Relevant Covered Persons who are sales representatives, with regard to whether the systems, policies, processes, and procedures are designed to ensure that financial incentives do not inappropriately motivate such individuals to engage in the improper promotion, sales, and marketing of Government Reimbursed Products. This shall include a review of the bases upon which compensation is determined and the extent to which compensation is based on product performance. To the extent that Shire establishes different systems, processes, policies, or procedures relating to compensation for different Government Reimbursed Products, the IRO shall review each type of compensation arrangement separately;
- 5) Shire's systems, processes, policies, and procedures relating to the development and review of call plans (as described in Section III.B.3.h of the CIA). This shall include a review of the bases upon which HCPs and HCIs belonging to specified medical specialties are included in, or excluded from, the call plans based on, among other factors, expected utilization of Government Reimbursed Products for FDA-approved uses or non-FDA-approved uses;
- 6) Shire's systems, processes, policies, and procedures relating to sample distribution (as described in Section III.B.3.i of the CIA). This shall include a review of the bases upon, and circumstances under, which HCPs and HCIs belonging to specified medical specialties or types of clinical practice may receive samples from Shire (including, separately, from sales representatives and other personnel or components). It shall also include a review of whether samples of Government Reimbursed Products are distributed through sales representatives or are distributed from a central location and the rationale for the manner of distribution;
- 7) Shire's systems (including any centralized electronic system), processes, policies, and procedures relating to speaker programs, speaker training programs, and all events and expenses relating to such engagements or arrangements;
- 8) Shire's systems, processes, policies, and procedures relating to non-speaker related consultant or other fee-for-service arrangements entered into with HCPs or HCIs (including, but not limited to, presentations, consultant meetings, advisory boards, and ad hoc advisory activities, and any other financial engagement or arrangement with an HCP or HCI) and all events and expenses relating to such engagements or arrangements;

9) Shire's systems, processes, policies and procedures relating to the submission of information about any Government Reimbursed Product to any compendia such as Drugdex or other published source of information used in connection with the determination of coverage by a Federal health care program for the Government Reimbursed Product ("Compendia"). This includes any initial submission of information to any Compendia and the submission of any additional, updated, supplemental, or changed information, (*e.g.*, any changes based on Shire's discovery of erroneous or scientifically unsound information or data associated with the information in the Compendia.) The review shall also assess Shire's processes relating to its annual review of all arrangements with, and processing fees or other payments or financial support (if any) provided by the company to any Compendia;

10) Shire's systems, processes, policies and procedures relating to RAMP, including but not limited to, a review of: (a) the sources and types of information used in connection with the risk assessment (*e.g.*, the individual personnel, departments or functional areas, and/or any data and systems involved); and (b) the timing for development of the risk assessment and risk mitigation plans;

11) An assessment of whether, in developing the risk assessment or risk mitigation plans: (a) additional or different sources of information should be utilized; (b) additional or different types of data or information should be utilized; and (c) additional or different timing cycles should be utilized;

12) A review of the experience, background, and training of personnel responsible for the development of the risk assessment and risk mitigation plans; and an assessment of the completeness and appropriateness of the relevant training, policies, procedures, standard operating procedures, and guidance each such individual receives;

13) An assessment of whether risk monitoring, review, and, as appropriate, audit activities related to RAMP: (a) adequately monitor all relevant identified risks; (b) identify any actual problems that have occurred in connection with the identified potential sales, marketing or promotional risk; and/or (c) prevent reoccurrence of any problems associated with an identified risk;

14) An assessment of whether risk monitoring, review, and, as appropriate, audit activities related to Shire's RAMP should be: (a) enhanced, revised, or refined; (b) changed to include additional or different mitigation/monitoring options to be considered based upon specific identified risks; and/or (c) tracked and reviewed more frequently than prescribed by current policies to ensure that the mitigation/monitoring options address all relevant risks for the specific Government Reimbursed Products reviewed; and

15) A review of the systems, policies, procedures, and processes by which Shire tracks and manages RAMP activities and an assessment of whether the systems, policies,

procedures and processes ensure that risk mitigations plans are appropriately implemented (including by identifying individuals responsible for the follow-up action items).

### **III. IRO Systems Review Report**

The IRO shall prepare a report based upon each Systems Review. For each of the Reviewed Policies and Procedures identified in Section II. above, the report shall include the following items:

- 1) a description of the documentation (including policies) reviewed and any personnel interviewed;
- 2) a detailed description of Shire's systems, policies, processes, and procedures relating to the items identified in Sections II.1-15 above, including a general description of Shire's control and accountability systems (*e.g.*, documentation and approval requirements, and tracking mechanisms) and written policies regarding the Reviewed Policies and Procedures;
- 3) a description of the manner in which the control and accountability systems and the written policies relating to the items identified in Sections II.1-15 above are made known or disseminated within Shire;
- 4) a detailed description of any system(s) used to track and respond to requests for information about Government Reimbursed Products (including the Inquiries Databases);
- 5) a detailed description of Shire's incentive compensation system, if any, for Covered Persons who are sales representatives, including a description of the bases upon which compensation is determined and the extent to which compensation is based on Government Reimbursed Product performance. To the extent that Shire may establish compensation differently for individual products, the IRO shall report separately on each such type of compensation arrangement;
- 6) findings and supporting rationale regarding any weaknesses in Shire's systems, processes, policies, and procedures relating to the Reviewed Policies and Procedures, if any;
- 7) recommendations to improve any of the systems, policies, processes, or procedures relating to the Reviewed Policies and Procedures, if any;
- 8) whether the risk monitoring and risk mitigation action associated with RAMP identify relevant risks and address identified risks;

- 9) whether sufficient controls exist to ensure that all monitoring, review, and auditing activities and risk mitigation action items are tracked appropriately;
- 10) whether RAMP (including the options for risk mitigation activities) potentially mitigates identified risks; and
- 11) whether sufficient controls exist to ensure that all agreed-upon risk monitoring, review, and audit activities and risk mitigation action items are completed as planned.

#### **IV. IRO Transactions Review**

As described more fully below in Sections IV.A-D, the Transactions Review shall include: (1) a review of a sample of Inquiries reflected in the Inquiries Databases; (2) a review of call plans and the call plan review process described at Section III.B.3.h of the CIA; (3) a review of records relating to a sample of the Payments that are reported by Shire pursuant to Section III.M of the CIA; (4) a review of Shire's promotional materials review and approval process; and (5) as described in IV.E below, a review of up to three additional items identified by OIG in accordance with Section III.E.1.b of the CIA (hereafter "Additional Items".) The IRO shall report on all aspects of its reviews in the Transactions Review Reports.

##### **A. Review of Inquiries and Inquiries Databases**

###### **1) Description of Inquiries Databases**

As set forth in Section III.B.3.f of the CIA, Shire shall establish databases (Inquiries Databases) to track information relating to all requests for information received by medical affairs personnel about Government Reimbursed Products (Inquiries). Shire shall record in the Inquiries Databases the following information for each Inquiry received: (a) date of Inquiry; (b) form of Inquiry (*e.g.*, fax, phone, medical information request form); (c) name of requesting HCP or HCI; (d) nature and topic of request including exact language of the Inquiry (if made in writing); (e) an evaluation of whether the Inquiry relates to information about off-label use for the Government Reimbursed Product; (f) nature/form of the response from Shire (including a record of any materials provided in response to the request); and (g) the name of the Shire representative who called upon or interacted with the HCP or HCI, if known.

###### **2) Internal Review of Inquiries Databases**

On a semi-annual basis, the CCRO, or a designee, shall review the Inquiries Databases and related information, as appropriate, and shall generate a report summarizing the items of information outlined in Section IV.A.1 above for each

Inquiry received during the preceding two quarters (Inquiry Report). The CCRO (or designee) shall review the Inquiry Reports to assess whether the information contained in the report suggests that improper (including but not limited to off-label) promotion may have occurred in connection with any Inquiry(ies). If the CCRO (or designee), in consultation with other appropriate Shire personnel, suspects that improper (including but not limited to off-label) promotion may have occurred in connection with any Inquiry, the CCRO shall initiate a follow-up review of the Inquiry (Improper Promotion Review), make specific findings based on his/her Improper Promotion Review, and take all appropriate responsive action (including disciplinary action of the Covered Person and reporting of the conduct, including disclosing Reportable Events pursuant to Section III.I of the CIA, if applicable).

### 3) IRO Review of Inquiries Reflected in Inquiries Databases

The IRO shall select and review a random sample of 50 Inquiries from among the Inquiries reflected in the Inquiries Databases for each Reporting Period. 40 of the Inquiries reviewed by the IRO shall be Inquiries for which Shire conducted an Improper Promotion Review, and the other 10 shall be Inquiries for which Shire did not conduct an Improper Promotion Review. For each Inquiry reviewed, the IRO shall determine:

- a) Whether each item of information listed above in Section IV.A.1 is reflected in the Inquiries Databases for each reviewed Inquiry; and
- b) For each Inquiry for which the CCRO (or designee) conducted an Improper Promotion Review, the basis for suspecting that improper off-label promotion may have occurred; the steps undertaken as part of the Improper Promotion Review; the findings of the Compliance Officer as a result of the Improper Promotion Review; and any follow-up actions taken by Shire based on the Improper Promotion Review findings.

### B. IRO Review of Call Plans and Call Plan Review Process

The IRO shall conduct a review and assessment of Shire's review of call plans described in Section III.B.3.h of the CIA. Shire shall provide the IRO with: (1) a list of Government Reimbursed Products promoted during the Reporting Period; (2) information about the FDA-approved uses for each Government Reimbursed Product; and (3) the call plans for each Government Reimbursed Product. Shire shall also provide the IRO with information about the reviews of call plans that Shire conducted during the Reporting Period and any modifications to the call plans made as a result of Shire's reviews.

For each call plan, the IRO shall select a sample of 50 of the HCPs and HCIs included on the call plan. For each call plan, the IRO shall compare the sampled HCPs and HCIs against the criteria (*e.g.*, medical specialty or practice area) used by Shire in conducting its review and/or modification of the call plan in order to determine whether Shire followed its criteria and Policies and Procedures in reviewing and modifying the call plan.

The IRO shall note any instances in which it appears that the sampled HCPs and HCIs on a particular call plan are inconsistent with the criteria applicable to the call plan and/or Shire's Policies and Procedures. The IRO shall also note any instances in which it appears that Shire failed to follow its criteria or Policies and Procedures.

### C. IRO Review of Physician Covered Recipient Payment Reports

#### 1) Information Contained in Physician Covered Recipient Payment Reports

As set forth in Section III.M of the CIA, Shire shall post the partial 2013 report and annual reports of Physician Covered Recipients who received Payments, as defined in the CIA, directly or indirectly from Shire. For each Physician Covered Recipient, each report shall include the following information: (i) physician's full name; (ii) city and state of the physician's practice; and (iii) the aggregate value of the Payments from August 1, 2013 through December 31, 2013, for the partial 2013 report; or (iv) the aggregate value of the Payment(s) in the preceding calendar year, for each annual report.

For purposes of this IRO review, the term "Control Documents" shall include all documents or electronic records associated with each Payment reflected in the report for the sampled Physician Covered Recipient. For example, the term "Control Documents" includes, but is not limited to, documents relating to the nature, purpose, and amount of all Payments reflected in the report; contracts relating to the Payment(s) reflected in the report; documents relating to the occurrence of Payment(s) reflected in the report; documents reflecting any work product generated in connection with the Payment(s); documents submitted by sales representatives or headquarters personnel to request approval for the Payment(s); and business rationale or justification forms relating to the Payment(s).

#### 2) Selection of Sample for Review

For each Reporting Period, the OIG shall have the discretion to identify up to 50 Physician Covered Recipients from the applicable report that will be subject to the IRO review described below. If the OIG elects to exercise this discretion, it shall notify the IRO of the Physician Covered Recipients subject to the IRO review.

If the OIG elects not to exercise its discretion as described above, the IRO shall randomly select 50 Physician Covered Recipients to be included in the review. For each selected Physician Covered Recipient, the IRO shall review the entry in the report and the Control Documents relating to Payments reflected in the report identified by the IRO as necessary and sufficient to validate the Payment information in the report.

### 3) IRO Review of Control Documents for Sampled Physician Covered Recipients

For each Physician Covered Recipient selected as part of the sample, the IRO shall review the Control Documents identified by the IRO as necessary and sufficient to validate each Payment reflected in the report to evaluate the following:

- a) Whether Control Documents are available relating to each Payment reflected in the report for the sampled Physician Covered Recipient;
- b) Whether the Control Documents were completed and archived in accordance with the requirements set forth in Shire's policies;
- c) Whether the aggregate value of the Payment(s) as reflected in the report for the sampled Physician Covered Recipient is consistent with the value of the Payment(s) reflected in the Control Documents; and
- d) Whether the Control Documents reflect that Shire's policies were followed in connection with Payment(s) reflected in the report (*e.g.*, all required written approvals for the activity were obtained in accordance with Shire's policies.)

### 4) Identification of Material Errors and Additional Review

A Material Error is defined as any of the following:

- a) A situation in which all required Control Documents relating to Payments reflected in the report for the sampled Physician Covered Recipient do not exist and:
  - i. no corrective action was initiated prior to the selection of the sampled Physician Covered Recipients; or
  - ii. the IRO cannot confirm that Shire otherwise followed its policies and procedures relating to the entry in the report for the sampled Physician Covered Recipient, including its policies and procedures relating to any Payment(s) reflected in the report; or



- b) Information or data is omitted from key fields in the Control Documents that prevents the IRO from assessing compliance with Shire's policies and procedures, and the IRO cannot obtain this information or data from reviewing other Control Documents.

If a Control Document does not exist, but Shire has initiated corrective action prior to the selection of the sampled Physician Covered Recipient, or if a Control Document does not exist but the IRO can determine that Shire otherwise followed its policies and procedures with regard to each entry in the report for a sampled Physician Covered Recipient, the IRO shall consider such a situation to be an exception (rather than a Material Error) and the IRO shall report the situation as such. Similarly, the IRO shall note as exceptions any Control Documents for which non-material information or data is omitted.

If the IRO identifies any Material Errors, the IRO shall conduct such Additional Review of the underlying Payment associated with the erroneous Control Documents as may be necessary to determine the root cause of the Material Errors. For example, the IRO may need to review additional documentation and/or conduct interviews with appropriate personnel to identify the root cause of the Material Error(s) discovered.

#### D. IRO Review of Promotional Materials Review and Approval Process

Shire shall provide the IRO with a list of all promotional materials: (1) reviewed by Shire during the Reporting Period; (2) approved for dissemination outside of Shire; and (3) containing claims or information about Government Reimbursed Products actively promoted during the Reporting Period ("Reviewed Promotional Materials"). From this list, the IRO shall select a sample of 50 Reviewed Promotional Materials. Shire shall provide the IRO with documents and information relating to the sample of Reviewed Promotional Materials sufficient to enable the IRO to conduct the review outlined below.

For each item of Reviewed Promotional Material, the IRO will review whether: (1) unique identifiers, such as unique serial numbers and date of preparation, identify the item of Reviewed Promotional Material in accordance with Shire policies and procedures; (2) appropriate Shire personnel reviewed and approved it consistent with Shire's policies and procedures; (3) completion of the review and the determination to approve was correctly noted in the appropriate electronic system, in accordance with Shire's policies and procedures; (4) a determination was made concerning how the item of Reviewed Promotional Material could be disseminated and by whom; (5) all changes required during the review were incorporated into the final version of the item of Reviewed Promotional Material, and if not, whether appropriate steps were taken in accordance with Shire's policies and procedures, to assure dissemination of the approved version of the item of Reviewed Promotional Material; (6) submission of the item of Reviewed Promotional Material to FDA was required and appropriately submitted, if required; (7) the age of the item of Reviewed Promotional Material was accurately

reflected in the electronic system that tracks the lifecycle (including but not limited to the approval and expiration dates) of Promotional Materials; and (8) the item of Reviewed Promotional Material was deemed no longer authorized for dissemination outside of Shire, and if so, why.

#### E. IRO Review of Additional Items

As set forth in Section III.E.1.b of the CIA, for each Reporting Period, OIG at its discretion may identify up to three additional items for the IRO to review (hereafter “Additional Items”.) No later than 150 days prior to the end of the applicable Reporting Period, OIG shall notify Shire of the nature and scope of the IRO review to be conducted for each of the Additional Items. Prior to undertaking the review of the Additional Items, the IRO and/or Shire shall submit an audit work plan to OIG for approval and the IRO shall conduct the review of the Additional Items based on a work plan approved by OIG. The IRO shall include information about its review of each Additional Item in the Transactions Review Report (including a description of the review conducted for each Additional Item; the IRO’s findings based on its review for each Additional Item; and the IRO’s recommendations for any changes in Shire’s systems, processes, policies, and procedures based on its review of each Additional Item.)

Shire may propose to OIG that its internal audit(s) and/or reviews conducted as part of the Sales and Marketing Monitoring Program (SMMP) described in Section III.K of the CIA or the Non-Promotional Monitoring Program (NPMP) described in Section III.L of the CIA be substituted for one or more of the Additional Items that would otherwise be reviewed by the IRO for the applicable Reporting Period. OIG retains sole discretion over whether, and in what manner, to allow Shire’s internal audit work and monitoring activities to be substituted for a portion of the Additional Items review conducted by the IRO.

In making its decision, OIG agrees to consider, among other factors, the nature and scope of Shire’s planned monitoring activities and internal audit work, the results of the Transactions Review(s) during prior Reporting Period(s), and Shire’s demonstrated audit capabilities to perform the proposed audit work internally. If OIG denies Shire’s request to permit its monitoring activities or internal audit work to be substituted for a portion of the IRO’s review of Additional Items in a given Reporting Period, Shire shall engage the IRO to perform the Review as outlined in this Section IV.

If OIG agrees to permit certain of Shire’s monitoring activities or internal audit work for a given Reporting Period to be substituted for a portion of Additional Items review, such internal work would be subject to verification by the IRO (Verification Review). In such an instance, OIG would provide additional details about the scope of the Verification Review to be conducted by the IRO. However, for purposes of any Verification Review,

the IRO shall review at least 20% of the sampling units reviewed by Shire in its internal audits.

#### F. Transactions Review Report

For each Reporting Period, the IRO shall prepare a report based on its Transactions Reviews. The report shall include the following:

##### 1) General Elements to Be Included in Report

- a) Review Objectives: A clear statement of the objectives intended to be achieved by each part of the review;
- b) Review Protocol: A detailed narrative description of the procedures performed and a description of the sampling unit and universe utilized in performing the procedures for each sample reviewed; and
- c) Sources of Data: A full description of documentation and other information, if applicable, relied upon by the IRO in performing the Transactions Review.

##### 2) Results to be Included in Report

The following results shall be included in each Transactions Review Report:

(Relating to the Review of Inquiries)

- a) in connection with the review of Inquiries, a description of each type of sample unit reviewed, including the number of each type of sample units reviewed (*e.g.*, the number of Inquiries) and an identification of the types of documents and information reviewed for the Inquiries;
- b) for each Inquiry sample unit, the IRO shall summarize the information about the Inquiry contained in the Inquiries Databases;
- c) for each Inquiry sample unit, findings and supporting rationale as to whether:
  - (i) each item of information listed in Section IV.A.1 is reflected in the Inquiries Databases; and
  - (ii) for each Inquiry for which an Improper Promotion Review was conducted, the basis for suspecting that improper (including but not limited to off-label) promotion may have occurred; the steps undertaken as part of the Improper Promotion Review; the findings of the Compliance Officer as a result of the

Improper Promotion Review; and any follow-up actions taken by Shire as a result of the CCRO's findings;

d) the findings and supporting rationale regarding any weaknesses in Shire's systems, processes, policies, procedures, and practices relating to the Inquiries, and the Inquiries Databases, if any; and

e) recommendations for improvement in Shire's systems, processes, policies, procedures, and practices relating to the Inquiries and the Inquiries Databases, if any;

(Relating to the Call Plan Reviews)

f) a list of the Government Reimbursed Products promoted during the Reporting Period and a summary of the FDA-approved uses for such products;

g) for such Government Reimbursed Products: i) a description of the criteria used in developing or reviewing the call plans and for including or excluding specified types of HCPs or HCIs from the call plans; ii) a description of the review conducted by Shire of the call plans and an indication of whether Shire reviewed the call plans as required by Section III.B.3.h of the CIA; iii) a description of all instances for each call plan in which it appears that the HCPs and HCIs included on the call plan are inconsistent with Shire's criteria relating to the call plan and/or Shire's Policies and Procedures; and iv) a description of all instances in which it appears that Shire failed to follow its criteria or Policies and Procedures relating to call plans or the review of the call plans;

h) the findings and supporting rationale regarding any weaknesses in Shire's systems, processes, policies, procedures, and practices relating to the call plans or the review of the call plans, if any; and

i) recommendations, if any, for changes in Shire's systems, processes, policies, procedures, and practices that would correct or address any weaknesses or deficiencies uncovered during the Transactions Review with respect to call plans or the review of the call plans;

(Relating to the Physician Covered Recipient Payment Reports)

j) a description of the entries in the report for each Physician Covered Recipient sampled and a description of Control Documents reviewed in connection with each selected Physician Covered Recipient;

k) for each sampled Physician Covered Recipient, findings and supporting rationale as to whether: (i) all required Control Documents exist; (ii) each Control Document was completed in accordance with all of the requirements set forth in the applicable Shire policy; (iii) the aggregate value of the Payment(s) as reflected in the report for the sampled Physician Covered Recipient is consistent with the value of the Payment(s) reflected in the Control Documents; (iv) each Control Document reflects that Shire's policies were followed in connection with the underlying activity reflected in the document (*e.g.*, all required approvals were obtained); and (v) any corrective action or disciplinary action was undertaken in those instances in which Shire policies were not followed;

l) for each sampled Physician Covered Recipient, an identification and description of all exceptions discovered. The report shall also describe those instances in which corrective action was initiated prior to the selection of the sampled Physician Covered Recipient, including a description of the circumstances requiring corrective action and the nature of the corrective action; and

m) if any Material Errors are discovered, a description of each error, the Additional Review procedures performed and a statement of findings as to the root cause(s) of the Material Error;

(Relating to the Promotional Materials Review and Approval Process)

n) a description of each item of Reviewed Promotional Material, including unique identifiers, and the types of documents and information reviewed in connection with each sampled item of Reviewed Promotional Material;

o) for each item of Reviewed Promotional Material reviewed, an assessment of whether it was reviewed and approved by appropriate Shire personnel consistent with Shire's policies and procedures;

p) for each item of Reviewed Promotional Material, whether completion of the review and the decision to approve was correctly noted in the appropriate electronic system in accordance with Shire's policies and procedures;

q) for each approved item of Reviewed Promotional Material, whether a determination was made concerning how the item could be disseminated and by whom;

r) for each item of Reviewed Promotional Material, whether all changes required during the review were incorporated into the final version of the Reviewed Promotional Material, and if not, whether appropriate steps were taken in

accordance with Shire's policies and procedures to assure dissemination of the approved version of the item of Reviewed Promotional Material;

s) whether submission of each item of Reviewed Promotional Material to FDA was required and appropriately submitted, if required;

t) whether the age of each item of Reviewed Promotional Material was accurately reflected in the electronic system that tracks the lifecycle (including but not limited to the approval and expiration dates) of promotional materials;

u) whether the item of Reviewed Promotional Material was deemed unauthorized for dissemination outside of Shire, and if so, why, and steps taken by Shire to ensure no further dissemination of the item of Reviewed Promotional Material;

v) the IRO's findings and supporting rationale regarding any weaknesses or deficiencies in Shire's systems, processes, policies, procedures, and/or practices relating to Shire's promotional materials review and approval activities; and

w) IRO recommendations, if any, for changes in Shire's systems, processes, policies, and procedures that would correct or address any weaknesses or deficiencies uncovered during the Transactions Review with respect to Shire's promotional materials review and approval activities;

(Relating to the Review of Additional Items)

x) for each Additional Item reviewed, a description of the review conducted;

y) for each Additional Item reviewed, the IRO's findings based on its review;

z) for each Additional Item reviewed, the findings and supporting rationale regarding any weaknesses in Shire's systems, processes, policies, procedures, and practices relating to the Additional Item, if any; and

aa) for each Additional Item reviewed, recommendations, if any, for changes in Shire's systems, processes, policies, and procedures that would correct or address any weaknesses or deficiencies uncovered during the review.