

Section VIII.

Isis Policy and Procedures Manual

CODE OF ETHICS AND BUSINESS CONDUCT

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ISIS PHARMACEUTICALS, INC.
1896 Rutherford Road
Carlsbad, CA 92008

Code of Ethics and Business Conduct

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PHILOSOPHY OF ISIS CODE OF ETHICS AND BUSINESS CONDUCT

Isis Pharmaceuticals, Inc. (hereinafter referred to as “Isis” or the “Company”) will adhere to high legal and ethical standards. As such, this Code of Ethics and Business Conduct (hereinafter referred to as the “Code of Ethics”) applies to each of Isis’ employees (including its executive officers) and each member of the Isis Board of Directors.

COMPLIANCE WITH LAWS AND REGULATIONS

As a U.S. company, Isis is governed by and required to comply with U.S. federal law. In addition to complying with federal law, Isis will conduct all its activities in compliance with all applicable national, state and local laws, regulations and judicial decrees wherever it conducts business.

At no time will you take any action on behalf of the Company that you know, or reasonably should know, violates any law or regulation. Whenever possible, you will strive to comply with the spirit of the law as well as its letter.

No code of conduct can cover all circumstances or anticipate every situation. When you encounter situations not addressed specifically by this Code of Ethics, you should apply its overall philosophy and concepts to the situation. You should also refer to specific Company policies on the subject in question or similar subjects. If you still have a question about the appropriateness of an action, you should review the particular circumstances with Isis’ COO, CEO or the Audit Committee of the Board of Directors.

ETHICAL CONDUCT

You should strive to act in a manner using good judgment, high ethical standards and honesty in your business dealings on behalf of the Company. Unethical practices and activities do not serve the interests of the Company or the community, even if they do not technically violate the law.

Your Responsibilities

- Know and comply with the Isis Code of Ethics and Company policies that apply to business activities.
- Be honest, fair and trustworthy in all business activities and relationships.
- Provide and support a culture that values integrity and ethical conduct.
- Avoid all conflicts of interest between work and personal affairs.

- Report suspected violations of law, the Isis Code of Ethics or Company Policies.
- Cooperate in any investigation into possible violations of law, the Isis Code of Ethics or Company Policies.

Business Practices

It is Isis’ policy to deal with its business associates, partners, suppliers, competitors and any governments or governmental agencies with which it interacts in an ethical manner. As such, you will comply with the principles outlined below and will take steps to ensure similar compliance by the persons you directly manage.

Interaction with Competitors

As a vigorous competitor in the marketplace, Isis will seek economic knowledge about our competitors. However, you will not engage in illegal or improper acts to acquire any competitor information. In addition, you will not hire competitors' employees for the purpose of obtaining confidential information, urge competitors' personnel, customers or suppliers to disclose confidential information, or seek such information from competitors' employees subsequently hired by the Company.

Bribes, Kickbacks and Similar Payments

You are prohibited from paying or receiving any bribe, kickback or other similar payment to or from any public official, or government, or other individual, to secure any concession, contract or other favorable treatment for Isis or you. This prohibition extends to the payment or receipt of money or anything else of substantial value when you have reason to believe that some part of the payment or "fee" will be used for a bribe, kickback or other similar activity.

Because Isis is a global company and does business worldwide, you must comply with the United States Foreign Corrupt Practices Act of 1977. For more detail, please read the "Foreign Corrupt Practices Act," attached as Appendix A.

Books, Records and Information Management

Isis' books of account and records must be accurately maintained and fully disclose the nature of transactions reflected in them. Penalties for violating the laws and regulations in this area could be severe for the Company and the employees involved. Isis will maintain these books according to the following record-keeping requirements and in compliance with the spirit and letter of applicable laws and regulations:

- All books, records and accounts must be kept in reasonable detail and must accurately and fairly reflect all transactions and dispositions of the Company's assets.
- All disbursements of funds and all receipts must be properly and promptly recorded.
- No undisclosed or unrecorded fund or account may be established for any purposes.
- False or artificial entries must never be made in any of the books or records of the Company, or in any public record for any reason, nor should the Company's records be falsely altered in any way.

Retention of Records

Legal practice requires the retention of certain records for various periods of time, particularly those relating to taxes, personnel, contracts and corporate structure. When litigation or a government investigation or audit is pending or imminent, you must not destroy any relevant records until the matter is closed. Destruction of records to avoid disclosure in a legal proceeding or investigation may constitute a criminal offense.

Audit Integrity

No officer or director of Isis, or any other person acting under their direction, will take any action to fraudulently influence, coerce, manipulate, or mislead any independent accountant engaged in the performance of an audit of the Company's financial statements for the purpose of rendering the Company's financial statements materially misleading.

Conflicts of Interest

As an employee you cannot without the Company's express written consent, engage in any employment or business activity other than for the Company. Unless expressly consented to in writing by the Company, your personal activities should not involve the use of Company property, facilities, influence or other resources, and should not reflect discredit upon the Company.

You will not engage in any activity through which you stand to benefit personally from any sale or purchase of goods and services by the Company. This provision does not apply to benefits arising out of your employment with the Company, or to ownership of equity in a publicly traded company which was purchased on the open market and represents (i) less than 1% of such company's outstanding equity and (ii) less than 5% of your equity portfolio.

You must promptly disclose in writing any actual or potential conflicts of interest to Isis' COO, CEO or General Counsel. Isis will review the matter, as set forth above, and communicate its position in writing.

Pre-Clearance Procedure

All employees must pre-clear any employment or business activity other than for the Company. To do so, you should contact either (i) the CEO, (ii) COO or (iii) General Counsel and explain to them the proposed business activity you wish to engage in. If you are an executive officer, the Nominating, Governance and Review Committee will evaluate the proposed business activity and will notify you whether such activity has been approved. For all other employees, the CEO or COO will evaluate the proposed business activity and will notify you whether such activity has been approved. In some cases, the individual(s) reviewing your request may discuss your request with other members of the Isis management team. Remember, just because you have to pre-clear a certain activity, does not mean that Isis will prevent you doing it.

Members of the Board of Directors must request and receive a determination of no conflict from the Nominating, Governance and Review Committee before engaging in any activity, including acting as an employee or director for any entity that directly or indirectly competes with Isis.

Certain Pre-Cleared Business Activities

Isis' management has already pre-cleared certain business activities that should not cause a conflict of interest. For these activities, employees generally do not need to obtain written permission from the Company. However, please use your common sense because even with pre-cleared activities, conflicts of interest can arise. If you are ever in doubt, you should follow the pre-clearance procedures outlined above. The pre-cleared business activities include:

- Working in the food service or hospitality industry after normal business hours;
- Owning rental property (unless Isis rents the property);
- Philanthropic or pro bono activities;
- Farming;
- Home-based retail (e.g. Amway, Tupperware, cosmetics), provided you do not solicit sales during Isis business hours or at the Isis workplace; and
- Fitness instructor.

Dishonesty and Theft

You will not knowingly:

- Engage in fraud or embezzlement affecting Company property, funds, securities or other assets; or
- Willfully damage or destroy property or materials belonging to the Company, its employees or customers.

In addition, without proper supervisory authorization, you will not knowingly:

- Remove property, material or money from the Company, its employees, or its customers for personal gain, personal use, resale or to give to another party;
- Receive property, materials or money belonging to the Company, its employees or its customers for personal gain, personal use, resale or to give to another party;
- Access, remove, publish, destroy or alter private or confidential information existing in physical Company records or electronically stored information;
- Remove, publish, destroy or alter other physical Company records or electronically stored information affecting the Company, its employees or corporate partners; or
- Copy, reprint, duplicate, or recreate in whole or in part, computer programs or related systems developed or modified by Isis personnel, or acquired from outside vendors.

Insider Trading

During the course of your employment, you may receive important information which is not yet publicly available (“inside information”) about Isis or about other publicly traded companies

with which the Company has business dealings. Because of your access to this information, you may be in a position to profit financially by buying or selling or in some other way dealing in Company stock or the stock of another publicly traded company. Similarly, you may be in a position to benefit financially or otherwise by passing this information on to some other person. Whether you personally benefit or another benefits, this is considered “insider trading” and is illegal.

You may not disclose inside information to anyone inside the Company who is not authorized to access it or to anyone outside the Company. When you have access to inside information, you may not buy or sell Isis stock regardless of the number of shares nor may you encourage or discourage others from trading on Company stock.

WAIVERS FOR EXECUTIVE OFFICERS AND DIRECTORS

Any waiver of this Code of Ethics for executive officers or members of the Board of Directors must be approved by the Nominating, Governance and Review Committee and must be promptly disclosed to the Company’s stockholders, including the reasons for the waiver.

REPORTING SUSPECTED VIOLATIONS

Isis is committed to complying with all applicable securities laws and to filing fair and accurate disclosures with the SEC. Each Employee who reports suspected accounting improprieties or violations of this Code of Ethics or of any laws specifically including federal mail fraud, wire fraud, or securities fraud statutes will be taken seriously and the allegations will be thoroughly investigated.

An employee who suspects accounting improprieties or violations of this Code of Ethics or of any laws specifically including federal mail fraud, wire fraud, or securities fraud statutes should take the following steps:

1. The employee should immediately communicate his/her concern to the General Counsel, the COO or the CEO. To ensure the highest quality response, employees should communicate directly with one of these designated Isis officials. However, any concern may be made anonymously and will be taken seriously.
2. Any officer receiving such a complaint will immediately communicate the complaint to the Audit Committee or you may directly report a suspected violation to the Chairman of the Audit Committee.
3. The Audit Committee together with management will conduct, if appropriate, a confidential, but not anonymous investigation which will involve talking to the complainant (if known), the accused, and as circumstances warrant, any witnesses, and anyone who may have similar complaints.
4. All parties involved in the investigation will be required to cooperate fully, maintain complete confidentiality and take no action which might be considered retaliatory.
5. Once the investigation is complete, the Audit Committee will make a determination as to what happened, the level of severity and the appropriate remedial action, and will take such action.

Isis will not discharge, demote, suspend, threaten, harass, or in any other manner discriminate against an employee because you (1) have provided information, caused information to be

provided, or otherwise assisted in an investigation regarding any conduct which you reasonably believe constitutes a violation of this Code of Ethics or of the federal mail fraud, wire fraud, or securities fraud statutes, any SEC rule or any provision of federal law relating to fraud against stockholders, when the information or assistance is provided to or the investigation is conducted by a federal regulatory or law enforcement agency, any Member of Congress or Congressional committee, or a person with supervisory authority over the employee or (2) have filed, caused to be filed, testified, participated in or otherwise assisted in a proceeding filed or about to be filed (with any knowledge of Isis) relating to an alleged violation of the federal mail fraud, wire fraud, or securities fraud statutes, any SEC rule or any provision of federal law relating to fraud against stockholders. An employee who alleges such discharge or discrimination may file a civil complaint with the Secretary of Labor.

CONSEQUENCES OF VIOLATING ISIS' CODE OF ETHICS

If you violate the law, the Isis Code of Ethics or Isis' policies, you may be subject to disciplinary action, up to and including termination. If necessary, Isis may suspend your employment during an investigation into an alleged breach. Additional actions may include reassignment of work duties and limitation in future job opportunities. Isis may refer violations of law to local or federal law enforcement authorities for possible prosecution.

The Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act (FCPA) prohibits U.S. companies from making improper payments or gifts to foreign officials. Company policy requires that all directors, officers, employees, agents and consultants of Isis comply with the FCPA.

A. Definition of Foreign Official

Under the FCPA, the term “foreign official” includes elected and appointed governmental officials, candidates for public office, foreign political parties, officers and employees of government owned or controlled enterprises, and public international organizations. When in doubt, Isis employees should consult the Company’s Legal Counsel for advice on whether a potential recipient of a payment is a “foreign official.”

B. Prohibited Acts

The following acts are prohibited by the FCPA:

1. Authorizing, paying, promising or delivering any payment, gift or favor intended to influence any foreign official on a matter within that person’s responsibilities. For example, any payment to any foreign official for the purposes of obtaining or retaining sales of products or services to Isis, sales by Isis of Isis products or services, to win a bid or contract, or to obtain more favorable tax treatment is prohibited.
2. Any indirect payment to a third party if the payor knows that the third party may make a prohibited payment. For example, any payment to an Isis agent or consultant where the payor is aware or has firm belief that such agent or consultant may make an improper payment to a foreign official is prohibited. The Isis payor may not avoid this prohibition by deliberately ignoring or purposefully avoiding knowledge that a bribe may be paid.
3. Establishing any undisclosed or unrecorded “slush” funds or assets; making any false or artificial entries in company books or records; failing to keep books, records and accounts in reasonable detail to reflect accurately the handling of money and other assets; and failing to maintain internal accounting controls sufficient to verify that no improper payments have been made.

C. Permissible Payments

The following payments may be made:

1. Payments to a foreign official for the purpose of expediting or securing the performance of a routine governmental action. Payments for the following routine governmental actions are permissible: obtaining permits, licenses or other official documents to qualify to do business in a foreign country; processing governmental papers, such as visas and work orders; assuring police protection, mail pickup and delivery, or scheduling inspections associated with contract performance or inspections related to the transit of goods across country; and providing phone service, power and water supply, loading and unloading cargo or protecting perishable products or commodities from deterioration. Routine governmental action does not include any decision by a foreign official to encourage, to award, to continue or to modify the terms relating to any business with any Isis entity.
2. Any payment that is lawful under the written laws and regulations of the foreign country.
3. Any reasonable expenditure directly related to the promotion, demonstration or explanation of Isis products or services or the execution or performance of a contract with a foreign government or agency, such as the travel and lodging expenses of a foreign official on a trip for such purposes.

D. Penalties

Violations of the anti-bribery provisions of the FCPA may result in criminal fines of up to \$2,000,000 for corporations and \$100,000 and five years imprisonment for individuals. Violations of the accounting provisions may result in fines of up to \$2,500,000 for corporations and \$1,000,000 and ten years imprisonment for individuals. Under alternative fine provisions, a violator may be fined up to twice the amount of the gain or loss resulting from a violation.

Payments and the FCPA

Neither Isis nor any director, officer, employee, agent or consultant of the Company will directly or indirectly make or promise illegal payments or contributions, or engage in any other illegal conduct in order to influence customers, suppliers or governmental entities, including their officials or employees, to secure or retain business, to encourage any such employees or officials to fail to perform or to perform improperly their official functions or to influence legislation, nor undertake any of the acts prohibited by the FCPA, as summarized above. Neither Isis nor any director, officer, employee, agent or consultant of the Company will submit to extortion as a condition of doing business.