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## **FORM F-6EF**

**Shire plc - N/A**

**Filed: May 04, 2016 (period: )**

Filing to become effective immediately upon filing

As filed with the Securities and Exchange Commission on May 4, 2016

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549**

**FORM F-6  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933 FOR AMERICAN DEPOSITARY SHARES EVIDENCED BY  
AMERICAN DEPOSITARY RECEIPTS**

**SHIRE PLC**

(Exact name of issuer of deposited securities as specified in its charter)

N/A

(Translation of issuer's name into English)

**Jersey, Channel Islands**

(Jurisdiction of incorporation or organization of issuer)

**CITIBANK, N.A.**

(Exact name of depositary as specified in its charter)

399 Park Avenue  
New York, New York 10043  
(212) 816-6690

(Address, including zip code, and telephone number, including area code, of depositary's principal executive offices)

Jeffrey Poulton  
Shire Pharmaceuticals LLC  
1200 Morris Drive  
Wayne, Pennsylvania 19087  
(484) 595-8800

(Address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

**John B. Meade**  
**Davis Polk & Wardwell LLP**  
**450 Lexington Avenue**  
**New York, New York 10017**  
**(212) 450-4077**

**Herman H. Raspé, Esq.**  
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**1133 Avenue of the Americas**  
**New York, New York 10036**  
**(212) 336-2301**

It is proposed that this filing become effective under Rule 466 ☒ immediately upon filing.  
☐ on (Date) at (Time).

If a separate registration statement has been filed to register the deposited shares, check the following box : ☐

**CALCULATION OF REGISTRATION FEE**

Title of Each Class of Securities to be Registered	Amount to be Registered	Proposed Maximum Aggregate Price Per Unit*	Proposed Maximum Aggregate Offering Price**	Amount of Registration Fee
American Depositary Shares ("ADSs"), each ADS representing three (3) ordinary shares of Shire plc.	300,000,000 ADSs	\$5.00	\$15,000,000	\$1,510.50

\* Each unit represents 100 ADSs.

\*\* Estimated solely for the purpose of calculating the registration fee. Pursuant to Rule 457(k), such estimate is computed on the basis of the maximum aggregate fees or charges to be imposed in connection with the issuance of ADSs.

This Registration Statement may be executed in any number of counterparts, each of which shall be deemed an original, and all of such counterparts together shall constitute one and the same instrument.

**PART I**  
**INFORMATION REQUIRED IN PROSPECTUS**

**Cross Reference Sheet**

**Item 1. DESCRIPTION OF SECURITIES TO BE REGISTERED**

<b><u>Item Number and Caption</u></b>	<b><u>Location in Form of American Depository Receipt ("Receipt") Filed Herewith as Prospectus</u></b>
1. Name of Depositary and address of its principal executive office	<u>Face of Receipt</u> - Introductory Article.
2. Title of Receipts and identity of deposited securities	<u>Face of Receipt</u> - Top Center.
Terms of Deposit:	
(i) The amount of deposited securities represented by one American Depositary Share ("ADSs")	<u>Face of Receipt</u> - Upper right corner.
(ii) The procedure for voting, if any, the deposited securities	<u>Reverse of Receipt</u> - Paragraph (12).
(iii) The collection and distribution of dividends	<u>Face of Receipt</u> - Paragraphs (4), (5) and (7) <u>Reverse of Receipt</u> - Paragraphs (10) and (11).
(iv) The transmission of notices, reports and proxy soliciting material	<u>Face of Receipt</u> - Paragraphs (3), (5) and (8); <u>Reverse of Receipt</u> - Paragraphs (12) and (13).
(v) The sale or exercise of rights	<u>Face of Receipt</u> - Paragraphs (3), (4) and (5); <u>Reverse of Receipt</u> - Paragraph (10).
(vi) The deposit or sale of securities resulting from dividends, splits or plans of reorganization	<u>Face of Receipt</u> - Paragraphs (3), (4) and (5); <u>Reverse of Receipt</u> - Paragraphs (10) and (13).

<b><u>Item Number and Caption</u></b>	<b><u>Location in Form of American Depositary Receipt ("Receipt") Filed Herewith as Prospectus</u></b>
(vii) Amendment, extension or termination of the deposit agreement	<u>Reverse of Receipt</u> - Paragraphs (16) and (17).
(viii) Rights of holders of Receipts to inspect the transfer books of the Depositary and the list of holders of ADSs	<u>Face of Receipt</u> - Paragraph (3).
(ix) Restrictions upon the right to deposit or withdraw the underlying securities	<u>Face of Receipt</u> – Paragraphs (2), (3), (4), (5), (6) and (7); <u>Reverse of Receipt</u> – Paragraph (10).
(x) Limitation upon the liability of the Depositary	<u>Face of Receipt</u> - Paragraph (5); <u>Reverse of Receipt</u> - Paragraphs (10) and (14).
3. Fees and charges which may be imposed directly or indirectly on holders of ADSs	<u>Face of Receipt</u> - Paragraph (7). <u>Face of Receipt</u> - Paragraph (8).

**Item 2. AVAILABLE INFORMATION**

The Company is subject to the periodic reporting requirements of the Securities Exchange Act of 1934 and accordingly files certain reports with, and submits certain reports to, the United States Securities and Exchange Commission (the "Commission"). Such reports and other information can be retrieved from the Commission's internet website (<http://www.sec.gov>), and can be inspected and copied at the public reference facilities maintained by the Commission at 100 F Street, N.E., Washington, D.C. 20549.

## **PROSPECTUS**

The Prospectus consists of the proposed form of American Depositary Receipt included as Exhibit (a)(i) to this Registration Statement on Form F-6 and is incorporated herein by reference.

## PART II

### INFORMATION NOT REQUIRED IN PROSPECTUS

#### Item 3. EXHIBITS

- (a)(i) Form of American Depositary Receipt to be issued to evidence American Depositary Shares representing ordinary shares of Shire plc (the “Company”). — Filed herewith as Exhibit (a)(i).
- (a)(ii) Amended and Restated Deposit Agreement, dated as of May 23, 2011, by and among the Company, Citibank, N.A., as successor depositary (the “Depositary”), and all Holders and Beneficial Owners of American Depositary Receipts issued thereunder evidencing American Depositary Shares representing deposited ordinary shares (the “Deposit Agreement”). — Previously filed and incorporated by reference to Registration Statement on Form F-6 filed on November 14, 2014 (Reg. No. 333-200206).
- (b) Any other agreement to which the Depositary is a party relating to the issuance of the American Depositary Shares registered hereunder or the custody of the deposited securities represented thereby. — None.
- (c) Every material contract relating to the deposited securities between the Depositary and the issuer of the deposited securities in effect at any time within the last three years. — None.
- (d) Opinion of counsel for the Depositary as to the legality of the securities to be registered. — Filed herewith as Exhibit (d).
- (e) Certificate under Rule 466. — Filed herewith as Exhibit (e).
- (f) Powers of Attorney for certain officers and directors and the authorized representative of the Company. — Set forth on the signature pages hereto.

**Item 4. UNDERTAKINGS**

- (a) The Depositary hereby undertakes to make available at the principal office of the Depositary in the United States, for inspection by holders of ADRs, any reports and communications received from the issuer of the deposited securities which are both (1) received by the Depositary as the holder of the deposited securities, and (2) made generally available to the holders of the underlying securities by the issuer.
- (b) If the amounts of fees charged are not disclosed in the prospectus, the Depositary undertakes to prepare a separate document stating the amount of any fee charged and describing the service for which it is charged and to deliver promptly a copy of such fee schedule without charge to anyone upon request. The Depositary undertakes to notify each registered holder of an ADR thirty days before any change in the fee schedule.



## **SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, as amended, Citibank, N.A., acting solely on behalf of the legal entity to be created by the Amended and Restated Deposit Agreement, dated as of May 23, 2011, by and among Shire plc and its successors, Citibank, N.A., as successor depositary, and all Holders and Beneficial Owners from time to time of American Depositary Receipts issued thereunder evidencing American Depositary Shares representing deposited ordinary shares, certifies that it has reasonable grounds to believe that all the requirements for filing on Form F-6 are met and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of New York, State of New York, on the 29<sup>th</sup> day of April, 2016.

Legal entity created by the Amended and Restated Deposit Agreement under which the American Depositary Shares registered hereunder are to be issued, each American Depositary Share representing three (3) ordinary shares of Shire plc

CITIBANK, N.A., solely in its capacity as Depositary

By: /s/ Thomas R. Wood

Name: Thomas R. Wood

Title: Vice President

## **SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, as amended, Shire plc certifies that it has reasonable grounds to believe that all the requirements for filing on Form F-6 are met and has duly caused this Registration Statement on Form F-6 to be signed on its behalf by the undersigned thereunto duly authorized, in Dublin, Ireland, on April 29, 2016.

Shire plc

By: /s/ Jeffrey Poulton

Name: Jeffrey Poulton

Title: Authorized signatory

## **POWERS OF ATTORNEY**

**KNOW ALL PERSONS BY THESE PRESENTS**, that each person whose signature appears below constitutes and appoints Flemming Orskov, Jeffrey Poulton and Bill Mordan, each of them acting individually, his true and lawful attorney-in-fact and agent, each with full power of substitution and resubstitution, for him and in his name, place and stead, in any and all such capacities, to sign any and all amendments, including post-effective amendments and supplements to this Registration Statement and any and all related registration statements pursuant to Rule 462(b) of the Securities Act of 1933, as amended, and to file the same, with all exhibits thereto and other documents in connection therewith, with the United States Securities and Exchange Commission, granting unto said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or any of them, or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof. The Power of Attorney may be executed in multiple counterparts, each of which shall be deemed an original, but which taken together, shall constitute one instrument.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement on Form F-6 has been signed by the following persons in the following capacities on April 29, 2016.

<u>Signature</u>	<u>Title</u>
<u>/s/ Susan Kilsby</u> Susan Kilsby	Chairman
<u>/s/ Dr. Flemming Orskov</u> Dr. Flemming Orskov	Chief Executive Officer
<u>/s/ Jeffrey Poulton</u> Jeffrey Poulton	Chief Financial Officer and Principal Accounting Officer
<u>/s/ Dominic Blakemore</u> Dominic Blakemore	Non-Executive Director

Signature

Title

/s/ Olivier Bohuon  
Olivier Bohuon

Non-Executive Director

/s/ William Burns  
William Burns

Non-Executive Director

/s/ Dr. Steven Gillis  
Dr. Steven Gillis

Non-Executive Director

/s/ Dr. David Ginsburg  
Dr. David Ginsburg

Non-Executive Director

/s/ Sara Mathew  
Sara Mathew

Non-Executive Director

/s/ Anne Minto  
Anne Minto

Non-Executive Director

Authorized Representative in the U.S.

/s/ Jeffrey Poulton  
Jeffrey Poulton

## Index to Exhibits

<u>Exhibit</u>	<u>Document</u>	<u>Sequentially Numbered Page</u>
(a)(i)	Form of American Depositary Receipt	
(d)	Opinion of counsel to the Depositary	
(e)	Certificate under Rule 466	

Exhibit (a)(i)  
[FORM OF FACE OF ADR]

Number

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CUSIP NUMBER:

American Depositary Shares (each American Depositary Share  
representing the right to receive three (3) fully paid  
ordinary shares)

AMERICAN DEPOSITARY RECEIPT  
evidencing

AMERICAN DEPOSITARY SHARES

representing

ORDINARY SHARES, NOMINAL VALUE 5P EACH

of

SHIRE plc

(Incorporated under the laws of Jersey)

Citibank, N.A., a national banking association organized and existing under the laws of the United States of America, as depositary (the "Depositary"), hereby certifies that \_\_\_\_\_ is the registered owner (a "Holder") of \_\_\_\_\_ American Depositary Shares ("ADSs"), each (subject to paragraphs (10) and (13)) representing three ordinary shares ("Shares") (including the rights to receive Shares described in paragraph (1), and, together with any other securities, cash or property from time to time held by the Depositary in respect or in lieu of deposited Shares, the "Deposited Securities"), of Shire plc, a corporation organized under the laws of Jersey (the "Company"), deposited with the Custodian appointed under the Deposit Agreement (subject to paragraph (15), the "Custodian"), under the Amended and Restated Deposit Agreement, dated as of May 23, 2011 (as amended from time to time, the "Deposit Agreement") among the Company, the Depositary and all Holders and Beneficial Owners from time to time of American Depositary Receipts evidencing ADSs issued thereunder ("ADRs"), each of whom, by accepting an ADR becomes a party thereto. The Deposit Agreement and this ADR (which includes the provisions set forth on the reverse hereof) shall be governed by and construed in accordance with the laws of the State of New York. Notwithstanding anything contained in the Deposit Agreement, this ADR or any present or future provisions of the laws of the State of New York, the rights of holders of Shares and of any other Deposited Securities and the obligations and duties of the Company in respect of the holders of Shares and other Deposited Securities, as such, shall be governed by the laws of Jersey (or, if applicable, such other laws as may govern the Deposited Securities). The terms and conditions of the Deposit Agreement are hereby incorporated by reference and all capitalized terms used herein which are not otherwise defined herein shall have the meanings ascribed thereto in the Deposit Agreement.

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(1) Issuance of ADRs. This ADR is one of the ADRs issued under the Deposit Agreement to evidence ADSs outstanding thereunder. Subject to paragraph (4), the Depositary may so issue ADRs for delivery at the Transfer Office (defined in paragraph (3)) only against deposit with the Custodian of: (a) Shares in form satisfactory to the Custodian; (b) rights to receive Shares from the Company or any registrar, transfer agent, clearing agent or other entity recording Share ownership or transactions on behalf of the Company; or, (c) unless requested in writing by the Company to cease doing so at least two business days in advance of the proposed deposit, other rights to receive Shares (until such Shares are actually deposited pursuant to (a) or (b) above, "Pre-released ADRs"), only if (i) Pre-released ADRs are fully collateralized (marked to market daily) with cash or U.S. government securities held by the Depositary for the benefit of Holders (but such collateral shall not constitute Deposited Securities), (ii) each recipient of Pre-released ADRs agrees in writing with the Depositary that such recipient (a) owns such Shares, (b) assigns all beneficial right, title and interest therein to the Depositary in its capacity as such, (c) holds such Shares for the account of the Depositary, (d) will deliver such Shares to the Custodian as soon as practicable and promptly upon demand therefor and (e) will not take any action with respect to the Pre-released ADRs and Shares that is inconsistent with the transfer of the Depositary's beneficial ownership thereof, and (iii) no new Pre-released ADRs will be issued if the total outstanding Pre-released ADRs is or would become more than 20% of the outstanding ADR balance (excluding then outstanding Pre-released ADRs) at the time of issuance, unless the Depositary: 1) determines that unusual market conditions require the issuance of Pre-released ADRs in addition to 20% of all such ADRs and 2) receives the prior written approval of the Company. The Depositary may retain for its own account any earnings on collateral for Pre-released ADRs and its charges for issuance thereof. At the request, risk and expense of the person depositing Shares, the Depositary may accept deposits for forwarding to the Custodian and may deliver ADRs at a place other than its office. Every person depositing Shares under the Deposit Agreement represents and warrants that such Shares are free and clear of any lien, encumbrance, security interest, charge, mortgage, pledge or restriction on transfer, validly issued and outstanding, fully paid, nonassessable and free of pre-emptive rights, that the person making such deposit is duly authorized so to do and that such Shares (A) are not "restricted securities" as such term is defined in Rule 144 under the Securities Act of 1933 unless at the time of deposit they may be freely transferred in accordance with Rule 144 and may otherwise be offered and sold freely in the United States or (B) have been registered under the Securities Act of 1933. Such representations and warranties shall survive the deposit of Shares and issuance of ADRs. The Depositary will not knowingly accept for deposit under the Deposit Agreement any Shares required to be registered under the Securities Act of 1933 and not so registered; the Depositary may refuse to accept for such deposit any Shares identified by the Company in order to facilitate the Company's compliance with such Act.

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(2) Withdrawal of Deposited Securities. Subject to paragraphs (4) and (5), upon surrender of this ADR in form satisfactory to the Depositary at the Transfer Office, the Holder hereof is entitled to delivery at the Custodian's office of the Deposited Securities at the time represented by the ADSs evidenced by this ADR. At the request, risk and expense of the Holder hereof, the Depositary may deliver such Deposited Securities at such other place as may have been requested by the Holder. Notwithstanding any other provision of the Deposit Agreement or this ADR, the withdrawal of Deposited Securities may be restricted only for the reasons set forth in General Instruction I.A.(1) of Form F-6 (as such instructions may be amended from time to time) under the Securities Act of 1933.

(3) Transfers of ADRs. The Depositary or its agent will keep, at a designated transfer office in the Borough of Manhattan, The City of New York (the "Transfer Office"), (a) a register (the "ADR Register") for the registration, registration of transfer, combination and split-up of ADRs, which at all reasonable times will be open for inspection by Holders and the Company for the purpose of communicating with Holders in the interest of the business of the Company or a matter relating to the Deposit Agreement and (b) facilities for the delivery and receipt of ADRs. Title to this ADR (and to the Deposited Securities represented by the ADSs evidenced hereby), when properly endorsed or accompanied by proper instruments of transfer, is transferable by delivery with the same effect as in the case of negotiable instruments under the laws of the State of New York; provided that the Depositary, notwithstanding any notice to the contrary, may treat the person in whose name this ADR is registered on the ADR Register as the absolute owner hereof for all purposes. Subject to paragraphs (4) and (5), this ADR is transferable on the ADR Register and may be split into other ADRs or combined with other ADRs into one ADR, evidencing the same number of ADSs evidenced by this ADR, by the Holder hereof or by duly authorized attorney upon surrender of this ADR at the Transfer Office properly endorsed or accompanied by proper instruments of transfer and duly stamped as may be required by applicable law; provided that the Depositary may close the ADR Register at any time or from time to time when deemed expedient by it or requested by the Company. At the request of a Holder, the Depositary shall, for the purpose of substituting a certificated ADR with uncertificated Direct Registration ADRs, or vice versa, execute (if applicable) and deliver a certificated ADR or uncertificated Direct Registration ADRs, as the case may be, for any authorized number of ADSs requested, evidencing the same aggregate number of ADSs as those evidenced by the certificated ADR or designated as uncertificated Direct Registration ADRs, as the case may be, substituted.

(4) Certain Limitations. Prior to the issue, registration, registration of transfer, split-up or combination of any ADR, the delivery of any distribution in respect thereof, or, subject to the last sentence of paragraph (2), the withdrawal of any Deposited Securities, and from time to time in the case of clause (b)(ii) of this paragraph (4), the Company, the Depositary or the Custodian may require: (a) payment with respect thereto of (i) any stamp duty, stamp duty reserve tax or other transfer duty or stock transfer or other tax or other governmental charge, (ii) any stock transfer or registration fees in effect for the registration of transfers of Shares or other Deposited Securities upon any applicable register and (iii) any applicable charges as provided in paragraph (7) of this ADR; (b) the production of proof satisfactory to it of (i) the identity and genuineness of any signature and (ii) such other information, including without limitation, information as to citizenship, residence, exchange control approval, beneficial ownership of any securities, compliance with applicable law, regulations, provisions of or governing Deposited Securities and terms of the Deposit Agreement and this ADR, as it may deem necessary or proper; and (c) compliance with such regulations as the Depositary may establish consistent with the Deposit Agreement. The issuance of ADRs, the acceptance of deposits of Shares, the registration, registration of transfer, split-up or combination of ADRs or, subject to the last sentence of paragraph (2), the withdrawal of Deposited Securities may be suspended, generally or in particular instances, when the ADR Register or any register for Deposited Securities is closed or when any such action is deemed advisable by the Depositary or the Company.

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(5) Taxes. If any tax or other governmental charge shall become payable by or on behalf of the Custodian or the Depositary with respect to this ADR, any Deposited Securities represented by the ADSs evidenced hereby or any distribution thereon, such tax or other governmental charge shall be paid by the Holder hereof to the Depositary and neither the Company nor the Depositary shall have any liability therefore. The Depositary may refuse to effect any registration, registration of transfer, split-up or combination hereof or, subject to the last sentence of paragraph (2), any withdrawal of such Deposited Securities until such payment is made. The Depositary may also deduct from any distributions on or in respect of Deposited Securities, or may sell by public or private sale for the account of the Holder hereof any part or all of such Deposited Securities (after attempting by reasonable means to notify the Holder hereof prior to such sale), and may apply such deduction or the proceeds of any such sale in payment of such tax or other governmental charge, the Holder and Beneficial Owner hereof remaining liable for any deficiency, and shall reduce the number of ADSs evidenced hereby to reflect any such sales of Deposited Securities. In connection with any distribution to Holders, the Company will remit to the appropriate governmental authority or agency all amounts (if any) required to be withheld and owing to such authority or agency by the Company; and the Depositary and the Custodian will remit to the appropriate governmental authority or agency all amounts (if any) required to be withheld and owing to such authority or agency by the Depositary or the Custodian. If the Depositary determines that any distribution in property other than cash (including Shares or rights) on Deposited Securities is subject to any tax that the Depositary or the Custodian is obligated to withhold, the Depositary may dispose of all or a portion of such property in such amounts and in such manner as the Depositary deems necessary and practicable to pay such taxes, by public or private sale, and the Depositary shall distribute the net proceeds of any such sale or the balance of any such property after deduction of such taxes to the Holders entitled thereto.

(6) Disclosure of Interests. To the extent that the provisions of or governing or to which such Deposited Securities are otherwise subject may require disclosure of or impose limits on beneficial or other ownership of Deposited Securities, other Shares and other securities and may provide for blocking transfer, voting or other rights to enforce such disclosure or limits, Holders, Beneficial Owners and all persons holding ADSs (or any interest therein) agree to comply with all such disclosure requirements and ownership limitations and to cooperate with the Depositary in the Depositary's compliance with any Company instructions in respect thereof, and the Depositary will use reasonable efforts to comply with such Company instructions.

Notwithstanding any provision of the Deposit Agreement or of this ADR and without limiting the foregoing, by being a Holder of an ADR, each such Holder and Beneficial Owner agrees to provide such information as the Company may request in a disclosure notice (a "Disclosure Notice") given pursuant to the Articles of the Company. By accepting or holding this ADR, each Holder and Beneficial Owner acknowledges that it understands that failure to comply with a Disclosure Notice may result in the imposition of sanctions against the holder of the Shares in respect of which the non-complying person is or was, or appears to be or has been, interested as provided in the Articles which currently include, the withdrawal of the voting rights of such Shares and the imposition of restrictions on the rights to receive dividends on and to transfer such Shares. In addition, by accepting or holding this ADR each Holder and Beneficial Owner agrees to comply with the provisions of the Articles with regard to the notification to the Company of interests in Shares, which currently provide, inter alia, that any member must comply with certain notification obligations to the Company set forth in the Articles, as if the Company were a UK-issuer (and not a non-UK Issuer) for the purposes of these provisions. Such notification obligations are extended to each Holder and Beneficial Owner where such Holder and Beneficial Owner is aware that another person for whom it holds such ADRs is so interested.

(7) Charges of Depositary. The Depositary may charge the following fees:

- (a) Issuance Fee: to any person depositing Shares or to whom ADSs are issued upon the deposit of Shares (excluding issuances as a result of distributions described in paragraph (iv) below), a fee not in excess of U.S. \$5.00 per 100 ADSs (or fraction thereof) so issued under the terms of the Deposit Agreement, *provided, however*, that the Depositary shall not charge an issuance fee to any person depositing Shares for purposes of the issuance of ADSs in connection with the Company's employee share plans;
- (b) Cancellation Fee: to any person surrendering ADSs for cancellation and withdrawal of Deposited Securities or to any person to whom Deposited Securities are delivered, a fee not in excess of U.S. \$5.00 per 100 ADSs (or fraction thereof) surrendered;
- (c) Cash Distribution Fee: to any Holder of ADSs, a fee not in excess of U.S. \$2.00 per 100 ADSs (or fraction thereof) held for the distribution of cash dividends or other cash distributions (*i.e.*, sale of rights and other entitlements);
- (d) Stock Distribution /Rights Exercise Fee: to any Holder of ADS(s), a fee not in excess of U.S. \$2.00 per 100 ADSs (or fraction thereof) held for (a) the distribution of stock dividends or other free stock distributions or (b) the exercise of rights to purchase additional ADSs;
- (e) Other Distribution Fee: to any Holder of ADS(s), a fee not in excess of U.S. \$2.00 per 100 ADSs (or fraction thereof) held for the distribution of securities other than ADSs or rights to purchase additional ADSs; and
- (f) Depositary Services Fee: to any Holder of ADS(s), a fee not in excess of U.S. \$2.00 per 100 ADSs (or fraction thereof) held on the applicable record date(s) established by the Depositary.

In addition, in connection with any action to deposit Shares or surrender ADSs for cancellation for the purpose of withdrawal of Deposited Securities instigated by, or on behalf of, any Holders or Beneficial Owners, the Depositary shall be entitled to charge the following:

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- (a) taxes (including applicable interest and penalties) and other governmental charges;
- (b) such registration fees as may from time to time be in effect for the registration of Shares or other Deposited Securities on the share register and applicable to transfers of Shares or other Deposited Securities to or from the name of the Custodian, the Depositary or any nominees upon the making of deposits and withdrawals, respectively;
- (c) such cable, telex and facsimile transmission and delivery expenses as are expressly provided in the Deposit Agreement to be at the expense of the person depositing or withdrawing Shares or Holders and Beneficial Owners of ADSs;
- (d) the expenses and charges incurred by the Depositary in the conversion of foreign currency;
- (e) such fees and expenses as are incurred by the Depositary in connection with compliance with exchange control regulations and other regulatory requirements applicable to Shares, Deposited Securities, ADSs and ADRs; and
- (f) the fees and expenses incurred by the Depositary, the Custodian, or any nominee in connection with the delivery or servicing of Deposited Securities.

For the avoidance of doubt, any fees and charges incurred by the Depositary in connection with its general operations and not triggered by a specific deposit or withdrawal transaction instigated for or on behalf of a Holder or Beneficial Owner shall be met by the Depositary and not passed on to Holders or Beneficial Owners.

All fees and charges may, at any time and from time to time, be changed by agreement between the Depositary and Company but, in the case of fees and charges payable by Holders or Beneficial Owners, only in the manner contemplated by paragraph 16 and as contemplated in the Deposit Agreement. The Depositary will provide, without charge, a copy of its latest fee schedule to anyone upon request.

Depositary fees payable upon (i) deposit of Shares against issuance of ADSs and (ii) surrender of ADSs for cancellation and withdrawal of Deposited Securities will be charged by the Depositary to the person to whom the ADSs so issued are delivered (in the case of ADS issuances) and to the person who delivers the ADSs for cancellation to the Depositary (in the case of ADS cancellations). In the case of ADSs issued by the Depositary into DTC or presented to the Depositary via DTC, the ADS issuance and cancellation fees will be payable to the Depositary by the DTC Participant(s) receiving the ADSs from the Depositary or the DTC Participant(s) surrendering the ADSs to the Depositary for cancellation, as the case may be, on behalf of the Beneficial Owner(s) and will be charged by the DTC Participant(s) to the account(s) of the applicable Beneficial Owner(s) in accordance with the procedures and practices of the DTC participant(s) as in effect at the time. Depositary fees in respect of distributions and the Depositary services fee are payable to the Depositary by Holders as of the applicable ADS Record Date established by the Depositary. In the case of distributions of cash, the amount of the applicable Depositary fees is deducted by the Depositary from the funds being distributed. In the case of distributions other than cash and the Depositary service fee, the Depositary will invoice the applicable Holders as of the ADS Record Date established by the Depositary. For ADSs held through DTC, the Depositary fees for distributions other than cash and the Depositary service fee are charged by the Depositary to the DTC Participants in accordance with the procedures and practices prescribed by DTC from time to time and the DTC Participants in turn charge the amount of such fees to the Beneficial Owners for whom they hold ADSs.

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The Depositary may reimburse the Company for certain expenses incurred by the Company in respect of the ADR program established pursuant to the Deposit Agreement, by making available a portion of the Depositary fees charged in respect of the ADR program or otherwise, upon such terms and conditions as the Company and the Depositary agree from time to time. The Company shall pay to the Depositary such fees and charges and reimburse the Depositary for such out-of-pocket expenses as the Depositary and the Company may agree from time to time. Responsibility for payment of such charges and reimbursements may from time to time be changed by agreement between the Company and the Depositary. Unless otherwise agreed, the Depositary shall present its statement for such expenses and fees or charges to the Company once every three months. The charges and expenses of the Custodian are for the sole account of the Depositary.

The right of the Depositary to receive payment of fees, charges and expenses as provided above shall survive the termination of the Deposit Agreement. As to any Depositary, upon the resignation or removal of such Depositary as described in this ADR, such right shall extend for those fees, charges and expenses incurred prior to the effectiveness of such resignation or removal.

(8) Available Information. The Deposit Agreement, the provisions of or governing Deposited Securities and any written communications from the Company, which are both received by the Custodian or its nominee as a holder of Deposited Securities and made generally available to the holders of Deposited Securities, are available for inspection by Holders and Beneficial Owners at the offices of the Depositary and the Custodian and at the Transfer Office. The Depositary will mail copies of such communications (or English translations or summaries thereof) to Holders if and when furnished by the Company. The Company is subject to the periodic reporting requirements of the Securities Exchange Act of 1934 and accordingly files certain reports with the United States Securities and Exchange Commission (the "Commission"). Such reports and other information may be inspected and copied at public reference facilities maintained by the Commission located at the date hereof at 100 F Street, N.E., Washington, D.C. 20549.

(9) Execution. This ADR shall not be valid for any purpose unless executed by the Depositary by the manual or facsimile signature of a duly authorized officer of the Depositary.

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Dated:

CITIBANK, N.A., as Depositary

By: \_\_\_\_\_  
Authorized Officer

The Depositary's principal executive office is located at 388 Greenwich Street, New York, New York 10013.

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[FORM OF REVERSE OF ADR]

(10) Distributions on Deposited Securities. Subject to paragraphs (4) and (5), to the extent practicable and provided timely written notice is delivered to the Depositary, the Depositary will distribute by mail to each Holder entitled thereto on the record date set by the Depositary therefor at such Holder's address shown on the ADR Register, in proportion to the number of Deposited Securities (on which the following distributions on Deposited Securities are received by the Custodian) represented by ADSs evidenced by such Holder's ADRs and, in each case, without unreasonable delay. (a) Cash. Any U.S. dollars available to the Depositary resulting from a cash dividend or other cash distribution or the net proceeds of sales of any other distribution or portion thereof authorized in this paragraph (10) ("Cash"), on an averaged or other practicable basis, subject to (i) appropriate adjustments for taxes withheld, (ii) such distribution being impermissible or impracticable with respect to certain Holders, and (iii) deduction of the Depositary's expenses in (1) converting any foreign currency to U.S. dollars by sale or in such other manner as the Depositary may determine to the extent that it determines that such conversion may be made on a reasonable basis, (2) transferring foreign currency or U.S. dollars to the United States by such means as the Depositary may determine to the extent that it determines that such transfer may be made on a reasonable basis, (3) obtaining any approval or license of any governmental authority required for such conversion or transfer, which is obtainable at a reasonable cost and within a reasonable time and (4) making any sale by public or private means in any commercially reasonable manner. If the Depositary determines in its reasonable judgment that such foreign currency is not convertible, in whole or in part, on a reasonable basis into U.S. dollars transferable to the United States, or if any approval or license which is required for such conversion is denied or in the opinion of the Depositary, is not obtainable or is not obtained within a reasonable period or at a reasonable cost, the Depositary may distribute all or part of the foreign currency (or an appropriate document evidencing the right to receive such foreign currency) to, or in its discretion may hold such foreign currency uninvested and without liability for interest thereon for the respective accounts of, the Holders entitled thereto. All expenses of any such conversion shall be deducted from the proceeds thereof. On the date on which the Company pays any cash dividend to the holders of Shares or other Deposited Securities, the Company may convert or cause to be converted, in a commercially reasonable manner, such foreign currency into U.S. dollars and distribute the same to the Depositary for distribution to Holders. No deductions shall be made by the Company from the proceeds of such conversion; provided that actual and customary commissions paid by the Company on account of such conversion shall not be considered a deduction by the Company. To the extent any holder of Deposited Securities is permitted to elect to receive distributions from Shire Biopharmaceutical Holdings, a subsidiary of the Company resident for tax purposes in the United Kingdom, or from the Company, a company resident for tax purposes in the Republic of Ireland, the Holders and Beneficial Owners shall be deemed to have instructed the Depositary to elect and the Depositary hereby elects, on behalf of Holders and Beneficial Owners, to receive all such distributions from Shire Biopharmaceutical Holdings. The Depositary agrees to execute all further documentation reasonably requested by the Company to implement the foregoing election. The Depositary shall not be deemed to exercise any discretion in connection with such election and shall be entitled to any and all protections afforded to the Depositary under the Deposit Agreement in connection with such election. (b) Shares. (i) Additional ADRs evidencing whole ADSs representing any Shares available to the Depositary resulting from a dividend or free distribution on Deposited Securities consisting of Shares (a "Share Distribution") and (ii) U.S. dollars available to it resulting from the net proceeds of sales of Shares received in a Share Distribution, which Shares would give rise to fractional ADSs if additional ADRs were issued therefor, as in the case of Cash. (c) Rights. (i) Warrants or other instruments in the discretion of the Depositary representing rights to acquire additional ADRs in respect of any rights to subscribe for additional Shares or rights of any nature available to the Depositary as a result of a distribution on Deposited Securities ("Rights"), to the extent that the Company timely furnishes to the Depositary evidence satisfactory to the Depositary that the Depositary may lawfully distribute the same (the Company has no obligation to so furnish such evidence), or (ii) to the extent the Company does not so furnish such evidence and sales of Rights are practicable, any U.S. dollars available to the Depositary from the net proceeds of sales of Rights as in the case of Cash, or (iii) to the extent the Company does not so furnish such evidence and such sales cannot practicably be accomplished by reason of the nontransferability of the Rights, whether by their terms, pursuant to applicable law or otherwise, limited markets therefor, their short duration or otherwise, nothing (and any Rights may lapse). (d) Other Distributions. (i) Securities or property available to the Depositary resulting from any distribution on Deposited Securities other than Cash, Share Distributions and Rights ("Other Distributions"), by any means that the Depositary may deem equitable and practicable, or (ii) to the extent the Depositary deems distribution of such securities or property not to be equitable and practicable, any U.S. dollars available to the Depositary from the net proceeds of sales of Other Distributions as in the case of Cash. Before effecting any such sale of a Share Distribution, Rights or Other Distribution, the Depositary will provide notice to the Company of its intended action. Such U.S. dollars available will be distributed by checks drawn on a bank in the United States for whole dollars and cents (any fractional cents being withheld without liability for interest and dealt with by the Depositary in accordance with its then current practices).

(11) Record Dates. The Depositary may, after consultation with the Company, if practicable, fix a record date (which shall be as near as practicable to any corresponding record date set by the Company) for the determination of the Holders who shall be entitled to receive any distribution on or in respect of Deposited Securities, to give instructions for the exercise of any voting rights, to receive any notice or to act in respect of other matters and only such Holders shall be so entitled.

(12) Voting of Deposited Securities. As soon as practicable after receipt from the Company of notice of any meeting or solicitation of consents or proxies of holders of Shares or other Deposited Securities, the Depositary shall fix a record date in accordance with paragraph (11) hereof and, unless otherwise requested in writing by the Company in order to comply with applicable law, mail to Holders a notice stating (a) such information as is contained in such notice and any solicitation materials, (b) that each Holder on the record date set by the Depositary therefor will be entitled to instruct the Depositary as to the exercise of the voting rights, if any, pertaining to the Deposited Securities represented by the ADSs evidenced by such Holder's ADRs and (c) the manner in which such instructions may be given, including instructions to give a discretionary proxy to a person designated by the Company subject to any applicable provisions of the laws of Jersey and the Memorandum and Articles of the Company and the provisions of or governing Deposited Securities. Upon receipt of instructions of a Holder on such record date in the manner and on or before the date established by the Depositary for such purpose, the Depositary shall endeavor insofar as practicable and permitted under the provisions of or governing Deposited Securities to vote or cause to be voted (or to grant a discretionary proxy to a person designated by the Company to vote) the Deposited Securities represented by the ADSs evidenced by such Holder's ADRs in accordance with such instructions. The Depositary will not itself exercise any voting discretion in respect of any Deposited Security. Subject to the provisions of the next succeeding paragraph, to the extent such instructions are not so received by the Depositary from any Holder, the Holder shall be deemed to have instructed the Depositary to give a discretionary proxy to a person designated by the Company to vote the Deposited Securities represented by ADSs as to which the Depositary has not received instructions from the Holders, provided that no such instruction shall be deemed to be given and no discretionary proxy shall be given with respect to which the Company informs the Depositary (and the Company agrees to provide such information promptly in writing) that the Company does not wish such proxy given.

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Notwithstanding anything to the contrary contained in the preceding paragraph, the Depositary shall not be obligated to give any such discretionary proxy and the Holders shall not have been deemed to have so instructed the Depositary unless and until the Depositary has been provided with an opinion of counsel to the Company, which may be given at the time of entering into the Deposit Agreement, satisfactory to the Depositary (which may be internal counsel), in form and substance satisfactory to the Depositary, substantially to the effect that (i) the granting of such discretionary proxy does not subject the Depositary to any additional disclosure obligations related to interests in shares under the Articles or the laws of Jersey or the listing rules of the United Kingdom Listing Authority, (ii) the granting of such proxy does not result in a breach of the laws of Jersey or the listing rules of the United Kingdom Listing Authority and (iii) the Depositary or the Custodian, or the nominee of any of them, whichever is the registered holder entitled to attend and vote at meetings of the Company in respect of such Shares, has the right to appoint the proxy to attend and vote instead of him. The Company undertakes to inform the Depositary of any substantial change in the Articles or the laws of Jersey which would subject the Depositary to disclosure obligations under the listing rules of the United Kingdom Listing Authority to which the Depositary, the Custodian or the nominee of any of them would not otherwise be subject but for the grant of such discretionary proxy.

(13) Changes Affecting Deposited Securities. Subject to paragraphs (4) and (5) the Depositary may, in its discretion, and after consultation with the Company if practicable, amend this ADR or distribute additional or amended ADRs or ADSs (with or without calling this ADR for exchange) or cash, securities or property on the record date set by the Depositary therefor to reflect any change in par value, split-up, consolidation, cancellation or other reclassification of Deposited Securities, any Share Distribution or Other Distribution not distributed to Holders or any cash, securities or property available to the Depositary in respect of Deposited Securities from (and the Depositary is hereby authorized to surrender any Deposited Securities to any person and to sell by public or private sale any property received in connection with) any recapitalization, reorganization, merger, consolidation, liquidation, receivership, bankruptcy or sale of all or substantially all the assets of the Company, and to the extent the Depositary does not so amend the terms and conditions of the ADRs or ADSs or make a distribution to Holders to reflect any of the foregoing, or the net proceeds thereof, whatever cash, securities or property results from any of the foregoing shall constitute Deposited Securities and each ADS evidenced by this ADR shall automatically represent its pro rata interest in the Deposited Securities as then constituted.

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(14) Exoneration. Without limiting Section 16 of the Deposit Agreement as between the Company and the Depositary, the Depositary, the Company, their respective officers, directors, employees and agents and each of them shall: (a) incur no liability (i) if any present or future law, regulation, the provisions of or governing any Deposited Securities, act of God, war or other circumstance beyond its control shall prevent, delay or subject to any civil or criminal penalty any act which the Deposit Agreement or this ADR provides shall be done or performed by it, or (ii) by reason of any exercise or failure to exercise any discretion given it in the Deposit Agreement or this ADR; (b) assume no obligation nor shall any of them be subject to any liability to any Holders or beneficial owners of ADSs or any other person except to perform its obligations to the extent they are specifically set forth in this ADR and the Deposit Agreement without gross negligence or bad faith; (c) in the case of the Depositary and its agents, be under no obligation to appear in, prosecute or defend any action, suit or other proceeding in respect of any Deposited Securities or this ADR; or (d) in the case of the Company and its agents hereunder be under no obligation to appear in, prosecute or defend any action, suit or other proceeding in respect of any Deposited Securities or this ADR, which in its opinion may involve it in expense or liability, unless indemnity satisfactory to it against all expense (including fees and disbursements of counsel) and liability be furnished as often as may be required; (e) not be liable for any action or inaction by it in reliance upon the advice of or information from legal counsel, accountants, any person presenting Shares for deposit, any Holder, Beneficial Owner or any other person believed by it to be competent to give such advice or information; or (f) not be liable for any consequential or punitive damages for any breach of the terms of the Deposit Agreement or this ADR. The Depositary and the Company, their respective agents and their respective directors, officers and employees acting hereunder may rely and shall be protected in acting upon any written notice, request, direction or other document believed by them to be genuine and to have been signed or presented by the proper party or parties. The Depositary and its agents will not be responsible for any failure to carry out any instructions to vote any of the Deposited Securities, for the manner in which any such vote is cast or for the effect of any such vote. The Depositary and its agents may own and deal in any class of securities of the Company and its affiliates and in ADRs. The Company has agreed to indemnify the Depositary and its agents under certain circumstances and the Depositary has agreed to indemnify the Company under certain circumstances. No disclaimer of liability under the Securities Act of 1933 is intended by any provision hereof.

(15) Resignation and Removal of Depositary: the Custodian. The Depositary may resign as Depositary by written notice of its election to do so delivered to the Company, or be removed as Depositary by the Company by written notice of such removal delivered to the Depositary; such resignation or removal shall take effect upon the appointment of and acceptance by a successor depositary. The Depositary may appoint substitute or additional Custodians and the term "Custodian" refers to each Custodian or all Custodians as the context requires.

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(16) Amendment. Subject to the last sentence of paragraph (2), the ADRs, the ADSs evidenced by the ADRs and the Deposit Agreement may be amended by the Company and the Depositary, provided that any amendment that imposes or increases any fees or charges (other than stock transfer or other taxes and other governmental charges, transfer or registration fees for the registration of transfer of Deposited Securities on any applicable register in connection with the deposit or withdrawal of Deposited Securities, cable, telex or facsimile transmission costs, delivery costs or other such expenses), or that shall otherwise prejudice any substantial existing right of Holders or Beneficial Owners, shall become effective 30 days after notice of such amendment shall have been given to the Holders and Beneficial Owners. Every Holder and Beneficial Owner of an ADS (or any interest therein) at the time any amendment to the Deposit Agreement so becomes effective shall be deemed, by continuing to hold such ADS (or any interest therein), to consent and agree to such amendment and to be bound by the Deposit Agreement and, if applicable, the ADR(s), as so amended thereby. In no event shall any amendment impair the right of the Holder of any ADR to surrender such ADR and receive the Deposited Securities represented thereby, except in order to comply with mandatory provisions of applicable law. The parties hereto agree that any amendments or supplements which (i) are reasonably necessary (as agreed by the Company and the Depositary) in order for (a) the ADSs to be registered on Form F-6 under the Securities Act of 1933 or (b) the ADSs or Shares to be traded solely in electronic book-entry form and (ii) do not in either such case impose or increase any fees or charges to be borne by Holders and Beneficial Owners, shall be deemed not to prejudice any substantial rights of Holders or Beneficial Owners. In no event shall any amendment or supplement impair the right of the Holder to surrender such ADR and receive therefor the Deposited Securities represented thereby except in order to comply with mandatory provisions of applicable law. Notwithstanding the foregoing, if any governmental body should adopt new laws, rules or regulations which would require amendment or supplement of the Deposit Agreement or the form of ADR to ensure compliance therewith, the Company and the Depositary may amend or supplement the Deposit Agreement, the ADRs and the ADSs evidenced by the ADRs at any time in accordance with such changed rules. Such amendment or supplement to the Deposit Agreement and, if applicable, the ADR, in such circumstances may become effective before a notice of such amendment or supplement is given to Holders and Beneficial Owners or within any other period of time as required for compliance.

(17) Termination. The Depositary shall at the written direction of the Company, terminate the Deposit Agreement and this ADR by mailing notice of such termination to the Holders at least 30 days prior to the date fixed in such notice for such termination. The Depositary may terminate the Deposit Agreement by giving the notice set forth in the preceding sentence of this paragraph (17) at any time after 60 days has elapsed after the Depositary shall have resigned hereunder, provided that no successor depositary shall have been appointed and accepted its appointment hereunder before the end of such 60 days. After the date so fixed for termination, the Depositary and its agents will perform no further acts under the Deposit Agreement and this ADR, except to advise Holders of such termination, receive and hold (or sell) distributions on Deposited Securities and deliver Deposited Securities being withdrawn. As soon as practicable after the expiration of six months from the date so fixed for termination, the Depositary shall sell the Deposited Securities and shall thereafter (as long as it may lawfully do so) hold in a segregated account the net proceeds of such sales, together with any other cash then held by it under the Deposit Agreement, without liability for interest, in trust for the pro rata benefit of the Holders of ADRs not theretofore surrendered. After making such sale, the Depositary shall be discharged from all obligations in respect of the Deposit Agreement and this ADR, except to account for such net proceeds and other cash. After the date so fixed for termination, the Company shall be discharged from all obligations under the Deposit Agreement except for its obligations to the Depositary and its agents.

May 4, 2016

Citibank, N.A. – ADR Department  
388 Greenwich Street  
New York, New York 10013

Ladies and Gentlemen:

We refer to the Registration Statement on Form F-6 (the “Registration Statement”) to be filed with the Securities and Exchange Commission (the “SEC”) by the legal entity created by the Deposit Agreement (as hereinafter defined) for the purpose of registering under the United States Securities Act of 1933, as amended (the “Securities Act”), 300,000,000 American Depositary Shares (the “ADSs”) to be issued under the Amended and Restated Deposit Agreement, dated as of May 23, 2011, by and among Citibank, N.A., as Depositary, Shire plc, a public limited company organized under the laws of Jersey (the “Company”), and the Holders and Beneficial Owners (each as defined in the Deposit Agreement and hereinafter used as so defined) from time to time of ADSs issued thereunder, a copy of which has been filed as Exhibit (a)(ii) to the Registration Statement (the “Deposit Agreement”). Each ADS represents, subject to the terms and conditions of the Deposit Agreement and, if applicable, the American Depositary Receipt (“ADR”) evidencing such ADS, the right to receive three (3) ordinary shares of the Company (the “Shares”).

Nothing contained herein or in any document referred to herein is intended by this firm to be used, and the addressees hereof cannot use anything contained herein or in any document referred to herein, as “tax advice” (within the meaning given to such term by the United States Internal Revenue Service (“IRS”) in IRS Circular 230 and any related interpretative advice issued by the IRS in respect of IRS Circular 230 prior to the date hereof, and hereinafter used within such meaning and interpretative advice). Without admitting that anything contained herein or in any document referred to herein constitutes “tax advice” for any purpose, notice is hereby given that, to the extent anything contained herein or in any document referred to herein constitutes, or is or may be interpreted by any court, by the IRS or by any other administrative body to constitute, “tax advice,” such “tax advice” is not intended or written to be used, and cannot be used, for the purpose of (i) avoiding penalties under the United States Internal Revenue Code of 1986, as amended, or (ii) promoting, marketing or recommending to any party any transaction or matter addressed herein.

Assuming that, at the time of their issuance, the Registration Statement will be effective and the Shares will have been legally issued, we are of the opinion that the ADSs, when issued in accordance with the terms of the Deposit Agreement and the Registration Statement, will be legally issued and will entitle the Holders to the rights specified in the Deposit Agreement and, if applicable, the ADR(s) evidencing the ADS(s).

This opinion is limited to the laws of the State of New York and the Federal laws of the United States. Without admitting that we are within the category of persons whose consent is required under Section 7 of the Securities Act, we hereby consent to the use of this opinion as Exhibit (d) to the Registration Statement.

Very truly yours,

**PATTERSON BELKNAP WEBB & TYLER LLP**

By: /s/ Herman H. Raspé

A Member of the Firm

Exhibit (e)

Rule 466 Certification

The depositary, Citibank, N.A., represents and certifies the following:

- (i) That it previously had filed a registration statement on Form F-6 (Registration No. 333-200206), which the U.S. Securities and Exchange Commission declared effective, with terms of deposit identical to the terms of deposit of this Form F-6 Registration Statement; and
- (ii) That its ability to designate the date and time of effectiveness under Rule 466 has not been suspended.

CITIBANK, N.A., as Depositary

By: /s/ Thomas R. Wood

Name: Thomas R. Wood

Title: Vice President