FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

	OMB APPROVAL									
1	OMB Number:	3235-0287								
	Estimated average burden									
	hours per response:	0.5								

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Reporting Person* <u>ECKER DAVID J</u>						2. Issuer Name and Ticker or Trading Symbol ISIS PHARMACEUTICALS INC [ISIS]						Relationship of Reporting Person(s) to Issuer (Check all applicable) Director 10% Owner Office (size title 2005)				
(Last) (First) (Middle) 2292 FARADAY AVENUE					3. Date of Earliest Transaction (Month/Day/Year) 01/01/2004						2	below)			Other (sp below) apeutics	pecify
(Street) CARLSBAD CA 92008 (City) (State) (Zip)				4.	4. If Amendment, Date of Original Filed (Month/Day/Year)						Line	Individual or Joint/Group Filing (Check Applicable ne) X Form filed by One Reporting Person Form filed by More than One Reporting Person				
		Tal	ole I - Non-D	erivativ	/e Se	curitie	s Ac	quired, Di	sposed o	of, or Ber	neficiall	y Owned				
1. Title of Security (Instr. 3) 2. Transac Date (Month/Date)					Execution Date,		Code (Instr. 5)		d (A) or r. 3, 4 and		s ally following	6. Owner Form: D (D) or Ir (I) (Insti	Direct II ndirect E r. 4) C	7. Nature of Indirect Beneficial Ownership		
									Amount	(A) or (D)	Price	Reported Transact (Instr. 3 a	ion(s)			(Instr. 4)
			Table II - De (e.ç					uired, Disp s, options,				Owned			•	
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security	Date Exec (Month/Day/Year) if an	3A. Deemed Execution Date, if any (Month/Day/Yea	Code		of I		6. Date Exercisable and Expiration Date (Month/Day/Year)		7. Title and Amo of Securities Underlying Derivative Secur (Instr. 3 and 4)		8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficial Owned Following Reported Transactio (Instr. 4)	ly D	0. Ownership Form: Direct (D) or Indirect (Instr. 4)	Beneficial Ownership (Instr. 4)
				Code	v	(A) (I		Date Exercisable	Expiration Date	Title	Amount or Number of Shares					
Employee Stock Option (right to	\$6.81	01/02/2004	01/02/2004	A		32,640		01/02/2008 ⁽¹⁾	01/01/2014	Common Stock	32,640	\$6.81	32,640)	D	

Explanation of Responses:

1. 25% of the shares subject to the option will vest and become exercisable on 1-2-05. Thereafter, the remaining shares subject to the option vest and become exercisable in 36 equal monthly installments, at the rate of 8,160 shares per year. The option is exercisable as to 0 shares on 1-2-04.

Remarks:

David J Ecker

01/05/2004

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.