Appendix A

Supporting Information

Phase transition studies of dutasterise crystalline forms

Marta Łaszcz*, Kinga Trzcińska, Anna Witkowska, Elżbieta Lipiec-Abramska,
Wojciech J. Szczepek

Pharmaceutical Research Institute (PRI), Warszawa 01-793, Poland

*Author to whom all correspondence should be addressed: e-mail: m.laszcz@ifarm.eu;
Tel.: +48-22-4563-903; Fax: +48-22-4563-838

Table of Contents

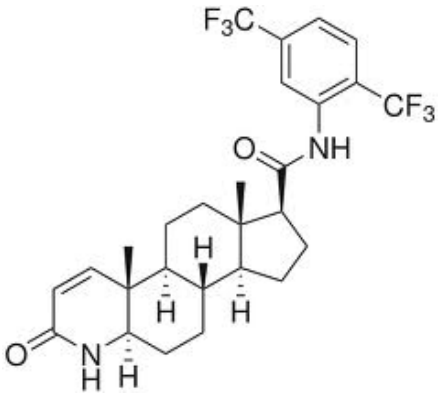
F3C
CF3
O
NH
H
H
H
O
N
H
H

Fig. A1

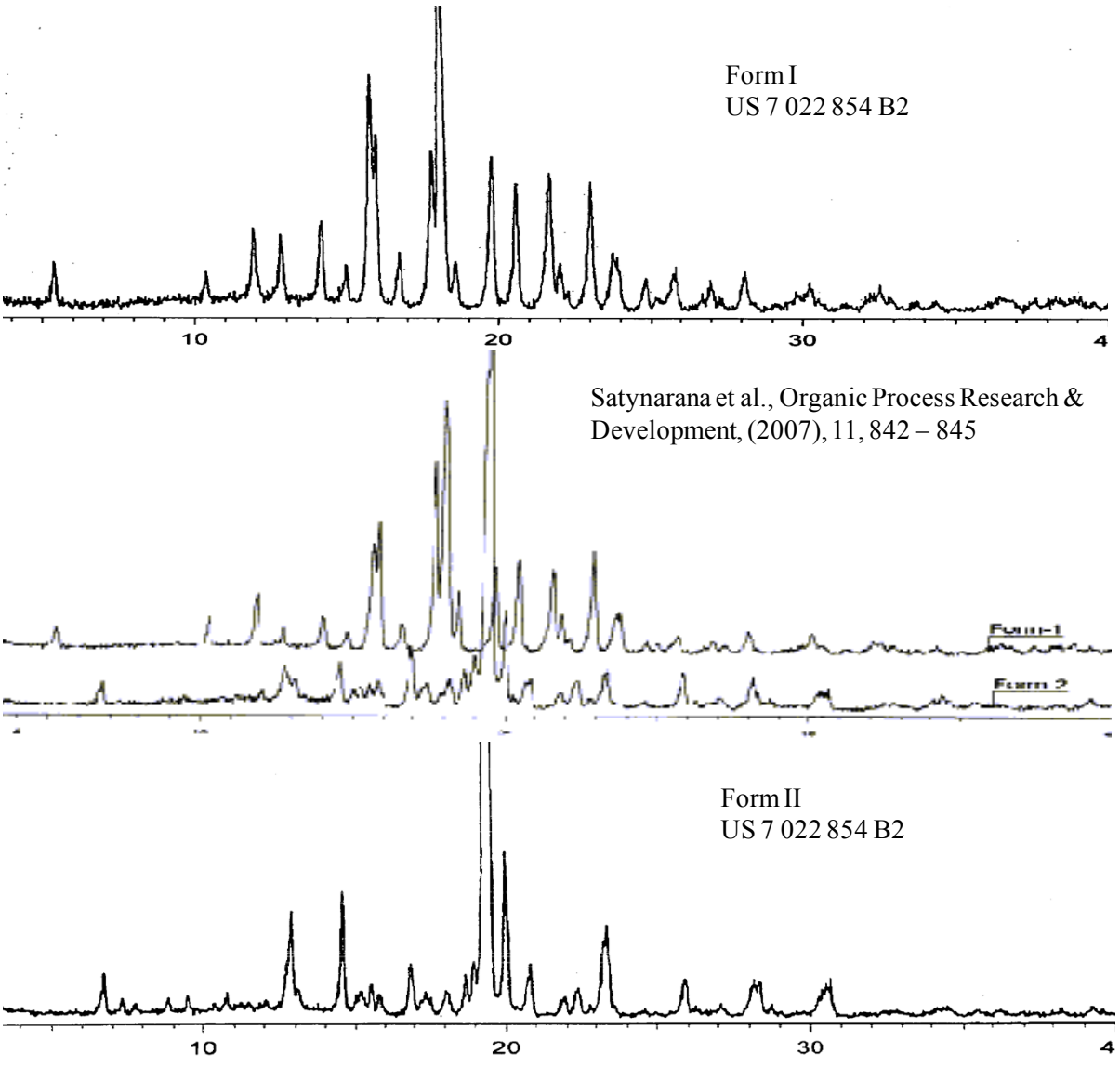
Form I
US 7 022 854 B2
10
20
30
4
Satynarana et al., Organic Process Research & Development, (2007), 11, 842 – 845
Form II
US 7 022 854 B2
10
20
30
4

Fig. A2

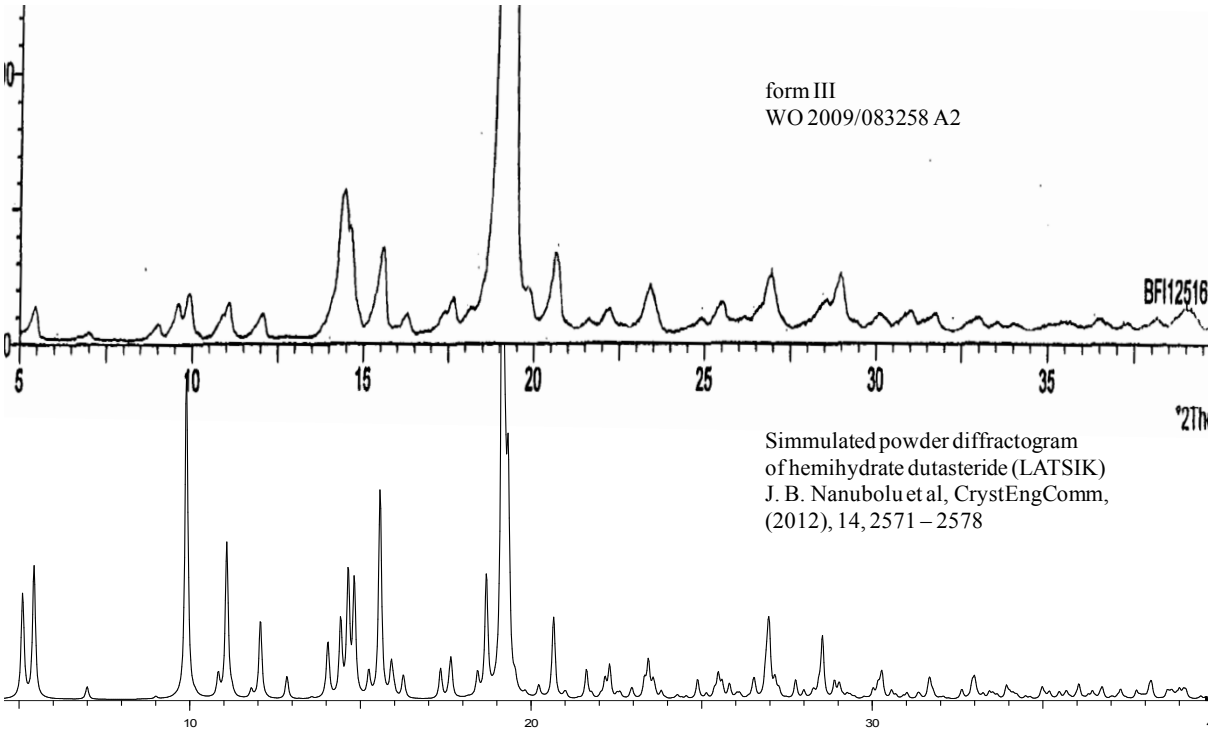
form III
WO 2009/083258 A2
BFI12516
5
10
15
20
25
30
35
°2Th
Simmulated powder diffractogram
of hemihydrate dutasteride (LATSIK)
J. B. Nanubolu et al, CrystEngComm,
(2012), 14, 2571 – 2578
10
20
30

Fig. A3

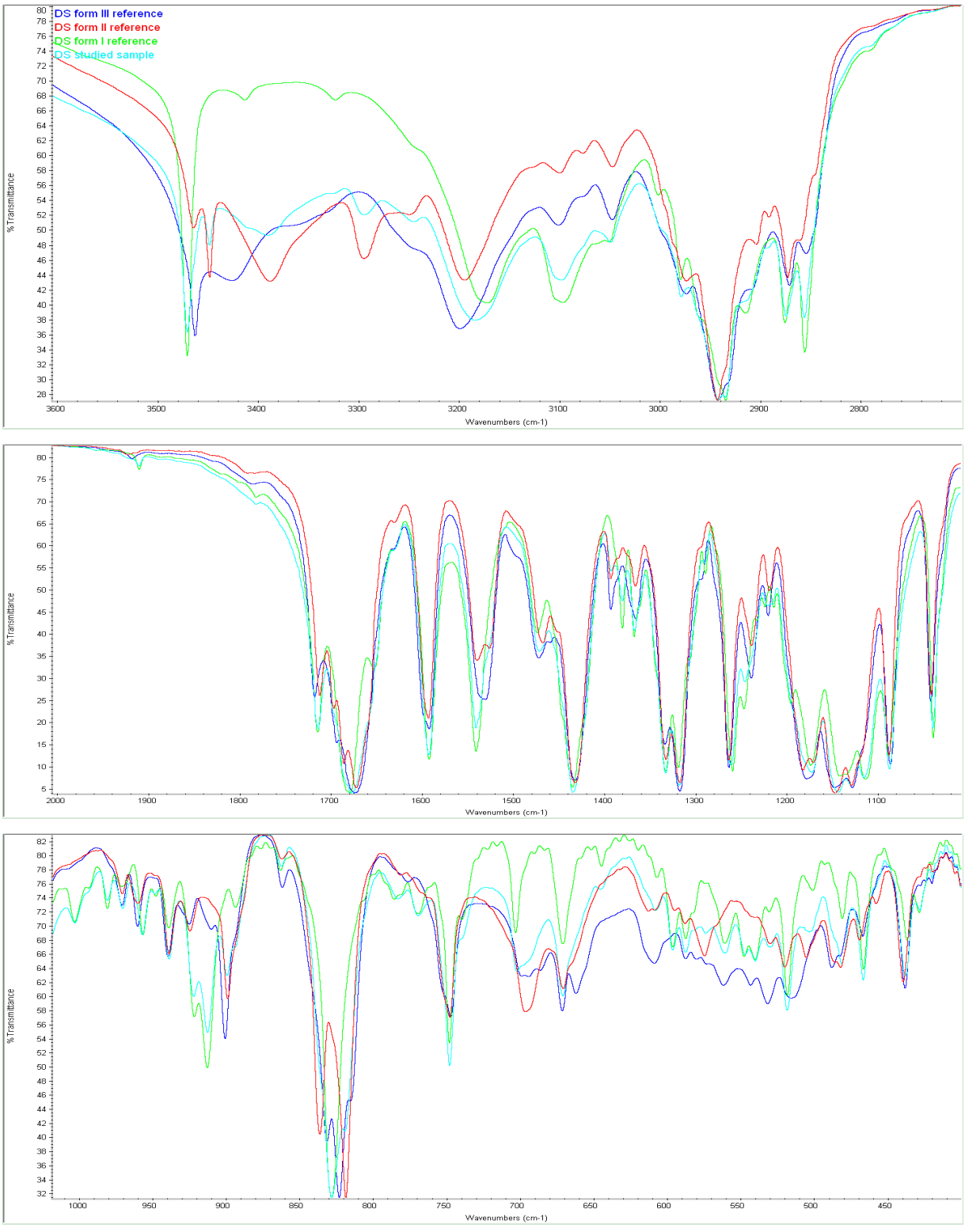

Fig. A4

Table A1. IR phase analysis of the dutasteride sample.

Main form	**Additional forms**
form I	form II: 3448, 3390, 3294, 3245, 2941, 1392, 899, 819, 573cm^{-1}.

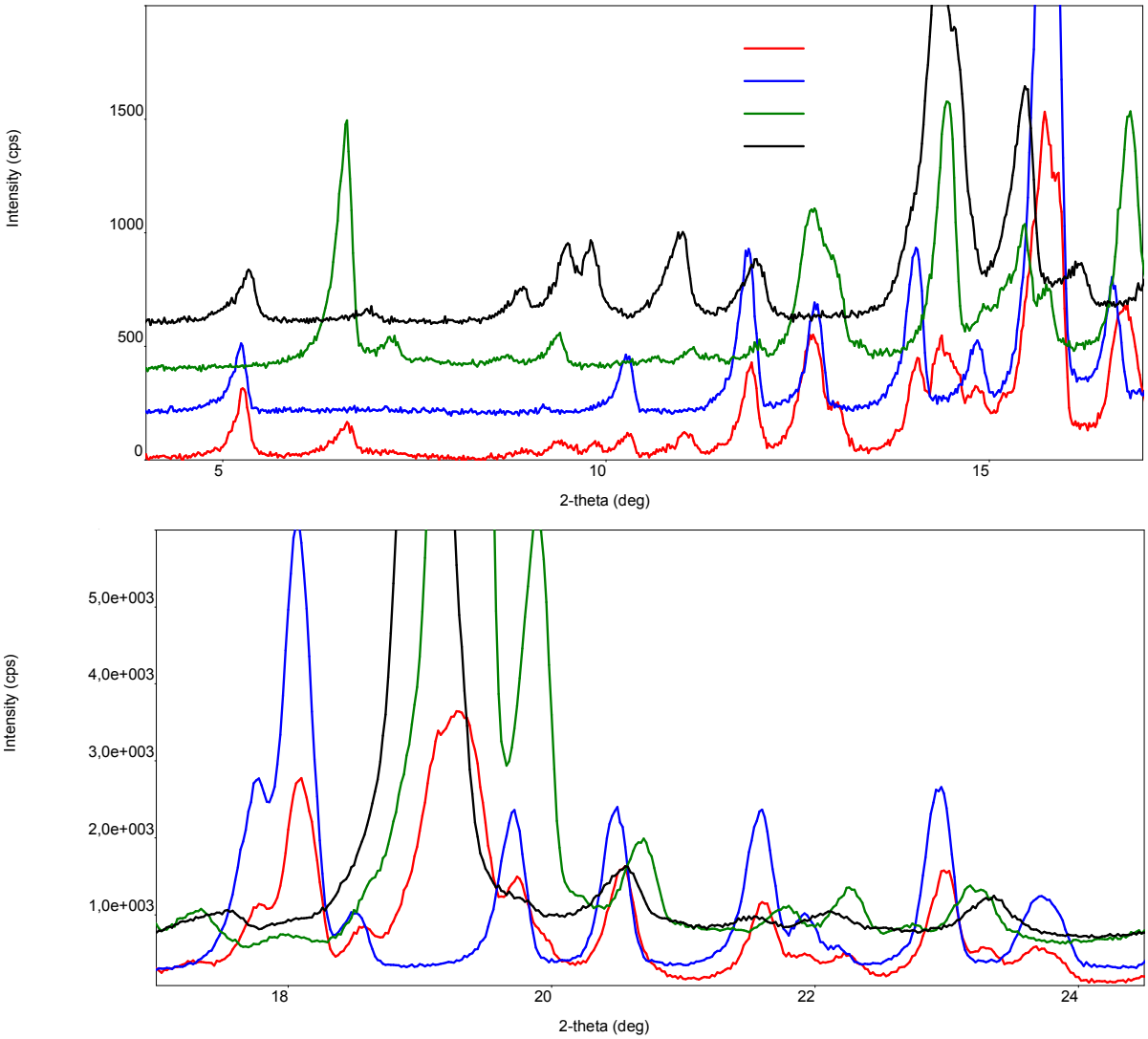

Fig. A5

Table A2. PXRD phase analysis of the dutasteride sample.

Main form	**Additional forms**
form I	form II: 6.63, 9.36, 11.02, 13.02, 14.37, 15.21, 16.78, 17.26, 19.30, 19.92, 22.24, 23.31, 28.82 °. form III: 9.84°.

Table A3. Bond lengths for the dutasteride form I molecule.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
F1	C26	1.340(3)	C7	C8	1.528(2)
F2	C26	1.357(2)	C8	C9	1.554(2)
F3	C26	1.327(2)	C8	C13	1.527(2)
F4	C27	1.301(13)	C9	C10	1.539(3)
F4A	C27A	1.335(6)	C10	C11	1.549(2)
F5	C27	1.301(14)	C11	C12	1.531(3)
F5A	C27A	1.332(5)	C12	C13	1.544(3)
F6	C27	1.307(13)	C12	C16	1.554(2)
F6A	C27A	1.321(5)	C12	C17	1.541(3)
O1	C1	1.241(2)	C13	C14	1.528(2)
O2	C19	1.215(3)	C14	C15	1.557(3)
N1	C1	1.334(2)	C15	C16	1.558(3)
N1	C5	1.459(2)	C16	C19	1.519(3)
N2	C19	1.385(2)	C20	C21	1.405(3)
N2	C20	1.410(2)	C20	C25	1.393(3)
C1	C2	1.486(3)	C21	C22	1.395(3)
C2	C3	1.333(3)	C21	C26	1.502(3)
C3	C4	1.517(2)	C22	C23	1.381(3)
C4	C5	1.539(3)	C23	C24	1.380(3)
C4	C9	1.558(2)	C24	C25	1.388(3)
C4	C18	1.541(3)	C24	C27	1.486(14)
C5	C6	1.516(2)	C24	C27A	1.515(4)
C6	C7	1.528(2)			

Table A4. Bond angles for the dutasteride form I molecule.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C1	N1	C5	121.67(16)	C19	C16	C12	114.07(16)
C19	N2	C20	127.89(17)	C19	C16	C15	117.42(16)
O1	C1	N1	122.18(18)	O2	C19	N2	122.73(18)
O1	C1	C2	122.03(18)	O2	C19	C16	122.23(18)
N1	C1	C2	115.76(16)	N2	C19	C16	114.97(17)
C3	C2	C1	121.03(17)	C21	C20	N2	119.18(17)
C2	C3	C4	121.59(17)	C25	C20	N2	121.90(17)
C3	C4	C5	105.54(15)	C25	C20	C21	118.91(17)
C3	C4	C9	114.13(15)	C20	C21	C26	121.29(17)
C3	C4	C18	106.02(15)	C22	C21	C20	120.42(18)
C5	C4	C9	107.42(14)	C22	C21	C26	118.28(18)
C5	C4	C18	112.23(15)	C23	C22	C21	120.2(2)
C18	C4	C9	111.44(15)	C24	C23	C22	119.20(19)
N1	C5	C4	110.67(15)	C23	C24	C25	121.8(2)
N1	C5	C6	110.50(15)	C23	C24	C27	122.2(7)

C6	C5	C4	113.99(15)	C23	C24	C27A	117.3(2)
C5	C6	C7	108.83(14)	C25	C24	C27	114.7(6)
C8	C7	C6	112.20(15)	C25	C24	C27A	120.8(2)
C7	C8	C9	111.11(15)	C27	C24	C27A	15.4(6)
C13	C8	C7	111.38(15)	C24	C25	C20	119.46(18)
C13	C8	C9	108.66(14)	F1	C26	F2	105.32(17)
C8	C9	C4	110.55(14)	F1	C26	C21	112.56(17)
C10	C9	C4	113.96(15)	F2	C26	C21	111.54(16)
C10	C9	C8	111.63(14)	F3	C26	F1	106.96(16)
C9	C10	C11	113.07(16)	F3	C26	F2	106.16(17)
C12	C11	C10	110.36(15)	F3	C26	C21	113.73(17)
C11	C12	C13	107.80(15)	F4	C27	F6	109.0(14)
C11	C12	C16	116.25(16)	F4	C27	C24	121.2(11)
C11	C12	C17	111.21(16)	F5	C27	F4	101.6(13)
C13	C12	C16	99.06(14)	F5	C27	F6	97.8(14)
C17	C12	C13	113.10(16)	F5	C27	C24	113.9(13)
C17	C12	C16	108.96(15)	F6	C27	C24	110.6(11)
C8	C13	C12	113.02(15)	F4A	C27A	C24	112.7(3)
C8	C13	C14	118.25(15)	F5A	C27A	F4A	106.1(3)
C14	C13	C12	104.76(15)	F5A	C27A	C24	109.4(4)
C13	C14	C15	104.06(15)	F6A	C27A	F4A	105.8(4)
C14	C15	C16	105.51(15)	F6A	C27A	F5A	109.5(4)
C12	C16	C15	105.09(15)	F6A	C27A	C24	113.0(3)

Table A5. Torsion angles for the dutasteride form I molecule.

A	**B**	**C**	**D**	**Angle/°**	**A**	**B**	**C**	**D**	**Angle/°**
O1	C1	C2	C3	163.0(2)	C15	C16	C19	O2	-164.9(2)
N1	C1	C2	C3	-15.0(3)	C15	C16	C19	N2	18.0(3)
N1	C5	C6	C7	176.14(15)	C16	C12	C13	C8	176.39(15)
N2	C20	C21	C22	179.15(18)	C16	C12	C13	C14	46.31(18)
N2	C20	C21	C26	0.0(3)	C17	C12	C13	C8	61.2(2)
N2	C20	C25	C24	-179.14(18)	C17	C12	C13	C14	-68.88(19)
C1	N1	C5	C4	45.4(2)	C17	C12	C16	C15	78.63(18)
C1	N1	C5	C6	172.64(18)	C17	C12	C16	C19	-51.4(2)
C1	C2	C3	C4	0.0(3)	C18	C4	C5	N1	61.7(2)
C2	C3	C4	C5	33.7(2)	C18	C4	C5	C6	-63.6(2)
C2	C3	C4	C9	151.47(19)	C18	C4	C9	C8	67.02(19)
C2	C3	C4	C18	-85.5(2)	C18	C4	C9	C10	-59.7(2)
C3	C4	C5	N1	-53.34(19)	C19	N2	C20	C21	-169.74(18)
C3	C4	C5	C6	-178.63(15)	C19	N2	C20	C25	10.0(3)
C3	C4	C9	C8	-172.93(15)	C20	N2	C19	O2	-7.0(3)
C3	C4	C9	C10	60.4(2)	C20	N2	C19	C16	170.10(17)
C4	C5	C6	C7	-58.5(2)	C20	C21	C22	C23	0.0(3)

C4	C9	C10	C11	178.53(16)	C20	C21	C26	F1	-57.8(2)
C5	N1	C1	O1	172.6(2)	C20	C21	C26	F2	60.3(3)
C5	N1	C1	C2	-9.5(3)	C20	C21	C26	F3	-179.68(17)
C5	C4	C9	C8	-56.29(19)	C21	C20	C25	C24	0.6(3)
C5	C4	C9	C10	177.03(15)	C21	C22	C23	C24	0.7(3)
C5	C6	C7	C8	55.3(2)	C22	C21	C26	F1	122.9(2)
C6	C7	C8	C9	-55.8(2)	C22	C21	C26	F2	-118.9(2)
C6	C7	C8	C13	-177.09(16)	C22	C21	C26	F3	1.1(3)
C7	C8	C9	C4	56.4(2)	C22	C23	C24	C25	-0.7(3)
C7	C8	C9	C10	-175.62(15)	C22	C23	C24	C27	165.5(6)
C7	C8	C13	C12	-178.09(16)	C22	C23	C24	C27A	-177.7(3)
C7	C8	C13	C14	-55.2(2)	C23	C24	C25	C20	0.0(3)
C8	C9	C10	C11	52.4(2)	C23	C24	C27	F4	-115.3(13)
C8	C13	C14	C15	-161.98(16)	C23	C24	C27	F5	6.4(15)
C9	C4	C5	N1	-175.49(14)	C23	C24	C27	F6	115.3(13)
C9	C4	C5	C6	59.22(19)	C23	C24	C27A	F4A	56.7(4)
C9	C8	C13	C12	59.2(2)	C23	C24	C27A	F5A	-61.1(5)
C9	C8	C13	C14	-177.94(16)	C23	C24	C27A	F6A	176.7(3)
C9	C10	C11	C12	-55.2(2)	C25	C20	C21	C22	-0.6(3)
C10	C11	C12	C13	57.6(2)	C25	C20	C21	C26	-179.84(18)
C10	C11	C12	C16	167.63(16)	C25	C24	C27	F4	51.9(15)
C10	C11	C12	C17	-66.9(2)	C25	C24	C27	F5	173.5(11)
C11	C12	C13	C8	-62.2(2)	C25	C24	C27	F6	-77.5(13)
C11	C12	C13	C14	167.75(16)	C25	C24	C27A	F4A	-120.3(3)
C11	C12	C16	C15	-154.79(16)	C25	C24	C27A	F5A	122.0(3)
C11	C12	C16	C19	75.2(2)	C25	C24	C27A	F6A	-0.3(5)
C12	C13	C14	C15	-35.06(19)	C26	C21	C22	C23	179.2(2)
C12	C16	C19	O2	-41.3(3)	C27	C24	C25	C20	-167.2(6)
C12	C16	C19	N2	141.57(17)	C27	C24	C27A	F4A	169(3)
C13	C8	C9	C4	179.29(15)	C27	C24	C27A	F5A	52(3)
C13	C8	C9	C10	-52.7(2)	C27	C24	C27A	F6A	-71(3)
C13	C12	C16	C15	-39.72(18)	C27A	C24	C25	C20	176.9(3)
C13	C12	C16	C19	-169.72(16)	C27A	C24	C27	F4	169(4)
C13	C14	C15	C16	9.2(2)	C27A	C24	C27	F5	-69(3)
C14	C15	C16	C12	19.5(2)	C27A	C24	C27	F6	40(2)
C14	C15	C16	C19	147.51(17)					

Single X-ray crystal data of the dutasteride form I were deposited at The Cambridge Crystallographic Data Centre. The deposition number CCDC 1032001 contains supplementary crystallographic data. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.htmL (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk).

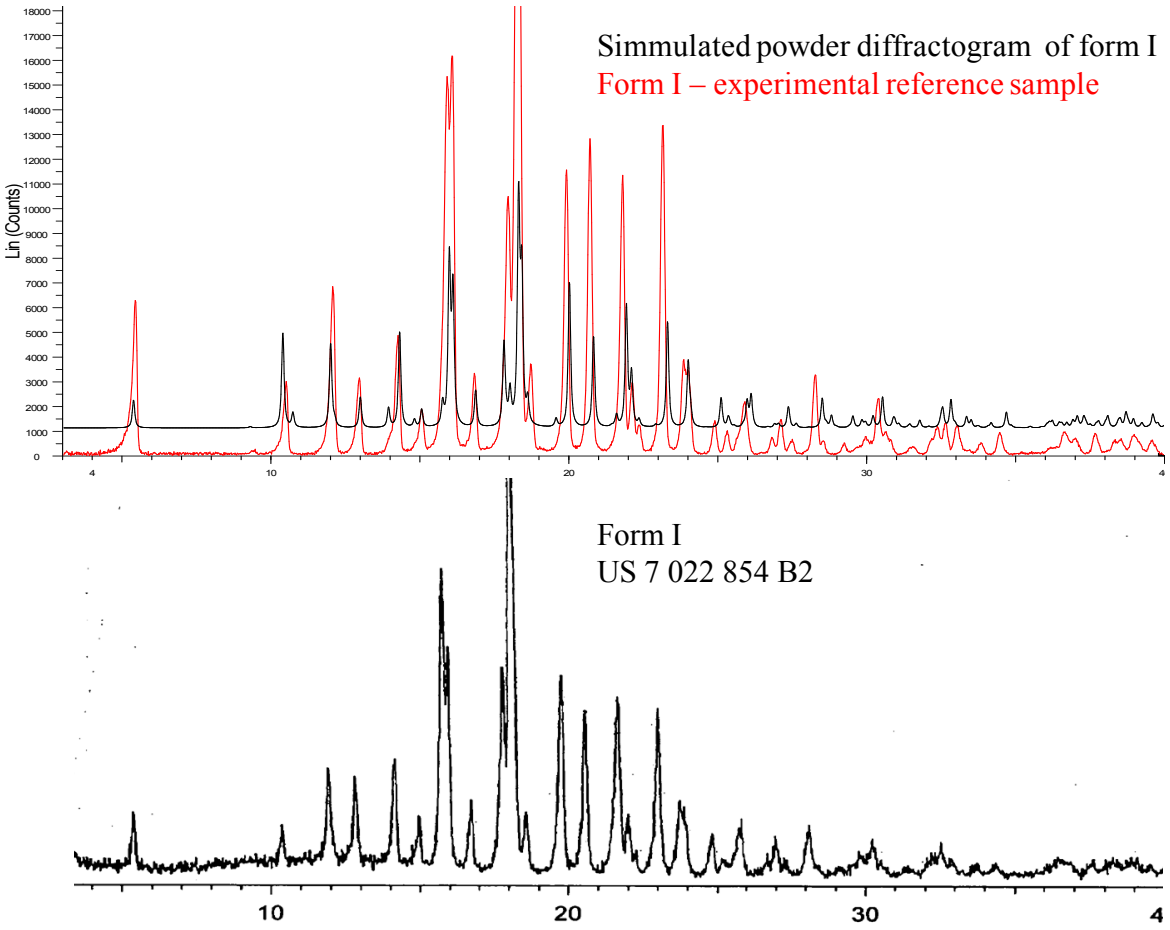
Simmulated powder diffractogram of form I
Form I – experimental reference sample
Lin (Counts)
Form I
US 7 022 854 B2

Fig. A6