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(54) Title: POLYMORPHIC FORMS OF TENOFOVIR DISOPROXIL FUMARATE

(57) Abstract: The present invention provides novel crystalline forms of Tenofovir disoproxil fumarate (Tenofovir DF), designated form ULT-4, ULT-5, ULT-6, ULT-7, ULT-8, ULT-IO, ULT-II, ULT-12, ULT-13, ULT-14, ULT-15, ULT-16, ULT-17, ULT-18, ULT-19, ULT-20, ULT-21 and ULT-22, methods for the preparation thereof and its use in pharmaceutical applications, in particular in anti-HIV medicaments. The crystalline form of Tenofovir DF can be used in combination with other anti-HIV medicaments such as Efavirenz and Emtricitabine.



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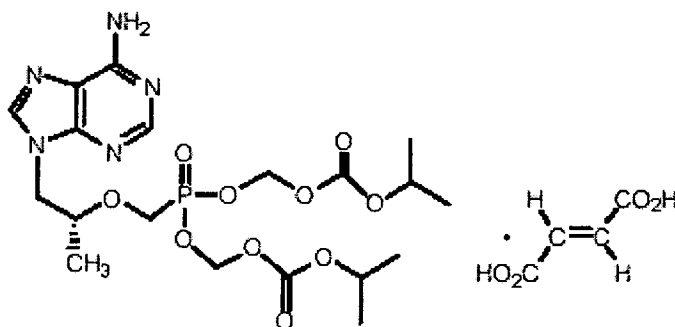
Title: Polymorphic forms of tenofovir disoproxil fumarate

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The present invention relates to novel crystalline forms of tenofovir disoproxil fumarate (tenofovir DF), methods for their preparation and their formulation and application in the field of medicine, in particular antiviral medicines.

Tenofovir disoproxil fumarate (also known as Viread(R), Tenofovir DF, Tenofovir disoproxil, TDF, Bis-POC-PMPA (U.S. Pat. Nos. 5,935,946, 5,922,695, 5,977,089, 6,043,230, 6,069,249) is a prodrug of tenofovir.

15 The chemical name of tenofovir disoproxil fumarate is 9-[(R)-2-[[bis[[[(isopropoxycarbonyl)oxy]methoxy]phosphinyl]methoxy]propyl]adenine fumarate (1:1). The CAS Registry number is 202138-50-9. It has a molecular formula of $C_{19}H_{30}N_5O_{10}P \cdot C_4H_4O_4$ and a molecular weight of 635.52. It has the following structural formula:



20 Tenofovir disoproxil fumarate (DF) is a nucleotide reverse transcriptase inhibitor approved in the United States for the treatment of HIV-I infection in combination with other antiretroviral agents. Tenofovir disoproxil DF is available as Viread(R) (Gilead Science, Inc.).

25 Among the anti-HIV drugs which have been developed are those which target the HIV reverse transcriptase (RT) enzyme or protease enzyme, both of which enzymes are necessary for the replication of the virus. Examples of RT inhibitors include nucleoside/nucleotide RT inhibitors (NRTIs) and non-nucleoside RT inhibitors (NNRTIs).

30 Currently, HIV-infected patients are routinely being treated with three-drug combinations. Regimens containing (at least) three NRTIs; two NRTIs in combination with one or two protease inhibitors (PI)(s);

5 or two NRTIs in combination with a NNRTI, are widely used. When two
or more PIs are used in these combinations, one of the PIs is often
ritonavir, given at a low sub-therapeutic dose, which acts as an
effective inhibitor of the elimination of the other PI(s) in the
regimen, resulting in maximal suppression of the virus and thereby
10 reducing the emergence of resistance.

Clinical studies have shown that three-drug combinations of
these anti-HIV drugs are much more effective than one drug used alone
or two-drug combinations in preventing disease progression and death.
Numerous studies of drug combinations with various combinations of
15 such drugs have established that such combinations greatly reduce
disease progression and deaths in people with HIV infections. The
name now commonly given to combinations of anti-HIV drugs is HAART
(Highly Active Anti-Retroviral Therapy).

Tenofovir DF is described *inter alia* in WO99/05150 and
20 EP998480. This crystalline form is characterised as having XRPD peaks
at about 4.9, 10.2, 10.5, 18.2, 20.0, 21.9, 24.0, 25.0, 25.5, 27.8,
30.1 and 30.4. Furthermore these crystals are described as opaque or
off-white and exhibit a DSC absorption peak at about 118 °C with an
onset at about 116 °C and an IR spectrum showing characteristic bands
25 expressed in reciprocal centimetres at approximately 3224, 3107-3052,
2986-2939, 1759, 1678, 1620, 1269 and 1102. Bulk densities have been
described of about 0.15-0.30 g/mL, usually about 0.2-0.25 g/mL.

Polymorphs:

30 Polymorphism is often characterised as the ability of a solid
substance to exist as two or more crystalline phases that have
different arrangements and/or conformations of the molecules in the
crystal lattice. The arrangement of the molecules in the space
(crystal packing) can affect the physical properties of the material
35 and can be influenced by controlling the conditions under which the
solid form is obtained.

Many pharmaceutical solids exhibit polymorphism and can exist
in different solid forms. The present invention relates to the
discovery of various solid forms of tenofovir DF and their solid
40 state physical properties .

These physical characteristics are influenced by the particular
solid form of a substance. One solid form may give rise to thermal
behaviour different from that of the amorphous material or other
solid forms. Thermal behaviour is measured in the laboratory by such

5 techniques as capillary melting point, thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) and can be used to distinguish some polymorphic forms from others. A particular solid form may also give rise to distinct spectroscopic properties that may be detectable by powder X-ray crystallography, solid state ¹³C NMR
10 spectrometry and infrared and Raman spectrometry.

Solid state physical properties affect the ease with which the material is handled during processing into a pharmaceutical product such as a tablet or capsule formulation. The physical properties impact the sort of excipients, for instance, to add to a tenofovir DF
15 formulation. Furthermore, the solid state physical property of a pharmaceutical compound is important to its dissolution in aqueous fluid or even in a patient's stomach fluid, which have therapeutic consequences. The rate of dissolution is also a consideration in liquid forms of medicine as well. The solid state form of a compound
20 may also affect its storage conditions.

Indications have been found by the present inventors that the solid form of Tenofovir DF in commercially available products experiences a conversion of its crystalline form when put under stress, indicating that the solid form currently used is not stable
25 or at least has a reduced stability.

The present invention relates to novel crystalline forms of tenofovir DF. The present inventors have identified novel crystalline forms, herein depicted as **ULT-4, ULT-5, ULT-6, ULT-7, ULT-8, ULT-10,**
30 **ULT-11, ULT-12, ULT-13, ULT-14, ULT-15, ULT-16, ULT-17, ULT-18, ULT-19, ULT-20, ULT-21 and ULT-22.**

Description of the Drawings:

35 **Figure 1A** illustrates the X-Ray Powder Diffraction pattern of Tenofovir DF Form **ULT-4**.

Figure 1B illustrates the DSC thermogram of Tenofovir DF Form **ULT-4**

Figure 1C illustrates the TGA thermogram of Tenofovir DF Form **ULT-4**.

Figure 2A illustrates the X-Ray Powder Diffraction pattern of
40 Tenofovir DF Form **ULT-5**.

Figure 3A illustrates the X-Ray Powder Diffraction pattern of Tenofovir DF Form **ULT-6**.

- 5 **Figure 4A** illustrates the X-Ray Powder Diffraction pattern of
Tenofovir DF Form **ULT-7**.
- Figure 4B** illustrates the DSC thermogram of Tenofovir DF Form **ULT-7**.
- Figure 4C** illustrates the TGA thermogram of Tenofovir DF Form **ULT-7**.
- Figure 5A** illustrates the X-Ray Powder Diffraction pattern of
10 Tenofovir DF Form **ULT-8**.
- Figure 5B** illustrates the DSC thermogram of Tenofovir DF Form **ULT-8**.
- Figure 5C** illustrates the TGA thermogram of Tenofovir DF Form **ULT-8**.
- Figure 7A** illustrates the X-Ray Powder Diffraction pattern of
Tenofovir DF Form **ULT-10**.
- 15 **Figure 8A** illustrates the X-Ray Powder Diffraction pattern of
Tenofovir DF Form **ULT-11**.
- Figure 8B** illustrates the DSC thermogram of Tenofovir DF Form **ULT-11**.
- Figure 8C** illustrates the TGA thermogram of Tenofovir DF Form **ULT-11**.
- Figure 6D** illustrates the molecular structure of base-acid-base
20 entity from the crystals of Tenofovir DF Form **ULT-11**.
- Figure 6E** illustrates the Crystal arrangement for Tenofovir DF Form
ULT-11.
- Figure 9A** illustrates the X-Ray Powder Diffraction pattern of
Tenofovir DF Form **ULT-12**.
- 25 **Figure 9B** illustrates the DSC thermogram of Tenofovir DF Form **ULT-12**.
- Figure 9C** illustrates the TGA thermogram of Tenofovir DF Form **ULT-12**.
- Figure 10A** illustrates the X-Ray Powder Diffraction pattern of
Tenofovir DF Form **ULT-13**.
- Figure 11A** illustrates the X-Ray Powder Diffraction pattern of
30 Tenofovir DF Form **ULT-14**.
- Figure 12A** illustrates the X-Ray Powder Diffraction pattern of
Tenofovir DF Form **ULT-15**.
- Figure 12B** illustrates the DSC thermogram of Tenofovir DF Form **ULT-15**.
- 35 **Figure 12C** illustrates the TGA thermogram of Tenofovir DF Form **ULT-15**. **Figure 13A** illustrates the X-Ray Powder Diffraction pattern of
Tenofovir DF Form **ULT-16**.
- Figure 14A** illustrates the X-Ray Powder Diffraction pattern of
Tenofovir DF Form **ULT-17**.
- 40 **Figure 15A** illustrates the X-Ray Powder Diffraction pattern of
Tenofovir DF Form **ULT-18**.

5 **Figure 16A** illustrates the X-Ray Powder Diffraction pattern of Tenofovir DF Form **ULT-19**.

Figure 16C illustrates the TGA thermogram of Tenofovir DF Form **ULT-19**. **Figure 17A** illustrates the X-Ray Powder Diffraction pattern of Tenofovir DF Form **ULT-20**.

10 **Figure 17C** illustrates the TGA thermogram of Tenofovir DF Form **ULT-20**.

Figure 18A illustrates the X-Ray Powder Diffraction pattern of Tenofovir DF Form **ULT-21**.

15 **Figure 18B** illustrates the DSC thermogram of Tenofovir DF Form **ULT-21**.

Figure 18C illustrates the TGA thermogram of Tenofovir DF Form **ULT-21**.

Figure 19A illustrates the X-Ray Powder Diffraction pattern of Tenofovir DF Form **ULT-22**.

5 Crystalline tenofovir DF form **ULT-4** (A1):

Thus, in one embodiment, Form **ULT-4** can be characterised by an XRPD substantially according to Fig 1A.

In another embodiment, Form **ULT-4** can be characterised by an DSC substantially according to Fig 1B.

10 In another embodiment, Form **ULT-4** can be characterised by an TGA substantially according to Fig 1C.

In another embodiment, Form **ULT-4** of the present invention can be characterised by DSC with an onset at 96.2°C and a characterising peak at 108.9°C. In a further embodiment, Form **ULT-4** of the present invention can be further characterised by DSC with an onset at
15 111.2°C and a characterising peak at 114.3°C.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-4** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a
20 suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-4** by evaporation of the solvent.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-4** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a
25 suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-4** by cooling and/or evaporation crystallization of a saturated solution.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-4** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a
30 suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-4** by anti-solvent addition as in Table III.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-4** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a
35 suitable solvent or mixture thereof as outlined herein elsewhere (paragraph on solvents) crystallising tenofovir DF Form **ULT-4** by slurry crystallisation and/or seed crystallisation.

Crystalline tenofovir DF form ULT-5 (A3):

Thus, in one aspect, the present invention provides crystalline tenofovir DF herein defined as Form **ULT-5**, characterised by an XRPD substantially according to Fig 2A.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-5** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-5** by evaporation of the solvent.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-5** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-5** by cooling and/or evaporation crystallization of a saturated solution.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-5** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-5** by anti-solvent addition as in Table III.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-5** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as outlined herein elsewhere (paragraph on solvents) crystallising tenofovir DF Form **ULT-5** by slurry crystallisation and/or seed crystallisation.

5 Crystalline tenofovir DF form ULT-6 (A4):

Thus, in one aspect, the present invention provides crystalline tenofovir DF herein defined as Form **ULT-6**, characterised by an XRPD substantially according to Fig 3A.

10 The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-6** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-6** by evaporation of the solvent.

15 The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-6** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-6** by cooling and/or evaporation crystallization of a saturated solution.

20 The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-6** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-6** by anti-solvent addition as in Table III.

25 The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-6** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as outlined herein elsewhere (paragraph on solvents) crystallising tenofovir DF Form **ULT-6** by
30 slurry crystallisation and/or seed crystallisation.

Crystalline tenofovir DF form ULT-7 (B1):

Thus, in one aspect, the present invention provides

crystalline tenofovir DF herein defined as Form **ULT-7**, characterised by the selection of at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group consisting of 5.0, 6.9, 8.9, 9.6, 10.2, 11.3, 13.2, 14.1, 17.8, 18.7, 20.0, 21.8, 23.8, 25.3, 27.8, 30.5, degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta. In a preferred embodiment, at least seven, more preferably at least eight, even more preferably at least nine, particularly preferred at least ten and most preferred eleven X-ray powder diffraction peaks are selected from the above group. In a more preferred embodiment, at least twelve, more preferably at least thirteen, even more preferably at least fourteen, particularly preferred at least fifteen and most preferred sixteen X-ray powder diffraction peaks are selected from the above group.

In another embodiment Form **ULT-7** can be characterised by the following set of XRPD peaks (Table 4) and, optionally, by the associated intensities:

Table 4	B1		Preferred embodiment	
Peak ID	Angle (2θ)	Intensity*	Angle (2θ)	Intensity*
1	5.0	M	5.00	M
2	6.9	M	6.94	M
3	8.9	L	8.94	L
4	9.6	L	9.58	L
5	10.2	H	10.20	H
6	11.3	M	11.30	M
7	13.2	L	13.18	L
8	14.1	M	14.10	M
9	17.8	M	17.82	M
10	18.7	M	18.74	M
11	20.0	H	20.00	H
12	21.8	L	21.76	L
13	23.8	M	23.80	M

14	25.3	H	25.34	H
15	27.8	L	27.84	L
16	30.5	L	30.49	L
normalised intensity values:		L	0	45
		M	45	70
		H	70	100

5

In another embodiment, Form **ULT-7** can be characterised by an XRPD substantially according to Fig 4A.

In another embodiment, Form **ULT-7** can be characterised by an DSC substantially according to Fig 4B.

10 In another embodiment, Form **ULT-7** can be characterised by an TGA substantially according to Fig 4C.

In another embodiment, Form **ULT-7** of the present invention can be characterised by DSC with an onset at 98.4°C and a characterising peak at 108.4°C. From the thermal analysis, it is concluded that
15 solid form **ULT-7** is anhydrous.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-7** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form
20 **ULT-7** by evaporation of the solvent.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-7** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising
25 tenofovir DF Form **ULT-7** by cooling and/or evaporation crystallization of a saturated solution.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-7** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising
30 tenofovir DF Form **ULT-7** by anti-solvent addition as in Table III.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-7** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as outlined herein elsewhere
35 (paragraph on solvents) crystallising tenofovir DF Form **ULT-7** by slurry crystallisation and/or seed crystallisation.

Crystalline tenofovir DF form ULT-8 (C):

Thus, in one aspect, the present invention provides

crystalline tenofovir DF herein defined as Form **ULT-8**, characterised by the selection of at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group consisting of 5.0, 10.3, 13.4, 14.7, 15.7, 17.3, 18.4, 19.1, 20.7, 21.2, 25.2 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta. In a preferred embodiment, at least seven, more preferably at least eight, even more preferably at least nine, particularly preferred at least ten and most preferred eleven X-ray powder diffraction peaks are selected from the above group. In another embodiment Form **ULT-8** can be characterised by the following set of XRPD peaks and, optionally, by the associated intensities:

Table 5	C		Preferred embodiment	
Peak ID	Angle (2θ)	Intensity*	Angle (2θ)	Intensity*
1	5.0	H	4.98	H
2	10.3	H	10.34	H
3	13.4	M	13.36	M
4	14.7	L	14.67	L
5	15.7	L	15.74	L
6	17.3	M	17.31	M
7	18.4	M	18.42	M
8	19.1	M	19.08	M
9	20.7	M	20.70	M
10	21.2	M	21.24	M
11	25.2	M	25.16	M
normalised intensity values:		L	0	35
		M	35	60
		H	60	100

In another embodiment, Form **ULT-8** can be characterised by an XRPD substantially according to Fig 5A.

5 In another embodiment, Form **ULT-8** can be characterised by an DSC substantially according to Fig 5B.

In another embodiment, Form **ULT-8** can be characterised by an TGA substantially according to Fig 5C.

10 In another embodiment, Form **ULT-8** of the present invention can be characterised by DSC with an onset at 104.8°C and a characterising peak at 113.0°C. From the thermal analysis, it is concluded that solid form **ULT-8** is anhydrous.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-8** of tenofovir DF comprising
15 the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-8** by evaporation of the solvent.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-8** of tenofovir DF
20 comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-8** by cooling and/or evaporation crystallization of a saturated solution.

The present invention in one aspect relates to a method for
25 the preparation of the crystalline form **ULT-8** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-8** by anti-solvent addition as in Table III.

The present invention in another aspect relates to a method
30 for the preparation of the crystalline form **ULT-8** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as outlined herein elsewhere (paragraph on solvents) crystallising tenofovir DF Form **ULT-8** by slurry crystallisation and/or seed crystallisation.

5 Crystalline tenofovir DF form ULT-10 (F):

Thus, in one aspect, the present invention provides crystalline tenofovir DF herein defined as Form **ULT-10**, characterised by the selection of at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group consisting of 5.0, 7.0, 10.6, 11.8, 12.7, 13.5, 15.2, 16.3, 17.3, 18.8, 20.7, 21.3, 22.2, 25.3, 27.3, degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta. In a preferred embodiment, at least seven, more preferably at least eight, even more preferably at least nine, particularly preferred at least ten and most preferred eleven X-ray powder diffraction peaks are selected from the above group. In a more preferred embodiment, at least twelve, more preferably at least thirteen, even more preferably at least fourteen, particularly preferred at least fifteen X-ray powder diffraction peaks are selected from the above group.

In another embodiment Form **ULT-10** can be characterised by the following set of XRPD peaks and, optionally, by the associated intensities:

Table 7		F		Preferred embodiment	
Peak ID	Angle (2 θ)	Intensity*	Angle (2 θ)	Intensity*	
1	5.0	M	5.04	M	
2	7.0	M	7.00	M	
3	10.6	H	10.60	H	
4	11.8	M	11.78	M	
5	12.7	M	12.74	M	
6	13.5	M	13.50	M	
7	15.2	L	15.21	L	
8	16.3	L	16.26	L	
9	17.3	L	17.32	L	
10	18.8	H	18.80	H	
11	20.7	M	20.68	M	
12	21.3	M	21.32	M	
13	22.2	M	22.18	M	
14	25.3	M	25.34	M	
15	27.3	H	27.26	H	
normalised intensity values:		L	0	30	

M	30	6
H	60	100

5

In another embodiment, Form **ULT-10** can be characterised by an XRPD substantially according to Fig 7A.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-10** of tenofovir DF comprising
10 the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-10** by evaporation of the solvent.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-10** of tenofovir DF
15 comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-10** by cooling and/or evaporation crystallization of a saturated solution.

The present invention in one aspect relates to a method for
20 the preparation of the crystalline form **ULT-10** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-10** by anti-solvent addition as in Table III.

The present invention in another aspect relates to a method
25 for the preparation of the crystalline form **ULT-10** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as outlined herein elsewhere (paragraph on solvents) crystallising tenofovir DF Form **ULT-10** by slurry crystallisation and/or seed crystallisation.

5 **Crystalline tenofovir DF form ULT-11 (F1):**

Thus, in one aspect, the present invention provides crystalline tenofovir DF herein defined as Form **ULT-11**, characterised by the selection of at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group consisting of 5.0, 7.0, 9.5, 10.6, 11.7, 13.5, 16.0, 17.4, 18.8, 20.4, 21.2, 22.0, 25.5 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta. In a preferred embodiment, at least seven, more preferably at least eight, even more preferably at least nine, particularly preferred at least ten and most preferred eleven X-ray powder diffraction peaks are selected from the above group. In a more preferred embodiment, at least twelve, more preferably at least thirteen X-ray powder diffraction peaks are selected from the above group.

In another embodiment Form **ULT-11** can be characterised by the following set of XRPD peaks and, optionally, by the associated intensities:

Table 8	F1		Preferred embodiment	
Peak ID	Angle (2θ)	Intensity*	Angle (2θ)	Intensity*
1	5.0	H	5.02	H
2	7.0	M	6.98	M
3	9.5	M	9.52	M
4	10.6	H	10.64	H
5	11.7	L	11.66	L
6	13.5	M	13.50	M
7	16.0	M	15.96	M
8	17.4	M	17.36	M
9	18.8	H	18.84	H
10	20.4	H	20.36	H
11	21.2	H	21.18	H
12	22.0	H	22.04	H
13	25.5	M	25.46	M
normalised intensity values:		L	0	45
		M	45	60
		H	60	100

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In another embodiment, Form **ULT-11** can be characterised by an XRPD substantially according to Fig 8A.

In another embodiment, Form **ULT-11** can be characterised by an DSC substantially according to Fig 8B.

10 In another embodiment, Form **ULT-11** can be characterised by an TGA substantially according to Fig 8C.

In another embodiment, Form **ULT-11** of the present invention can be characterised by DSC with an onset at 104.5°C and a characterising peak at 112.8°C. From the thermal analysis, it is
15 concluded that solid form **ULT-11** is anhydrous.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-11** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form
20 **ULT-11** by evaporation of the solvent.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-11** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising
25 tenofovir DF Form **ULT-11** by cooling and/or evaporation crystallization of a saturated solution.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-11** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a
30 suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-11** by anti-solvent addition as in Table III.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-11** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a
35 suitable solvent or mixture thereof as outlined herein elsewhere (paragraph on solvents) crystallising tenofovir DF Form **ULT-11** by slurry crystallisation and/or seed crystallisation.

The present invention in one aspect relates to the crystal structure of tenofovir DF Form **ULT-11** as depicted in figure 8D and/or
40 8E and/or in the table X1, Y1 and Z1 below:

Table X1. Crystal data and structure refinement for tenofovir form **ULT-11**.

Empirical formula	$C_{19}H_{31}N_5O_{10}P^+ \cdot C_4H_3O_4^-$
Formula weight	635.52
Temperature	120(2)
Wavelength	0.71073
Crystal system	Monoclinic
Space group	P 2 ₁
Unit cell dimensions	9.7440(3) [9.963(2)]* 18.0330(5) [18.410(5)] 17.4080(6) [18.160(2)] 102.759(2) [104.66(2)]
Volume	2983.3(2) [3222.4(11)]
Z	4
Density (calculated)	1.415 [1.310]
F(000)	1336
Crystal size	0.25 x 0.25 x 0.05
Theta range for data collection	2.5 → 27.5
Reflections collected	20281
Independent reflections	11699 [R(int) = 0.0812]
Data / restraints / parameters	11699 / 1 / 783
Goodness-of-fit on F ²	1.106
Final R indices [I>2sigma(I)]	R1 = 0.0774, wR2 = 0.1194
R indices (all data)	R1 = 0.1239, wR2 = 0.1340
Absolute structure parameter	0.07(13)

* Values in square brackets were taken at 293(2)K

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Crystalline tenofovir DF form ULT-12 (H):

Thus, in one aspect, the present invention provides crystalline tenofovir DF herein defined as Form **ULT-12**, characterised by the selection of at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group consisting of 4.2, 5.2, 9.5, 14.5, 16.7, 18.6, 19.2, 20.2, 11.1, 13.4, 17.3, 21.2, 25.4 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta. In a preferred embodiment, at least seven, more preferably at least eight, even more preferably at

10

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5 least nine, particularly preferred at least ten and most preferred eleven X-ray powder diffraction peaks are selected from the above group. In a more preferred embodiment, at least twelve, more preferably at least thirteen X-ray powder diffraction peaks are selected from the above group.

10 In another embodiment Form **ULT-12** can be characterised by the following set of XRPD peaks and, optionally, by the associated intensities:

Table 9	H		Preferred embodiment	
Peak ID	Angle (2 θ)	Intensity*	Angle (2 θ)	Intensity*
1	4.2	H	4.18	H
2	5.2	H	5.24	H
3	9.5	L	9.47	L
4	14.5	L	14.45	L
5	16.7	L	16.66	L
6	18.6	M	18.60	M
7	19.2	M	19.18	M
8	20.2	L	20.16	L
9	11.1	H	11.12	H
10	13.4	M	13.36	M
11	17.3	H	17.32	H
12	21.2	M	21.16	M
13	25.4	M	25.42	M
Normalised intensity values:		L	0	40
		M	40	65
		H	65	100

15 In another embodiment, Form **ULT-12** can be characterised by an XRPD substantially according to Fig 9A.

In another embodiment, Form **ULT-12** can be characterised by an DSC substantially according to Fig 9B.

20 In another embodiment, Form **ULT-12** can be characterised by an TGA substantially according to Fig 9C.

In another embodiment, Form **ULT-12** of the present invention can be characterised by DSC with an onset at 90.0°C and a characterising peak at 100.4°C. In a preferred embodiment, Form **ULT-12** of the present invention can be further characterised by DSC with an onset at 107.9°C and a characterising peak at 113.7°C. From the

25

5 thermal analysis, it is concluded that solid form **ULT-12** is a solvate with an alcohol, preferably cyclopentanol, cyclohexanol or isobutanol.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-12** of tenofovir DF comprising
10 the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-12** by evaporation of the solvent.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-12** of tenofovir DF
15 comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-12** by cooling and/or evaporation crystallization of a saturated solution.

The present invention in one aspect relates to a method for
20 the preparation of the crystalline form **ULT-12** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-12** by anti-solvent addition as in Table III.

The present invention in another aspect relates to a method
25 for the preparation of the crystalline form **ULT-12** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as outlined herein elsewhere (paragraph on solvents) crystallising tenofovir DF Form **ULT-12** by slurry crystallisation and/or seed crystallisation.

Crystalline tenofovir DF form ULT-13 (K):

Thus, in one aspect, the present invention provides

crystalline tenofovir DF herein defined as Form **ULT-13**, characterised by the selection of at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group consisting of 4.7, 5.6, 9.1, 10.4, 13.3, 14.8, 16.0, 16.0, 19.4, 21.4, 23.7, 28.6 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta. In a preferred embodiment, at least seven, more preferably at least eight, even more preferably at least nine, particularly preferred at least ten and most preferred eleven X-ray powder diffraction peaks are selected from the above group. In a more preferred embodiment twelve X-ray powder diffraction peaks are selected from the above group.

In another embodiment Form **ULT-13** can be characterised by the following set of XRPD peaks and, optionally, by the associated intensities:

Table 10		K		Preferred embodiment	
Peak ID	Angle (2θ)	Intensity*	Angle (2θ)	Intensity*	
1	4.7	L	4.74	L	
2	5.6	L	5.57	L	
3	9.1	L	9.10	L	
4	10.4	M	10.40	M	
5	13.3	M	13.31	M	
6	14.8	L	14.75	L	
7	16.0	L	15.98	L	
8	16.0	L	16.02	L	
9	19.4	M	19.39	M	
10	21.4	M	21.40	M	
11	23.7	M	23.74	M	
12	28.6	L	28.59	L	
normalised intensity values:		L	0	30	
		M	30	60	
		H	60	100	

5 In another embodiment, Form **ULT-13** can be characterised by an XRPD substantially according to Fig 10A.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-13** of tenofovir DF comprising
10 the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-13** by evaporation of the solvent.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-13** of tenofovir DF
15 comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-13** by cooling and/or evaporation crystallization of a saturated solution.

The present invention in one aspect relates to a method for
20 the preparation of the crystalline form **ULT-13** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-13** by anti-solvent addition as in Table III.

The present invention in another aspect relates to a method
25 for the preparation of the crystalline form **ULT-13** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as outlined herein elsewhere (paragraph on solvents) crystallising tenofovir DF Form **ULT-13** by slurry crystallisation and/or seed crystallisation.

5 Crystalline tenofovir DF form ULT-14 (K1):

Thus, in one aspect, the present invention provides crystalline tenofovir DF herein defined as Form **ULT-14**, characterised by the selection of at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five X-ray powder diffraction peaks selected from the group consisting of 4.7, 10.3, 18.4, 20.6, 21.5 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta. In another embodiment Form **ULT-14** can be characterised by the following set of XRPD peaks and, optionally, by the associated intensities:

Table 11	K1		Preferred embodiment	
Peak ID	Angle (2 θ)	Intensity*	Angle (2 θ)	Intensity*
1	4.7	H	4.70	H
2	10.3	H	10.30	H
3	18.4	M	18.38	M
4	20.6	M	20.62	M
5	21.5	H	21.46	H
normalised intensity values:		L	0	50
		M	50	80
		H	80	100

In another embodiment, Form **ULT-14** can be characterised by an XRPD substantially according to Fig 11A.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-14** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-14** by evaporation of the solvent.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-14** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-14** by cooling and/or evaporation crystallization of a saturated solution.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-14** of tenofovir DF

- 5 comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-14** by anti-solvent addition as in Table III.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-14** of tenofovir DF

10 comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as outlined herein elsewhere (paragraph on solvents) crystallising tenofovir DF Form **ULT-14** by slurry crystallisation and/or seed crystallisation.

Crystalline tenofovir DF form ULT-15 (L):

Thus, in one aspect, the present invention provides

crystalline tenofovir DF herein defined as Form **ULT-15**, characterised by the selection of at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group consisting of 4.7, 5.2, 9.4, 10.5, 13.2, 17.1, 18.3, 21.3, 24.4 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta. In a preferred embodiment, at least seven, more preferably at least eight, even more preferably nine X-ray powder diffraction peaks are selected from the above group. In another embodiment Form **ULT-15** can be characterised by the following set of XRPD peaks and, optionally, by the associated intensities:

Table 12		L		Preferred embodiment	
Peak ID	Angle (2θ)	Intensity*	Angle (2θ)	Intensity*	
1	4.7	M	4.74	M	
2	5.2	M	5.22	M	
3	9.4	L	9.42	L	
4	10.5	H	10.52	H	
5	13.2	M	13.18	M	
6	17.1	M	17.14	M	
7	18.3	H	18.26	H	
8	21.3	L	21.26	L	
9	24.4	L	24.36	L	
normalised intensity values:		L	0	45	
		M	45	65	
		H	65	100	

In another embodiment, Form **ULT-15** can be characterised by an XRPD substantially according to Fig 12A.

In another embodiment, Form **ULT-15** can be characterised by an DSC substantially according to Fig 12B.

In another embodiment, Form **ULT-15** can be characterised by an TGA substantially according to Fig 12C.

5 In another embodiment, Form **ULT-15** of the present invention can be characterised by DSC with an onset at 61.3°C and a characterising peak at 69.8°C. In a further embodiment, Form **ULT-15**
can be further characterised by DSC with an onset at 92.8°C and a characterising peak at 97.8°C. In another embodiment, Form **ULT-15** can
10 be characterised by DSC with an onset at 104.8°C and a characterising peak at 111.8°C.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-15** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-15** by evaporation of the solvent.
15

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-15** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a
20 suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-15** by cooling and/or evaporation crystallization of a saturated solution.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-15** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a
25 suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-15** by anti-solvent addition as in Table III.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-15** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a
30 suitable solvent or mixture thereof as outlined herein elsewhere (paragraph on solvents) crystallising tenofovir DF Form **ULT-15** by slurry crystallisation and/or seed crystallisation.

5 Crystalline tenofovir DF form **ULT-16** (Q):

Thus, in one aspect, the present invention provides crystalline tenofovir DF herein defined as Form **ULT-16**, characterised by the selection of at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group consisting of 4.7, 10.3, 13.4, 15.4, 18.5, 20.6, 21.5, 23.5 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta. In a preferred embodiment, at least seven, more preferably eight X-ray powder diffraction peaks are selected from the above group. In another embodiment Form **ULT-16** can be characterised by the following set of XRPD peaks and, optionally, by the associated intensities:

Table 13	Q		Preferred embodiment	
Peak ID	Angle (2 θ)	Intensity*	Angle (2 θ)	Intensity*
1	4.7	H	4.70	H
2	10.3	H	10.34	H
3	13.4	M	13.38	M
4	15.4	L	15.35	L
5	18.5	M	18.54	M
6	20.6	M	20.62	M
7	21.5	M	21.54	M
8	23.5	H	23.54	H
normalised intensity values:		L	0	55
		M	55	70
		H	70	100

In another embodiment, Form **ULT-16** can be characterised by an XRPD substantially according to Fig 13A.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-16** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-16** by evaporation of the solvent.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-16** of tenofovir DF

- 5 comprising the steps of dissolving or mixing tenofovir DF in a
suitable solvent or mixture thereof as in Table II and crystallising
tenofovir DF Form **ULT-16** by cooling and/or evaporation
crystallization of a saturated solution.
-

- 10 The present invention in one aspect relates to a method for
the preparation of the crystalline form **ULT-16** of tenofovir DF
comprising the steps of dissolving or mixing tenofovir DF in a
suitable solvent or mixture thereof as in Table III and crystallising
tenofovir DF Form **ULT-16** by anti-solvent addition as in Table III.

- 15 The present invention in another aspect relates to a method
for the preparation of the crystalline form **ULT-16** of tenofovir DF
comprising the steps of dissolving or mixing tenofovir DF in a
suitable solvent or mixture thereof as outlined herein elsewhere
(paragraph on solvents) crystallising tenofovir DF Form **ULT-16** by
slurry crystallisation and/or seed crystallisation.

Crystalline tenofovir DF form ULT-17 (R):

Thus, in one aspect, the present invention provides crystalline tenofovir DF herein defined as Form **ULT-17**, characterised by the selection of at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group consisting of 4.8, 10.2, 10.8, 11.8, 13.3, 15.6, 17.0, 18.0, 18.8, 20.5, 21.5, 23.2, 24.3 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta. In a preferred embodiment, at least seven, more preferably at least eight, even more preferably at least nine, particularly preferred at least ten and most preferred eleven X-ray powder diffraction peaks are selected from the above group. In a more preferred embodiment, at least twelve, more preferably thirteen X-ray powder diffraction peaks are selected from the above group.

In another embodiment Form **ULT-17** can be characterised by the following set of XRPD peaks and, optionally, by the associated intensities:

Table 14		R		Preferred embodiment	
Peak ID	Angle (2 θ)	Intensity*	Angle (2 θ)	Intensity*	
1	4.8	H	4.82	H	
2	10.2	H	10.20	H	
3	10.8	M	10.84	M	
4	11.8	L	11.76	L	
5	13.3	H	13.32	H	
6	15.6	L	15.58	L	
7	17.0	M	17.03	M	
8	18.0	H	18.06	H	
9	18.8	M	18.78	M	
10	20.5	M	20.50	M	
11	21.5	H	21.50	H	
12	23.2	M	23.22	M	
13	24.3	H	24.30	H	
normalised intensity values:		L	0	45	
		M	45	65	
		H	65	100	

In another embodiment, Form **ULT-17** can be characterised by an XRPD substantially according to Fig 14A.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-17** of tenofovir DF comprising
10 the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-17** by evaporation of the solvent.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-17** of tenofovir DF
15 comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-17** by cooling and/or evaporation crystallization of a saturated solution.

The present invention in one aspect relates to a method for
20 the preparation of the crystalline form **ULT-17** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-17** by anti-solvent addition as in Table III.

The present invention in another aspect relates to a method
25 for the preparation of the crystalline form **ULT-17** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as outlined herein elsewhere (paragraph on solvents) crystallising tenofovir DF Form **ULT-17** by slurry crystallisation and/or seed crystallisation.

5 Crystalline tenofovir DF form ULT-18 (S):

Thus, in one aspect, the present invention provides crystalline tenofovir DF herein defined as Form **ULT-18**, characterised by the selection of at least one, preferably two X-ray powder diffraction peaks selected from the group consisting of 4.3 and 10.3
10 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta. In another embodiment Form **ULT-18** can be characterised by the following set of XRPD peaks and, optionally, by the associated intensities:

15

Table 15	S		Preferred embodiment	
Peak ID	Angle (2 θ)	Intensity*	Angle (2 θ)	Intensity*
1	4.3	H	4.26	H
2	10.3	L	10.30	L
normalised intensity values:		L	0	60
		H	60	100

In another embodiment, Form **ULT-18** can be characterised by an XRPD substantially according to Fig 15A.

20 The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-18** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-18** by evaporation of the solvent.

25 The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-18** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-18** by cooling and/or evaporation crystallization of a saturated solution.

30 The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-18** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-18** by anti-solvent addition as in Table III.

35 The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-18** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a

- 5 suitable solvent or mixture thereof as outlined herein elsewhere (paragraph on solvents) crystallising tenofovir DF Form **ULT-18** by slurry crystallisation and/or seed crystallisation.

5 **Crystalline tenofovir DF form ULT-19 (T):**

Thus, in one aspect, the present invention provides crystalline tenofovir DF herein defined as Form **ULT-19**, characterised by the selection of at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group consisting of 5.3, 9.7, 10.5, 13.3, 17.1, 21.4, 30.5 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta. In a preferred embodiment seven X-ray powder diffraction peaks are selected from the above group. In another embodiment Form **ULT-19** can be characterised by the following set of XRPD peaks and, optionally, by the associated intensities:

Table 16			Preferred embodiment	
Peak ID	Angle (2θ)	Intensity*	Angle (2θ)	Intensity*
1	5.3	M	5.30	M
2	9.7	M	9.72	M
3	10.5	H	10.46	H
4	13.3	M	13.28	M
5	17.1	H	17.14	H
6	21.4	M	21.38	M
7	30.5	L	30.50	L
normalised intensity values:		L	0	50
		M	50	80
		H	80	100

In another embodiment, Form **ULT-19** can be characterised by an XRPD substantially according to Fig 16A.

In another embodiment, Form **ULT-19** can be characterised by an TGA substantially according to Fig 16C.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-19** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-19** by evaporation of the solvent.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-19** of tenofovir DF

5 comprising the steps of dissolving or mixing tenofovir DF in a
suitable solvent or mixture thereof as in Table II and crystallising
tenofovir DF Form **ULT-19** by cooling and/or evaporation
crystallization of a saturated solution.

10 The present invention in one aspect relates to a method for
the preparation of the crystalline form **ULT-19** of tenofovir DF
comprising the steps of dissolving or mixing tenofovir DF in a
suitable solvent or mixture thereof as in Table III and crystallising
tenofovir DF Form **ULT-19** by anti-solvent addition as in Table III.

15 The present invention in another aspect relates to a method
for the preparation of the crystalline form **ULT-19** of tenofovir DF
comprising the steps of dissolving or mixing tenofovir DF in a
suitable solvent or mixture thereof as outlined herein elsewhere
(paragraph on solvents) crystallising tenofovir DF Form **ULT-19** by
slurry crystallisation and/or seed crystallisation.

5 **Crystalline tenofovir DF form ULT-20 (U):**

Thus, in one aspect, the present invention provides crystalline tenofovir DF herein defined as Form **ULT-20**, characterised by the selection of at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group consisting of 5.1, 9.0, 10.4, 11.3, 13.3, 17.6, 18.7, 19.6, 20.3, 21.3, 23.7, 24.4, 25.6, 26.5, 27.6, 29.4, 30.8 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta. In a preferred embodiment, at least seven, more preferably at least eight, even more preferably at least nine, particularly preferred at least ten and most preferred eleven X-ray powder diffraction peaks are selected from the above group. In a more preferred embodiment, at least twelve, more preferably at least thirteen, even more preferably at least fourteen, particularly preferred at least fifteen and most preferred sixteen X-ray powder diffraction peaks are selected from the above group.

In another embodiment Form **ULT-20** can be characterised by the following set of XRPD peaks and, optionally, by the associated intensities:

Table 17		U		Preferred embodiment	
Peak ID	Angle (2θ)	Intensity*	Angle (2θ)	Intensity*	
1	5.1	M	5.06	M	
2	9.0	L	9.02	L	
3	10.4	H	10.42	H	
4	11.3	L	11.34	L	
5	13.3	H	13.32	H	
6	17.6	M	17.64	M	
7	18.7	M	18.16	M	
8	19.6	M	19.60	M	
9	20.3	M	20.30	M	
10	21.3	M	21.26	M	
11	23.7	L	23.66	L	
12	24.4	M	24.36	M	
13	25.6	M	25.60	M	
14	26.5	L	26.54	L	

15	27.6	L	27.63	L
16	29.4	L	29.42	L
17	30.8	L	30.82	L
normalised intensity values:		L	0	45
		M	45	70
		H	70	100

5

In another embodiment, Form **ULT-20** can be characterised by an XRPD substantially according to Fig 17A.

In another embodiment, Form **ULT-20** can be characterised by an TGA substantially according to Fig 17C.

10 From the thermal analysis, it is concluded that solid form **ULT-20** is anhydrous.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-20** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-20** by evaporation of the solvent.

15 The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-20** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-20** by cooling and/or evaporation crystallization of a saturated solution.

20 The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-20** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-20** by anti-solvent addition as in Table III.

25 The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-20** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as outlined herein elsewhere (paragraph on solvents) crystallising tenofovir DF Form **ULT-20** by slurry crystallisation and/or seed crystallisation.

30

Crystalline tenofovir DF form ULT-21 (V):

Thus, in one aspect, the present invention provides crystalline tenofovir DF herein defined as Form **ULT-21**, characterised by the selection of at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group consisting of 5.1, 9.0, 10.4, 11.3, 13.3, 17.6, 18.7, 19.6, 20.3, 21.3, 23.7, 24.4, 25.6, 26.5, 27.6, 29.4, 30.8 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta. In a preferred embodiment, at least seven, more preferably at least eight, even more preferably at least nine, particularly preferred at least ten and most preferred eleven X-ray powder diffraction peaks are selected from the above group. In a more preferred embodiment, at least twelve, more preferably at least thirteen, even more preferably at least fourteen, particularly preferred at least fifteen and most preferred sixteen X-ray powder diffraction peaks are selected from the above group.

In another embodiment Form **ULT-21** can be characterised by the following set of XRPD peaks and, optionally, by the associated intensities:

Table 18			Preferred embodiment	
Peak ID	Angle (2θ)	Intensity*	Angle (2θ)	Intensity*
1	5.0	H	5.00	H
2	9.6	M	9.64	M
3	10.3	M	10.34	M
4	10.8	L	10.76	L
5	11.1	M	11.06	M
6	11.7	M	11.74	M
7	13.3	H	13.26	H
8	15.0	L	14.99	L
9	17.2	L	17.15	L
10	18.5	H	18.50	H
11	20.3	M	20.30	M
12	21.6	M	21.56	M
13	25.3	M	25.34	M
normalised intensity values:		L	0	50

M	50	75
H	75	100

5

In another embodiment, Form **ULT-21** can be characterised by an XRPD substantially according to Fig 18A.

In another embodiment, Form **ULT-21** can be characterised by an DSC substantially according to Fig 18B.

10 In another embodiment, Form **ULT-21** can be characterised by an TGA substantially according to Fig 18C.

In another embodiment, Form **ULT-21** of the present invention can be characterised by DSC with an onset at 100.8°C and a characterising peak at 105.6°C. In a further embodiment, Form **ULT-21**
15 can be further characterised by DSC with an onset at 107.6°C and a characterising peak at 114.7°C. From the thermal analysis, it is concluded that solid form **ULT-21** is anhydrous.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-21** of tenofovir DF comprising
20 the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-21** by evaporation of the solvent.

The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-21** of tenofovir DF
25 comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-21** by cooling and/or evaporation crystallization of a saturated solution.

The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-21** of tenofovir DF
30 comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-21** by anti-solvent addition as in Table III.

The present invention in another aspect relates to a method
35 for the preparation of the crystalline form **ULT-21** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as outlined herein elsewhere (paragraph on solvents) crystallising tenofovir DF Form **ULT-21** by slurry crystallisation and/or seed crystallisation.

40

Crystalline tenofovir DF form **ULT-22** (X):

5 Thus, in one aspect, the present invention provides
 crystalline tenofovir DF herein defined as Form **ULT-22**, characterised
 by the selection of at least one, preferably at least two, more
 preferably at least three, even more preferably at least four,
 particularly preferred at least five and most preferred six X-ray
 10 powder diffraction peaks selected from the group consisting of 5.4,
 8.9, 9.3, 9.9, 10.4, 13.3, 17.6, 19.2, 21.2, 21.8, 23.0, 23.5, 25.7,
 26.3 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2
 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most
 preferably +/- 0.05 degrees two-theta. In a preferred embodiment, at
 15 least seven, more preferably at least eight, even more preferably at
 least nine, particularly preferred at least ten and most preferred
 eleven X-ray powder diffraction peaks are selected from the above
 group. In a more preferred embodiment, at least twelve, more
 preferably at least thirteen, even more preferably fourteen X-ray
 20 powder diffraction peaks are selected from the above group.

In another embodiment Form **ULT-22** can be characterised by the
 following set of XRPD peaks and, optionally, by the associated
 intensities:

25

Table 19			Preferred embodiment	
Peak ID	Angle (2θ)	Intensity*	Angle (2θ)	Intensity*
1	5.4	L	5.44	L
2	8.9	L	8.90	L
3	9.3	L	9.28	L
4	9.9	H	9.86	H
5	10.4	M	10.38	M
6	13.3	H	13.28	H
7	17.6	M	17.64	M
8	19.2	M	19.24	M
9	21.2	H	21.20	H
10	21.8	L	21.78	L
11	23.0	L	23.00	L
12	23.5	L	23.52	L
13	25.7	L	25.74	L
14	26.3	L	26.30	L
normalised intensity values:		L	0	40
		M	40	65

H	65	100
---	----	-----

5

In another embodiment, Form **ULT-22** can be characterised by an XRPD substantially according to Fig 19A.

10 The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-22** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-22** by evaporation of the solvent.

15 The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-22** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-22** by cooling and/or evaporation crystallization of a saturated solution.

20 The present invention in one aspect relates to a method for the preparation of the crystalline form **ULT-22** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-22** by anti-solvent addition as in Table III.

25 The present invention in another aspect relates to a method for the preparation of the crystalline form **ULT-22** of tenofovir DF comprising the steps of dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as outlined herein elsewhere (paragraph on solvents) crystallising tenofovir DF Form **ULT-22** by slurry crystallisation and/or seed crystallisation. In particular, 30 Form **ULT-22** was obtained by slow evaporation of saturated solution of tenofovir DF in methanol/water (50/50) at room temperature. During cooling of the saturated solution, solid material crystallized out. The solution was heated anew until dissolution of the solid material and as diluted to half the concentration. The solution was slowly 35 cooled to room temperature and aged for several days.

Purity

In one aspect of the invention, the forms **ULT-4, ULT-5, ULT-6, ULT-7, ULT-8, , ULT-10, ULT-11, ULT-12, ULT-13, ULT-14, ULT-15, ULT-16, ULT-17, ULT-18, ULT-19, ULT-20, ULT-21** and **ULT-22** of the present invention are, independently, in a substantially pure form, preferably substantially free from other amorphous, and/or crystalline solid forms such as **ULT-4, ULT-5, ULT-6, ULT-7, ULT-8, ULT-10, ULT-11, ULT-12, ULT-13, ULT-14, ULT-15, ULT-16, ULT-17, ULT-18, ULT-19, ULT-20, ULT-21** and **ULT-22** or the solid forms as described in the prior art as referred herein before or of **ULT-1, ULT-2** or **ULT-3** as described in applicant's copending US60/872999 and US60/873267 respectively, respectively. In this respect, "substantially pure" relates to at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% of the pure compound. In this respect, "substantially free from other amorphous, and/or crystalline solid forms" means that no more than about 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of these other amorphous, and/or crystalline solid forms are present in the form according to the invention.

Solvents

In certain embodiments of the method for the preparation of **ULT-4, ULT-5, ULT-6, ULT-7, ULT-8, ULT-10, ULT-11, ULT-12, ULT-13, ULT-14, ULT-15, ULT-16, ULT-17, ULT-18, ULT-19, ULT-20, ULT-21** and **ULT-22** of the present invention, the solvents for evaporation crystallisation, hot filtration anti-solvent addition , seed crystallisation and/or slurry crystallisation are preferably selected from the group consisting of: (R)-(-)-2-Octanol, 1,2-Diethoxyethane, 1,2-Dimethoxyethane, 1,4-Dioxane, 1-Butanol, 1-Heptanol, 1-Hexanol, 1-Methoxy-2-propanol, 1-Nitropropane, 1-Octanol, 2,2,2-Trifluoroethanol , 2-Butanone, 2-Ethoxyethanol, 2-Ethoxyethyl acetate, 2-Hexanol, 2-Methoxyethanol, 2-Nitropropane, 2-Pentanol, 2-Propanol, 4-Hydroxy-4-methyl-2-pentanone, Acetone, Acetonitrile, Butyronitrile, Cyclohexanol, Cyclopentanol, Cyclopentanone, Diethylene glycol dimethylether, Dimethylcarbonate, Dimethylcarbonate, Ethanol, Ethyl formate, Ethylacetate, Ethylene glycol monobutyl ether, Furfuryl alcohol, Isobutanol, Isopropyl acetate, Methanol, Methoxyethyl acetate, Methyl acetate, Methyl

5 butyrate, Methyl propionate, Methyl-4-2-Pentanol, N,N-Dimethylacetamide, N,N-Dimethylformamide, Nitrobenzene, Nitroethane, Nitromethane, N-Methyl Pyrrolidone, Propionitrile, Propyl acetate, Propylene glycol methyl ether acetate, tert-Butanol, Tetrahydrofuran, Tetrahydrofurfuryl alcohol, Tetrahydropyran, Water and mixtures
10 thereof.

In certain embodiments of the method for the preparation of ULT-4-21 of the present invention, the solvents for hot filtration crystallisation are preferably selected from the group consisting of: (R)-(-)-2-Octanol, 1,2-Diethoxyethane, 1,2-Dimethoxyethane, 1,4-Dioxane , 1-Butanol, 1-Nitropropane, 1-Propanol, 2-Butanone, 2-Ethoxyethyl acetate, 2-Methyl-4-pentanol, 2-Nitropropane, 2-Propanol, Acetone, Acetonitrile, Cyclopentanol, Ethanol, Isobutanol, Isopropyl acetate, Methanol, Methoxy-2-1-Propanol, Methyl propionate, N,N-Dimethylacetamide, N,N-Dimethylformamide, Nitromethane, tert-Butanol, Tetrahydrofuran, Water and mixtures thereof.
20

In certain embodiments of the method for the preparation of ULT-4-21 of the present invention, the solvents for solvent/anti-solvent crystallisation are preferably selected from the group consisting of: 1,2-Dichloroethane, 1,2-Dimethoxyethane, 1,4-Dioxane , 2,6-Dimethyl-4-heptanone, 2-Butanone, Acetone, Acetonitrile, Amyl ether, Butyl benzene, Chloroform, Cyclohexane, Cyclohexane, Cyclohexane, Cyclohexane, Dichloromethane, Hexafluorobenzene, Methanol, n-Heptane, Nitromethane, N-Methyl Pyrrolidone, tert-Butyl methyl ether, Tetrahydrofuran, Toluene, Water and mixtures thereof.
25
30

In certain embodiments of the method for the preparation of **ULT-4, ULT-5, ULT-6, ULT-7, ULT-8, ULT-10, ULT-11, ULT-12, ULT-13, ULT-14, ULT-15, ULT-16, ULT-17, ULT-18, ULT-19, ULT-20, ULT-21 and ULT-22** of the present invention, the anti-solvents for anti-solvent crystallisation are preferably selected from the group consisting of: 1,2-Dichloroethane, 2,6-Dimethyl-4-heptanone, Acetone, Amyl ether, Butyl benzene, Chloroform, Cyclohexane, Dichloromethane, Hexafluorobenzene, n-Heptane, Nitromethane, tert-Butyl methyl ether, Toluene and mixtures thereof.
35

In certain embodiments of the method for the preparation of **ULT-4, ULT-5, ULT-6, ULT-7, ULT-8, ULT-10, ULT-11, ULT-12, ULT-13, ULT-14, ULT-15, ULT-16, ULT-17, ULT-18, ULT-19, ULT-20, ULT-21 and ULT-22** of the present invention, the solvents for seeding crystallisation are preferably selected from the group consisting of:
40

- 5 methanol, water, 1,4-dioxane, acetonitrile, 2-ethoxyethylacetate, 2-methyl-4-pentanol, tetrahydrofuran, butyl benzene, amylether, tert-butyl methyl ether, cyclopentanone and mixtures thereof.

In certain embodiments of the method for the preparation of
ULT-4, ULT-5, ULT-6, ULT-7, ULT-8, ULT-10, ULT-11, ULT-12, ULT-13,
10 ULT-14, ULT-15, ULT-16, ULT-17, ULT-18, ULT-19, ULT-20, ULT-21 and
ULT-22 of the present invention, the solvents for slurring
crystallisation are preferably selected from the group consisting of:
water, methanol, acetonitrile, 1,4-dioxane and mixtures thereof.

5 **Pharmaceutical formulations.**

The present invention further relates to pharmaceutical formulations comprising the novel crystalline forms of tenofovir DF.

Pharmaceutical formulations of the present invention contain one or more of the crystalline forms according to the present
10 invention, such as **ULT-4, ULT-5, ULT-6, ULT-7, ULT-8, ULT-10, ULT-11, ULT-12, ULT-13, ULT-14, ULT-15, ULT-16, ULT-17, ULT-18, ULT-19, ULT-20, ULT-21** and **ULT-22** as disclosed herein. The invention also provides pharmaceutical compositions comprising one or more of the crystal forms according to the present invention. Pharmaceutical
15 formulations of the present invention contains one or more of the crystal form according to the present invention as active ingredient, optionally in a mixture with other crystal form(s).

The pharmaceutical formulations according to the invention, may further comprise, in addition to the forms **ULT-1, ULT-2, ULT-3,**
20 **ULT-4, ULT-5, ULT-6, ULT-7, ULT-8, ULT-10, ULT-11, ULT-12, ULT-13, ULT-14, ULT-15, ULT-16, ULT-17, ULT-18, ULT-19, ULT-20, ULT-21** and **ULT-22** additional pharmaceutical active ingredients, preferably Anti-HIV agents and more preferably Efavirenz and/or Emtricitabine.

25 In addition to the active ingredient(s), the pharmaceutical formulations of the present invention may contain one or more excipients. Excipients are added to the formulation for a variety of purposes.

Diluents increase the bulk of a solid pharmaceutical
30 composition, and may make a pharmaceutical dosage form containing the composition easier for the patient and caregiver to handle. Diluents for solid compositions include, for example, microcrystalline cellulose (e.g. Avicel(R)), micro fine cellulose, lactose, starch, pregelatinized starch, calcium carbonate, calcium sulfate, sugar,
35 dextrates, dextrin, dextrose, dibasic calcium phosphate dihydrate, tribasic calcium phosphate, kaolin, magnesium carbonate, magnesium oxide, maltodextrin, mannitol, polymethacrylates (e.g. Eudragit(R)), potassium chloride, powdered cellulose, sodium chloride, sorbitol and talc.

40 Solid pharmaceutical compositions that are compacted into a dosage form, such as a tablet, may include excipients whose functions include helping to bind the active ingredient and other excipients together after compression. Binders for solid pharmaceutical

5 compositions include acacia, alginic acid, carbomer (e.g. Carbopol),
carboxymethylcellulose sodium, dextrin, ethyl cellulose, gelatin,
guar gum, hydrogenated vegetable oil, hydroxyethyl cellulose,
hydroxypropyl cellulose (e.g. Klucel(R)), hydroxypropyl methyl
cellulose (e.g. Methocel(R)), liquid glucose, magnesium aluminum
10 silicate, maltodextrin, methylcellulose, polymethacrylates, povidone
(e.g. Kollidon(R), Plasdone(R)), pregelatinized starch, sodium
alginate and starch.

The dissolution rate of a compacted solid pharmaceutical
composition in the patient's stomach may be increased by the addition
15 of a disintegrant to the composition. Disintegrants include alginic
acid, carboxymethylcellulose calcium, carboxymethylcellulose sodium
(e.g. Ac-Di-Sol(R), Primellose(R)), colloidal silicon dioxide,
croscarmellose sodium, crospovidone (e.g. Kollidon(R),
Polyplasdone(R)), guar gum, magnesium aluminum silicate, methyl
20 cellulose, microcrystalline cellulose, polacrillin potassium, powdered
cellulose, pregelatinized starch, sodium alginate, sodium starch
glycolate (e.g. Explotab(R)) and starch.

Glidants can be added to improve the flowability of a non-
compacted solid composition and to improve the accuracy of dosing.
25 Excipients that may function as glidants include colloidal silicon
dioxide, magnesium trisilicate, powdered cellulose, starch, talc and
tribasic calcium phosphate.

When a dosage form such as a tablet is made by the compaction
30 of a powdered composition, the composition is subjected to pressure
from a punch and dye. Some excipients and active ingredients have a
tendency to adhere to the surfaces of the punch and dye, which can
cause the product to have pitting and other surface irregularities. A
lubricant can be added to the composition to reduce adhesion and ease
35 the release of the product from the dye. Lubricants include magnesium
stearate, calcium stearate, glyceryl monostearate, glyceryl
palmitostearate, hydrogenated castor oil, hydrogenated vegetable oil,
mineral oil, polyethylene glycol, sodium benzoate, sodium lauryl
sulfate, sodium stearyl fumarate, stearic acid, talc and zinc
40 stearate. Flavoring agents and flavor enhancers make the dosage form
more palatable to the patient. Common flavoring agents and flavor
enhancers for pharmaceutical products that may be included in the
composition of the present invention include maltol, vanillin, ethyl
vanillin, menthol, citric acid, fumaric acid, ethyl maltol and

5 tartaric acid. Solid and liquid compositions may also be dyed using
any pharmaceutically acceptable colorant to improve their appearance
and/or facilitate patient identification of the product and unit
dosage level.

10 In liquid pharmaceutical compositions of the present
invention, the crystalline forms according to the present invention
and any other solid excipients are suspended in a liquid carrier such
as water, vegetable oil, alcohol, polyethylene glycol, propylene
glycol or glycerin.

15 Liquid pharmaceutical compositions may contain emulsifying
agents to disperse uniformly throughout the composition an active
ingredient or other excipient that is not soluble in the liquid
carrier. Emulsifying agents that may be useful in liquid compositions
of the present invention include, for example, gelatin, egg yolk,
casein, cholesterol, acacia, tragacanth, chondrus, pectin, methyl
20 cellulose, carbomer, cetostearyl alcohol and cetyl alcohol.

Liquid pharmaceutical compositions of the present invention
may also contain a viscosity enhancing agent to improve the mouth-
feel of the product and/or coat the lining of the gastrointestinal
tract. Such agents include acacia, alginic acid bentonite, carbomer,
25 carboxymethylcellulose calcium or sodium, cetostearyl alcohol,
methylcellulose, ethylcellulose, gelatin guar gum, hydroxyethyl
cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose,
maltodextrin, polyvinyl alcohol, povidone, propylene carbonate,
propylene glycol alginate, sodium alginate, sodium starch glycolate,
30 starch tragacanth and xanthan gum.

Sweetening agents such as sorbitol, saccharin, sodium
saccharin, sucrose, aspartame, fructose, mannitol and invert sugar
may be added to improve the taste. Preservatives and chelating agents
such as alcohol, sodium benzoate, butylated hydroxyl toluene,
35 butylated hydroxyanisole and ethylenediamine tetraacetic acid may be
added at levels safe for ingestion to improve storage stability.
According to the present invention, a liquid composition may also
contain a buffer such as gluconic acid, lactic acid, citric acid or
acetic acid, sodium gluconate, sodium lactate, sodium citrate or
40 sodium acetate. Selection of excipients and the amounts used may be
readily determined by the formulation scientist based upon experience
and consideration of standard procedures and reference works in the
field.

5 For infections of the eye or other external tissues, e.g.
mouth and skin, the formulations are preferably applied as a topical
ointment or cream containing the active ingredient(s) in an amount
of, for example, 0.01 to 10% w/w (including active ingredient(s) in a
range between 0.1% and 5% in increments of 0.1% w/w such as 0.6% w/w,
10 0.7% w/w, etc), preferably 0.2 to 3% w/w and most preferably 0.5 to
2% w/w. When formulated in an ointment, the active ingredients may be
employed with either a paraffinic or a water-miscible ointment base.

Alternatively, the active ingredients may be formulated in a
cream with an oil-in-water cream base.

15 If desired, the aqueous phase of the cream base may include,
for example, at least 30% w/w of a polyhydric alcohol, i.e. an
alcohol having two or more hydroxyl groups such as propylene glycol,
butane 1,3-diol, mannitol, sorbitol, glycerol and polyethylene glycol
(including PEG 400) and mixtures thereof. The topical formulations
20 may desirably include a compound which enhances absorption or
penetration of the active ingredient through the skin or other
affected areas. Examples of such dermal penetration enhancers include
dimethyl sulphoxide and related analogs.

The oily phase of the emulsions of this invention may be
25 constituted from known ingredients in a known manner. While the phase
may comprise merely an emulsifier (otherwise known as an emulgent),
it desirably comprises a mixture of at least one emulsifier with a
fat or an oil or with both a fat and an oil. Preferably, a
hydrophilic emulsifier is included together with a lipophilic
30 emulsifier which acts as a stabiliser. It is also preferred to
include both an oil and a fat. Together, the emulsifier(s) with or
without stabiliser(s) make up the emulsifying wax, and the wax
together with the oil and fat make up the emulsifying ointment base
which forms the oily dispersed phase of the cream formulations.

35 Emulgents and emulsion stabilisers suitable for use in the
formulation of the present invention include Tween8 60, Spans 80,
cetostearyl alcohol, benzyl alcohol, myristyl alcohol, glyceryl
monostearate and sodium lauryl sulfate.

The choice of suitable oils or fats for the formulation is
40 based on achieving the desired cosmetic properties. Thus the cream
should preferably be a non-greasy, non-staining and washable product
with suitable consistency to avoid leakage from tubes or other
containers.

5 Straight or branched chain, mono- or dibasic alkyl esters such
as diisoadipate, isocetyl stearate, propylene glycol diester of
coconut fatty acids, isopropyl myristate, decyl oleate, isopropyl
palmitate, butyl stearate, 2-ethylhexyl palmitate or a blend of
10 branched chain esters known as Crodamol CAP may be used, the last
three being preferred esters. These may be used alone or in
combination depending on the properties required. Alternatively, high
melting point lipids such as white soft paraffin and/or liquid
paraffin or other mineral oils can be used.

15 Formulations suitable for topical administration to the eye
also include eye drops wherein the active ingredient is dissolved or
suspended in a suitable carrier, especially an aqueous solvent for
the active ingredient. The active ingredient is suitably present in
such formulations in a concentration of 0.01 to 20%, in some
embodiments 0.1 to 10%, and in others about 1.0% w/w.

20 Formulations suitable for topical administration in the mouth
include lozenges comprising the active ingredient in a flavored
basis, usually sucrose and acacia or tragacanth; pastilles comprising
the active ingredient in an inert basis such as gelatin and glycerin,
or sucrose and acacia; and mouthwashes comprising the active
25 ingredient in a suitable liquid carrier.

 Formulations for rectal administration may be presented as a
suppository with a suitable base comprising for example cocoa butter
or a salicylate.

30 Formulations suitable for nasal or inhalational administration
wherein the carrier is a solid include a powder having a particle
size for example in the range 1 to 500 microns (including particle
sizes in a range between 20 and 500 microns in increments of 5
microns such as 30 microns, 35 microns, etc). Suitable formulations
wherein the carrier is a liquid, for administration as for example a
35 nasal spray or as nasal drops, include aqueous or oily solutions of
the active ingredient.

 Formulations suitable for aerosol administration may be
prepared according to conventional methods and may be delivered with
other therapeutic agents. Inhalational therapy is readily
40 administered by metered dose inhalers.

 Formulations suitable for vaginal administration may be
presented as pessaries, tampons, creams, gels, pastes, foams or spray
formulations containing in addition to the active ingredient such
carriers as are known in the art to be appropriate.

5 The solid compositions of the present invention include
powders, granulates, aggregates and compacted compositions. The
dosages include dosages suitable for oral, buccal, rectal, parenteral
(including subcutaneous, intramuscular, and intravenous), inhalant
and ophthalmic administration. Although the most suitable
10 administration in any given case will depend on the nature and
severity of the condition being treated, the most preferred route of
the present invention is oral. The dosages may be conveniently
presented in unit dosage form and prepared by any of the methods
well-known in the pharmaceutical arts.

15 Dosage forms include solid dosage forms like tablets, powders,
capsules, suppositories, sachets, troches and lozenges, as well as
liquid syrups, suspensions and elixirs.

 The dosage form of the present invention may be a capsule
containing the composition, preferably a powdered or granulated solid
20 composition of the invention, within either a hard or soft shell. The
shell may be made from gelatin and optionally contain a plasticizer
such as glycerin and sorbitol, and an opacifying agent or colorant.

 The active ingredient and excipients may be formulated into
compositions and dosage forms according to methods known in the art.
25 A composition for tabletting or capsule filling may be prepared by
wet granulation. In wet granulation, some or all of the active
ingredients and excipients in powder form are blended and then
further mixed in the presence of a liquid, typically water, that
causes the powders to clump into granules. The granulate is screened
30 and/or milled, dried and then screened and/or milled to the desired
particle size. The granulate may then be tableted/compressed, or
other excipients may be added prior to tabletting, such as a glidant
and/or a lubricant.

 A tabletting composition may be prepared conventionally by dry
35 blending. For example, the blended composition of the actives and
excipients may be compacted into a slug or a sheet and then comminuted
into compacted granules. The compacted granules may subsequently be
compressed into a tablet.

 As an alternative to dry granulation, a blended composition
40 may be compressed directly into a compacted dosage form using direct
compression techniques. Direct compression produces a more uniform
tablet without granules. Excipients that are particularly well suited
for direct compression tableting include microcrystalline cellulose,
spray dried lactose, dicalcium phosphate dihydrate and colloidal

5 silica. The proper use of these and other excipients in direct compression tableting is known to those in the art with experience and skill in particular formulation challenges of direct compression tableting.

10 A capsule filling of the present invention may comprise any of the aforementioned blends and granulates that were described with reference to tableting, however, they are not subjected to a final tableting step.

Moreover, the crystalline forms according to the present invention can be formulated for administration to a mammal, preferably a human, via injection. The crystalline forms according to the present invention may be formulated, for example, as a viscous liquid solution or suspension, preferably a clear solution, for injection. The formulation may contain solvents. Among considerations for such solvent include the solvent's physical and chemical stability at various pH levels, viscosity (which would allow for syringeability), fluidity, boiling point, miscibility and purity. Suitable solvents include alcohol USP, benzyl alcohol NF, benzyl benzoate USP and Castor oil USP. Additional substances may be added to the formulation such as buffers, solubilizers, antioxidants, among others. Ansel *et al.* , Pharmaceutical Dosage Forms and Drug Delivery Systems, 7th Ed.

The present invention also provides pharmaceutical formulations comprising the crystalline form according to the present invention, optionally in combination with other polymorphic forms or co-crystals, to be used in a method of treatment of a mammal, preferably a human, in need thereof. A pharmaceutical composition of the present invention comprises the crystalline form **ULT-1**. The crystalline form according to the present invention may be used in a method of treatment of a mammal comprising administering to a mammal suffering from the ailments described herein before a therapeutically effective amount of such pharmaceutical composition. The invention further relates to the use of the crystalline form of the invention for the preparation of a medicament for the treatment of the ailments described herein before, in particular HIV.

40 Having described the invention with reference to certain preferred embodiments, other embodiments will become apparent to one skilled in the art from consideration of the specification. The invention is further defined by reference to the following examples describing in detail the preparation of the compounds of the present

5 invention. It will be apparent to those skilled in the art that many modifications, both to materials and methods, may be practiced without departing from the scope of the invention.

51
Examples

Experimental conditions

X-ray Powder Diffraction:

XRPD patterns were obtained using a T2 high-throughput XRPD set-up by Avantium technologies, The Netherlands. The plates were mounted on a Bruker GADDS diffractometer equipped with a Hi-Star area detector. The XRPD platform was calibrated using Silver Behenate for the long d-spacings and Corundum for the short d-spacings.

Data collection was carried out at room temperature using monochromatic CuK(alpha) radiation in the two-theta region between 1.5

° and 41.5 °. The diffraction pattern of each well is collected in two two-theta ranges ($1.5^\circ \leq 2\theta \leq 21.5^\circ$ for the first frame, and $19.5^\circ \leq 2\theta \leq 41.5^\circ$ for the second) with an exposure time of 120 s for each frame. One of ordinary skill in the art understands that experimental differences may arise due to differences in

instrumentation, sample preparation, or other factors. Typically XRPD data are collected with a variance of about 0.3 degrees two-theta, preferable about 0.2 degrees, more preferably 0.1 degrees, even more preferable 0.05 degrees. This has consequences for when X-ray peaks are considered overlapping.

Single-crystal X-ray diffraction

Suitable single crystals were selected and glued to a glass fibre, which was then mounted on an X-ray diffraction goniometer. X-ray diffraction data were collected for these crystals at a temperature of 120K and at room temperature, using a KappaCCD system and MoK α radiation, generated by a FR590 X-ray generator (Bruker Nonius, Delft, The Netherlands).

Unit-cell parameters and crystal structures were determined and refined using the software package MaXus.

Thermal analysis:

Melting properties were obtained from DSC thermograms, recorded with a heat flux DSC822e instrument (Mettler-Toledo GmbH, Switzerland). The DSC822e was calibrated for temperature and enthalpy with a small piece of indium (m.p. = 156.6°C; $\Delta H(f) = 28.45 \text{ J/g}$). Samples were sealed in standard 40 microliter aluminum pans and heated in the DSC from 25°C to 300°C, at a heating rate of 20°C/min. Dry N₂ gas, at

5 a flow rate of 50 ml/min, was used to purge the DSC equipment during measurement.

Mass loss due to solvent or water loss from the crystals was determined by TGA/SDTA. Monitoring of the sample weight, during heating in a TGA/SDTA851e instrument (Mettler-Toledo GmbH,

10 Switzerland), resulted in a weight vs. temperature curve. The TGA/SDTA851e was calibrated for temperature with indium and aluminium. Samples were weighed into 100 microliter aluminium crucibles and sealed. The seals were pin-holed and the crucibles heated in the TGA from 25°C to 300°C at a heating rate of 20°C/min.
15 Dry N₂ gas is used for purging. Melting point determinations based on DSC have a variability of +/- 2.0 degrees Celsius, preferably 1.0 degrees Celsius.

Raman spectroscopy:

20 The Raman spectra were collected with a Raman microscope mW (Kaiser Opticals Inc) at 0.96 cm⁻¹ resolution using a laser of 780 nm and a power output of 100.

Examples

25

Crystallisation of Tenofovir DF on microliter scale.

A small quantity, about 2-3 mg of the starting material was placed in a plate well. The starting material was stock-dosed in tetrahydrofuran/water (80/20 v/v) mixture. The solvent was removed by
30 evaporation under 20kPa for about 45-75 h and the starting material was dry. The crystallisation solvent or mixture of crystallisation solvents (50/50 v/v) was added in small amounts to the well containing the dry starting material at room temperature to a total volume of 40 microliter and a stock concentration of 50 or 80 mg/ml.

35 The solution was heated and maintained at 60°C for 30 minutes.

Following, controlled cooling was applied with a cooling rate of about 1°C/h or 50°C/h to a final temperature of 5°C or 20°C and remained at this temperature for 1, 48, 75, 117 or 139h.

Subsequently, the solvent was evaporated under pressure of 20 kPa at
40 RT for 48-120 h. The resulting residue was analysed by X-ray powder diffraction, DSC and TG-MS. The solvents employed are in Table I.

Crystallisation of Tenofovir DF on millilitre scale using hot filtration.

45

5 A small quantity, about 70-75 mg of the starting material was placed in a HPLC vial. The crystallisation solvent (or 50/50 v/v mixture of solvents) was added in small amounts to the vial containing the dry starting material at room temperature to a total volume of 200-1000 microliter. The solvents and conditions employed are in Table II.

10 Subsequently, the solutions were heated with a rate of 20 degrees Celsius to 60°C for 60 min and they were filtered at this temperature. The filtrated solutions were cooled with 1.1 or 50°C/h to a temperature of 3 or 20°C where they remained for 24h. Subsequently, the solvents were evaporated from the vial under 20 kPa pressure at 20-25°C for 15-200h (see table II, in the case of (R)-(-)-2-Octanol at 0,2 kPa for 500 h). The resulting residue was analysed by X-ray powder diffraction, DSC and TGA.

Crystallisation of Tenofovir DF on millilitre scale using anti-solvent addition.

20 The anti-solvent addition experiments were carried out following two different protocols. According to the first protocol (forward anti-solvent addition) for each solvent, a slurry was prepared at ambient temperature, which was equilibrated for about 17-19 hours before filtering into a vial. The anti-solvent was added, using a solvent:anti-solvent ratio of 1:1. This ratio was increased to 1:4 in those cases where no precipitation occurred, by subsequent anti-solvent additions. The time interval between the additions was 1h. The total volume of the anti-solvent was equal to that of the saturated solution.

30 For the second protocol (reverse anti-solvent addition), a slurry was prepared at ambient temperature, which was equilibrated for about 17-19 hours before filtering into a set of four vials. The content of each of these vials was added to a vial containing anti-solvent. The total volume of the four vials of saturated solutions was equal to that of the anti-solvent. The time interval between the additions was 1h.

35 Precipitates were recovered by centrifugation, and the solid products were dried and analyzed by XRPD. In the cases that no precipitation occurred the solutions were evaporated for 96-314 hrs at room temperature and the residues were analysed by XRPD.

See Table III for experimental details

5 Crystallisation of Tenofovir DF on millilitre scale using slurry
crystallisation.

About 50mg of the starting material was used to make a slurry with a solvent (see Table A). The slurries were stirred for the time
 10 interval of 2 and 10 days at RT or 35°C as shown in Table A. The materials were checked by XRPD in order to check for solid form changes.

Table A: Slurry experiments of Tenofovir DF

#	Solvent	Temperature (°C)	Time (days)	form	Time (days)	form
1	water	RT	2	ULT-9	10	ULT-9
2	water	35	2	ULT-9	10	ULT-9
3	Methanol	RT	2	ULT-20	10	ULT-20
4	Methanol	35	2	ULT-3	10	ULT-13+am
5	Acetonitrile	RT	2	SM	10	ULT-5
6	Acetonitrile	35	2	ULT-8	10	ULT-8
7	1,4-dioxane	RT	2	SM	10	SM
8	1,4-dioxane	35	2	ULT-8	10	ULT-8

SM = Starting Material, am = amorphous

15 Slurry experiments in water both at room temperature and at 35°C led to the conversion of the starting material to form ULT-9 after 2 days. An XRPD measurement of the materials in slurries after 10 days showed that the solid form was still form ULT-9.

Slurry experiments of the starting material in 1,4-dioxane and
 20 acetonitrile at RT did not lead to any solid form conversion after 2 and 10 days, while the same type of experiments performed at 35°C led to the conversion of the starting material to form ULT-8.

Slurry experiments of the starting material in methanol at room temperature led to form ULT-20 after 2 days while in the same
 25 experiment at 35°C ULT-3 was obtained. An XRPD measurement after 10 days of the materials in slurries showed that the solid form was still form ULT-20 in the case of the RT experiment while the material of the slurry at 35°C had been converted to form ULT-13 containing a large part of amorphous component.

30 Crystallisation of Tenofovir DF on milliliter scale using seeding
crystallisation.

5 Three types of seeding experiments were performed as described below:

Type 1

~~A slurry was made at RT using about 100mg of the starting material.~~
The slurry was filtered at RT and a small quantity of about 2mg of the corresponding seed was added. The solution remained at RT or 5°C
10 overnight. Subsequently the solution was evaporated and the solid material was checked by XRPD.

Type 2

The experiments were performed as described in the anti-solvent addition example with the following modification: immediately after
15 precipitation, a small quantity of about 2mg of the corresponding seed was added to the solution. The solution remained at RT or 5°C overnight. Subsequently the solution was evaporated and the solid material was checked by XRPD.

Type 3

20 A slurry was made at RT using about 100mg of the starting material. A small quantity of about 5 mg of the corresponding seed was added. The slurry was stirred for about 1h and there after it remained at RT for 2 days. Subsequently the solution was evaporated and the solid material was checked by XRPD.

25 The specific conditions and seeds used in each experiment are listed in Table B

**Table B. Seeding experiments performed using tenofovir form A. In all solvent mixtures the ration was 50/50. The anti-solvent addition was
30 reverse as described in the corresponding paragraph.**

Exp	solvent	anti solvent	type	Seed	Result
1	methanol/water		1	ULT-3	ULT-3
2	methanol/water		1	ULT-3	ULT-3
5	water		3	ULT-3	ULT-9
6	methanol/ 1,4-dioxane		1	ULT-8	ULT-8
7	methanol/ 1,4-dioxane		1	ULT-8	ULT-8
8	acetonitrile/ 1,4-dioxane		1	ULT-8	ULT-8

9	acetonitrile/ 1,4-dioxane		1	ULT-8	ULT-8
11	1,4-dioxane	butyl benzene	2	ULT-8	ULT-8
14	water		3	ULT-8	ULT-9
15	2-ethoxyethylacetate		1	ULT-9	ULT-9
16	2-ethoxyethylacetate		1	ULT-9	ULT-9
18	2-methyl-4-pentanol		1	ULT-9	ULT-9
19	water		3	ULT-9	ULT-9
20	tetrahydrofuran	amylether	2	ULT-9	ULT-9
22	tetrahydrofuran	tert-butyl methyl ether	2	ULT-9	ULT-9
23	tetrahydrofuran	tert-butyl methyl ether	2	ULT-9	ULT-9
24	cyclopentanone		1	ULT-11	ULT-8
25	cyclopentanone		1	ULT-11	ULT-8
32	water		3	ULT-11	ULT-9

5

From type 3 of seeding experiments it was shown that independently of the seed used in the water slurry, the outcome was form ULT-9.

Form ULT 22

- 10 Form ULT-22 was obtained by slow evaporation of saturated solution of tenofovir DF in methanol/water (50/50) at room temperature. During cooling of the saturated solution, solid material crystallized out. The solution was heated anew until dissolution of the solid material and as diluted to half the concentration. The solution was slowly
- 15 cooled to room temperature and aged for several days.

1. Crystalline tenofovir DF Form **ULT-4**, **ULT-5**, **ULT-6**, **ULT-7**, **ULT-8**, **ULT-10**, **ULT-11**, **ULT-12**, **ULT-13**, **ULT-14**, **ULT-15**, **ULT-16**, **ULT-17**, **ULT-18**, **ULT-19**, **ULT-20**, **ULT-21** and **ULT-22**.

10

2. Crystalline tenofovir DF Form **ULT-4**, characterised by one or more of:

- DSC with an onset at 96.2°C and a characterising peak at 108.9°C.

15

- DSC with an onset at 111.2°C and a characterising peak at 114.3°C.

3. Crystalline tenofovir DF Form **ULT-4** according to claim 1, characterised by one or more of:

20

- a XRPD pattern substantially as set out in Fig 1A;
- a DSC substantially as set out in Fig 1B;
- a TGA substantially as set out in Fig 1C.

4. Method for the preparation of the crystalline form **ULT-4** of tenofovir DF comprising the steps of

25

- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-4** by evaporation of the solvent; and/or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-4** by cooling and/or evaporation crystallization of a saturated solution; and /or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-4** by anti-solvent addition as in Table III; and/or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof and crystallising tenofovir DF Form **ULT-4** by slurry crystallisation and/or seed crystallisation.

30

35

40

5. Crystalline tenofovir DF Form **ULT-5**, characterised by an XRPD pattern substantially as set out in Fig 2A.

5

6. Method for the preparation of the crystalline form **ULT-5** of tenofovir DF comprising the steps of

10

- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-5** by evaporation of the solvent; and/or

- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-5** by cooling and/or evaporation crystallization of a saturated solution; and /or

15

- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-5** by anti-solvent addition as in Table III; and/or

20

- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof and crystallising tenofovir DF Form **ULT-5** by slurry crystallisation and/or seed crystallisation.

7. Crystalline tenofovir DF Form **ULT-6** characterised by an XRPD pattern substantially as set out in Fig 3A;

25

8. Method for the preparation of the crystalline form **ULT-6** of tenofovir DF comprising the steps of

30

- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-6** by evaporation of the solvent; and/or

- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-6** by cooling and/or evaporation crystallization of a saturated solution; and /or

35

- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-6** by anti-solvent addition as in Table III

40

- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof and crystallising tenofovir DF Form **ULT-6** by slurry crystallisation and/or seed crystallisation.

- 5 9. Crystalline tenofovir DF⁵⁹ Form **ULT-7**, characterised by one or more of:
- at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six
- 10 X-ray powder diffraction peaks selected from the group consisting of 5.0, 6.9, 8.9, 9.6, 10.2, 11.3, 13.2, 14.1, 17.8, 18.7, 20.0, 21.8, 23.8, 25.3, 27.8, 30.5, degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta,
- 15 most preferably +/- 0.05 degrees two-theta;
- DSC with an onset at 98.4°C and a characterising peak at 108.4°C.
- 20 10. Crystalline tenofovir DF Form **ULT-7** according to claim 1, characterised by one or more of:
- a XRPD pattern substantially as set out in Table 4 and/or Fig 4A;
 - a DSC substantially as set out in Fig 4B;
 - a TGA substantially as set out in Fig 4C.
- 25 11. Method for the preparation of the crystalline form **ULT-7** of tenofovir DF comprising the steps of
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir
- 30 DF Form **ULT-7** by evaporation of the solvent; and/or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-7** by cooling and/or evaporation crystallization of a saturated solution; and /or
- 35 -
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-7** by anti-solvent addition as in Table III; and/or
 - dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof and crystallising tenofovir DF Form **ULT-7** by slurry crystallisation and/or seed crystallisation.
- 40

- 5 12. Crystalline tenofovir DF Form **ULT-8**, characterised by one
or more of:
- at least one, preferably at least two, more preferably at
least three, even more preferably at least four,
particularly preferred at least five and most preferred six
10 X-ray powder diffraction peaks selected from the group
consisting of 5.0, 10.3, 13.4, 14.7, 15.7, 17.3, 18.4,
19.1, 20.7, 21.2, 25.2 degrees two-theta +/- 0.3 degrees
two-theta, preferably +/- 0.2 degrees two-theta, more
preferably +/- 0.1 degrees two-theta, most preferably +/-
15 0.05 degrees two-theta;
 - DSC with an onset at 104.8°C and a characterising peak at
113.0°C.
- 20 13. Crystalline tenofovir DF Form **ULT-8** according to claim 1,
characterised by one or more of:
- a XRPD pattern substantially as set out in Table 5 and/or
Fig. 5A;
 - a DSC substantially as set out in Fig 5B;
 - a TGA substantially as set out in Fig 5C.
- 25 14. Method for the preparation of the crystalline form **ULT-8** of
tenofovir DF comprising the steps of
- dissolving or mixing tenofovir DF in a suitable solvent or
mixture thereof as in Table I and crystallising tenofovir
30 DF Form **ULT-8** by evaporation of the solvent; and/or
 - dissolving or mixing tenofovir DF in a suitable solvent or
mixture thereof as in Table II and crystallising tenofovir
DF Form **ULT-8** by cooling and/or evaporation crystallization
of a saturated solution; and /or
 - 35 - dissolving or mixing tenofovir DF in a suitable solvent or
mixture thereof as in Table III and crystallising tenofovir
DF Form **ULT-8** by anti-solvent addition as in Table III
 - dissolving or mixing tenofovir DF in a suitable solvent or
mixture thereof and crystallising tenofovir DF Form **ULT-8**
40 by slurry crystallisation and/or seed crystallisation.

- 5 15. Crystalline tenofovir DF Form **ULT-10**, characterised by one or more of:
- at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six
- 10 X-ray powder diffraction peaks selected from the group consisting of 5.0, 7.0, 10.6, 11.8, 12.7, 13.5, 15.2, 16.3, 17.3, 18.8, 20.7, 21.3, 22.2, 25.3, 27.3, degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta,
- 15 theta, most preferably +/- 0.05 degrees two-theta.
16. Crystalline tenofovir DF Form **ULT-10** according to claim 1, characterised by an XRPD pattern substantially as set out in Table 7 and/or Fig 7A.
- 20 17. Method for the preparation of the crystalline form **ULT-10** of tenofovir DF comprising the steps of
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir
- 25 DF Form **ULT-10** by evaporation of the solvent; and/or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir
- 30 DF Form **ULT-10** by cooling and/or evaporation crystallization of a saturated solution; and /or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir
- 35 DF Form **ULT-10** by anti-solvent addition as in Table III; and/or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof and crystallising tenofovir DF Form **ULT-10**
- by slurry crystallisation and/or seed crystallisation.
18. Crystalline tenofovir DF Form **ULT-11**, characterised by one or more of:
- at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six
- 40 X-ray powder diffraction peaks selected from the group

- 5 consisting of 5.0, 7.0,⁶²9.5, 10.6, 11.7, 13.5, 16.0, 17.4, 18.8, 20.4, 21.2, 22.0, 25.5 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta;
- 10 - DSC with an onset at 104.5°C and a characterising peak at 112.8°C.
19. Crystalline tenofovir DF Form **ULT-11** according to claim 1, characterised by one or more of:
- 15 - a XRPD pattern substantially as set out in Table 8 and/or Fig 8A;
- a DSC substantially as set out in Fig 8B;
- a TGA substantially as set out in Fig 8C.
- 20 20. Method for the preparation of the crystalline form **ULT-11** of tenofovir DF comprising the steps of
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-11** by evaporation of the solvent; and/or
- 25 - dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-11** by cooling and/or evaporation crystallization of a saturated solution; and /or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir
- 30 DF Form **ULT-11** by anti-solvent addition as in Table III; and/or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof and crystallising tenofovir DF Form **ULT-11**
- 35 by slurry crystallisation and/or seed crystallisation.
21. Crystalline tenofovir DF Form **ULT-12**, characterised by one or more of:
- at least one, preferably at least two, more preferably at least three, even more preferably at least four,
- 40 particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group

- 5 consisting of 4.2, 5.2,⁶³ 9.5, 14.5, 16.7, 18.6, 19.2, 20.2, 11.1, 13.4, 17.3, 21.2, 25.4 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta;
- 10 - DSC with an onset at 90.0°C and a characterising peak at 100.4°C.
22. Crystalline tenofovir DF Form **ULT-12** according to claim 1, characterised by one or more of:
- 15 - a XRPD pattern substantially as set out in Table 9 and/or Fig 9A;
- a DSC substantially as set out in Fig 9B;
- a TGA substantially as set out in Fig 9C.
- 20 23. Method for the preparation of the crystalline form **ULT-12** of tenofovir DF comprising the steps of
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-12** by evaporation of the solvent; and/or
- 25 - dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-12** by cooling and/or evaporation crystallization of a saturated solution; and /or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir
- 30 DF Form **ULT-12** by anti-solvent addition as in Table III; and/or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof and crystallising tenofovir DF Form **ULT-12**
- 35 by slurry crystallisation and/or seed crystallisation.
24. Crystalline tenofovir DF Form **ULT-13**, characterised by one or more of:
- at least one, preferably at least two, more preferably at least three, even more preferably at least four,
- 40 particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group

5 consisting of 4.7, 5.6,⁶⁴9.1, 10.4, 13.3, 14.8, 16.0, 16.0, 19.4, 21.4, 23.7, 28.6 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta.

10

25. Crystalline tenofovir DF Form **ULT-13** according to claim 1, characterised by an XRPD pattern substantially as set out in Table 10 and/or Fig 10A;

15

26. Method for the preparation of the crystalline form **ULT-13** of tenofovir DF comprising the steps of

20

- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-13** by evaporation of the solvent; and/or

- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-13** by cooling and/or evaporation crystallization of a saturated solution; and /or

25

- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-13** by anti-solvent addition as in Table III; and/or

30

- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof and crystallising tenofovir DF Form **ULT-13** by slurry crystallisation and/or seed crystallisation.

27. Crystalline tenofovir DF Form **ULT-14**, characterised by one or more of:

35

- at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group consisting of 4.7, 10.3, 18.4, 20.6, 21.5 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta;

40

5 28. Crystalline tenofovir ⁶⁵DF Form **ULT-14** according to claim 1, characterised by an XRPD pattern substantially as set out in Table 11 and/or Fig 11A.

10 29. Method for the preparation of the crystalline form **ULT-14** of tenofovir DF comprising the steps of

- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-14** by evaporation of the solvent; and/or
- 15 - dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-14** by cooling and/or evaporation crystallization of a saturated solution; and /or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir
- 20 DF Form **ULT-14** by anti-solvent addition as in Table III; and/or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof and crystallising tenofovir DF Form **ULT-14** by slurry crystallisation and/or seed crystallisation.

25

30. Crystalline tenofovir DF Form **ULT-15**, characterised by one or more of:

- at least one, preferably at least two, more preferably at least three, even more preferably at least four,
- 30 particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group consisting of 4.7, 5.2, 9.4, 10.5, 13.2, 17.1, 18.3, 21.3, 24.4 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/-
- 35 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta;
- DSC with an onset at 104.8°C and a characterising peak at 111.8°C.

40

31. Crystalline tenofovir DF Form **ULT-15** according to claim 1, characterised by one or more of:

- a XRPD pattern substantially as set out in Table 12 and/or Fig 12A;

- 5 - a DSC substantially as set out in Fig 12B;
 - a TGA substantially as set out in Fig 12C.

32. Method for the preparation of the crystalline form **ULT-15** of tenofovir DF comprising the steps of

- 10 - dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-15** by evaporation of the solvent; and/or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir
- 15 DF Form **ULT-15** by cooling and/or evaporation crystallization of a saturated solution; and /or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir
- DF Form **ULT-15** by anti-solvent addition as in Table III;
- 20 and/or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof and crystallising tenofovir DF Form **ULT-15** by slurry crystallisation and/or seed crystallisation.

25 33. Crystalline tenofovir DF Form **ULT-16**, characterised by one or more of:

- at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six
- 30 X-ray powder diffraction peaks selected from the group consisting of 4.7, 10.3, 13.4, 15.4, 18.5, 20.6, 21.5, 23.5 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta;

35

34. Crystalline tenofovir DF Form **ULT-16** according to claim 1, characterised by an XRPD pattern substantially as set out in Table 13 and/or Fig 13A;

40 35. Method for the preparation of the crystalline form **ULT-16** of tenofovir DF comprising the steps of

- 5 - dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-16** by evaporation of the solvent; and/or
- 10 - dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-16** by cooling and/or evaporation crystallization of a saturated solution; and /or
- 15 - dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-16** by anti-solvent addition as in Table III; and/or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof and crystallising tenofovir DF Form **ULT-16** by slurry crystallisation and/or seed crystallisation.

20 36. Crystalline tenofovir DF Form **ULT-17**, characterised by one or more of:

- 25 - at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group consisting of 4.8, 10.2, 10.8, 11.8, 13.3, 15.6, 17.0, 18.0, 18.8, 20.5, 21.5, 23.2, 24.3 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta;
- 30 - Crystalline tenofovir DF Form **ULT-17** according to claim 1, characterised by an XRPD pattern substantially as set out in Table 14 and/or Fig 14A.

35

37. Method for the preparation of the crystalline form **ULT-17** of tenofovir DF comprising the steps of

- 40 - dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-17** by evaporation of the solvent; and/or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir

- 5 DF Form **ULT-17** by cooling and/or evaporation
crystallization of a saturated solution; and /or
- dissolving or mixing tenofovir DF in a suitable solvent or
mixture thereof as in Table III and crystallising tenofovir
DF Form **ULT-17** by anti-solvent addition as in Table III;
 - 10 and/or
 - dissolving or mixing tenofovir DF in a suitable solvent or
mixture thereof and crystallising tenofovir DF Form **ULT-17**
by slurry crystallisation and/or seed crystallisation.
- 15 38. Crystalline tenofovir DF Form **ULT-18**, characterised by one
or more of:
- at least one, preferably two X-ray powder diffraction peaks
selected from the group consisting of 4.3 and 10.3 degrees
two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2
20 degrees two-theta, more preferably +/- 0.1 degrees two-
theta, most preferably +/- 0.05 degrees two-theta;
39. Crystalline tenofovir DF Form **ULT-18** according to claim 1,
characterised by one or more of:
- 25 - a XRPD pattern substantially as set out in Table 15 and/or
Fig 15A.
40. Method for the preparation of the crystalline form **ULT-18**
of tenofovir DF comprising the steps of
- 30 - dissolving or mixing tenofovir DF in a suitable solvent or
mixture thereof as in Table I and crystallising tenofovir
DF Form **ULT-18** by evaporation of the solvent; and/or
 - dissolving or mixing tenofovir DF in a suitable solvent or
mixture thereof as in Table II and crystallising tenofovir
35 DF Form **ULT-18** by cooling and/or evaporation
crystallization of a saturated solution; and /or
 - dissolving or mixing tenofovir DF in a suitable solvent or
mixture thereof as in Table III and crystallising tenofovir
DF Form **ULT-18** by anti-solvent addition as in Table III;
 - 40 and/or

- 5 - dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof and crystallising tenofovir DF Form **ULT-18** by slurry crystallisation and/or seed crystallisation.

10 41. Crystalline tenofovir DF Form **ULT-19**, characterised by one or more of:

- at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six X-ray powder diffraction peaks selected from the group
15 consisting of 5.3, 9.7, 10.5, 13.3, 17.1, 21.4, 30.5 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta, most preferably +/- 0.05 degrees two-theta;

20 42. Crystalline tenofovir DF Form **ULT-19** according to claim 1, characterised by one or more of:

- a XRPD pattern substantially as set out in Table 16 and/or Fig 16A;
 - a TGA substantially as set out in Fig 16C.

25

43. Method for the preparation of the crystalline form **ULT-19** of tenofovir DF comprising the steps of

- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir
30 DF Form **ULT-19** by evaporation of the solvent; and/or
 - dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir DF Form **ULT-19** by cooling and/or evaporation crystallization of a saturated solution; and /or
35 - dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-19** by anti-solvent addition as in Table III; and/or
 - dissolving or mixing tenofovir DF in a suitable solvent or
40 mixture thereof and crystallising tenofovir DF Form **ULT-19** by slurry crystallisation and/or seed crystallisation.

- 5 44. Crystalline tenofovir DF Form **ULT-20**, characterised by one or more of:
- at least one, preferably at least two, more preferably at least three, even more preferably at least four, particularly preferred at least five and most preferred six
- 10 X-ray powder diffraction peaks selected from the group consisting of 5.1, 9.0, 10.4, 11.3, 13.3, 17.6, 18.7, 19.6, 20.3, 21.3, 23.7, 24.4, 25.6, 26.5, 27.6, 29.4, 30.8 degrees two-theta +/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-theta,
- 15 theta, most preferably +/- 0.05 degrees two-theta;
45. Crystalline tenofovir DF Form **ULT-20** according to claim 1, characterised by one or more of:
- a XRPD pattern substantially as set out in Table 17 and/or
- 20 Fig 17A;
- a TGA substantially as set out in Fig 17C.
46. Method for the preparation of the crystalline form **ULT-20** of tenofovir DF comprising the steps of
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table I and crystallising tenofovir DF Form **ULT-20** by evaporation of the solvent; and/or
 - dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table II and crystallising tenofovir
- 30 DF Form **ULT-20** by cooling and/or evaporation crystallization of a saturated solution; and /or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof as in Table III and crystallising tenofovir DF Form **ULT-20** by anti-solvent addition as in Table III;
- 35 and/or
- dissolving or mixing tenofovir DF in a suitable solvent or mixture thereof and crystallising tenofovir DF Form **ULT-20** by slurry crystallisation and/or seed crystallisation.
- 40 47. Crystalline tenofovir DF Form **ULT-21**, characterised by one or more of:
- at least one, preferably at least two, more preferably at least three, even more preferably at least four,

5 particularly preferred ⁷¹at least five and most preferred six
X-ray powder diffraction peaks selected from the group
consisting of 5.1, 9.0, 10.4, 11.3, 13.3, 17.6, 18.7, 19.6,
20.3, 21.3, 23.7, 24.4, 25.6, 26.5, 27.6, 29.4, 30.8
degrees two-theta +/- 0.3 degrees two-theta, preferably +/-
10 0.2 degrees two-theta, more preferably +/- 0.1 degrees two-
theta, most preferably +/- 0.05 degrees two-theta;

48. Crystalline tenofovir DF Form **ULT-21** according to claim 1,
characterised by a XRPD pattern substantially as set out in
15 Table 18 and/or Fig 18A.

49. Method for the preparation of the crystalline form **ULT-21**
of tenofovir DF comprising the steps of

- 20 - dissolving or mixing tenofovir DF in a suitable solvent or
mixture thereof as in Table I and crystallising tenofovir
DF Form **ULT-21** by evaporation of the solvent; and/or
- dissolving or mixing tenofovir DF in a suitable solvent or
mixture thereof as in Table II and crystallising tenofovir
DF Form **ULT-21** by cooling and/or evaporation
25 crystallization of a saturated solution; and /or
- dissolving or mixing tenofovir DF in a suitable solvent or
mixture thereof as in Table III and crystallising tenofovir
DF Form **ULT-21** by anti-solvent addition as in Table III;
and/or
- 30 - dissolving or mixing tenofovir DF in a suitable solvent or
mixture thereof and crystallising tenofovir DF Form **ULT-21**
by slurry crystallisation and/or seed crystallisation.

50. Crystalline tenofovir DF Form **ULT-22**, characterised by one
35 or more of:

- at least one, preferably at least two, more preferably at
least three, even more preferably at least four,
particularly preferred at least five and most preferred six
X-ray powder diffraction peaks selected from the group
40 consisting of of 5.4, 8.9, 9.3, 9.9, 10.4, 13.3, 17.6,
19.2, 21.2, 21.8, 23.0, 23.5, 25.7, 26.3 degrees two-theta
+/- 0.3 degrees two-theta, preferably +/- 0.2 degrees two-

5 theta, more preferably ± 0.1 degrees two-theta, most
preferably ± 0.05 degrees two-theta;

10 51. Crystalline tenofovir DF Form **ULT-21** according to claim 1,
characterised by a XRPD pattern substantially as set out in
Table 19 and/or Fig 19A.

15 52. Method for the preparation of the crystalline form **ULT-22**
of tenofovir DF comprising the steps of

- dissolving or mixing tenofovir DF in a suitable solvent or
mixture thereof as in Table I and crystallising tenofovir
DF Form **ULT-22** by evaporation of the solvent; and/or
- dissolving or mixing tenofovir DF in a suitable solvent or
mixture thereof as in Table II and crystallising tenofovir
DF Form **ULT-22** by cooling and/or evaporation
20 crystallization of a saturated solution; and /or
- dissolving or mixing tenofovir DF in a suitable solvent or
mixture thereof as in Table III and crystallising tenofovir
DF Form **ULT-22** by anti-solvent addition as in Table III;
and/or
- 25 - dissolving or mixing tenofovir DF in a suitable solvent or
mixture thereof and crystallising tenofovir DF Form **ULT-22**
by slurry crystallisation and/or seed crystallisation.

30 53. Pharmaceutical formulation comprising one or more
crystalline forms of tenofovir FD selected from the group
consisting of **ULT-4, ULT-5, ULT-6, ULT-7, ULT-8, ULT-10, ULT-11,**
ULT-12, ULT-13, ULT-14, ULT-15, ULT-16, ULT-17, ULT-18, ULT-19,
ULT-20, ULT-21 and ULT-22.

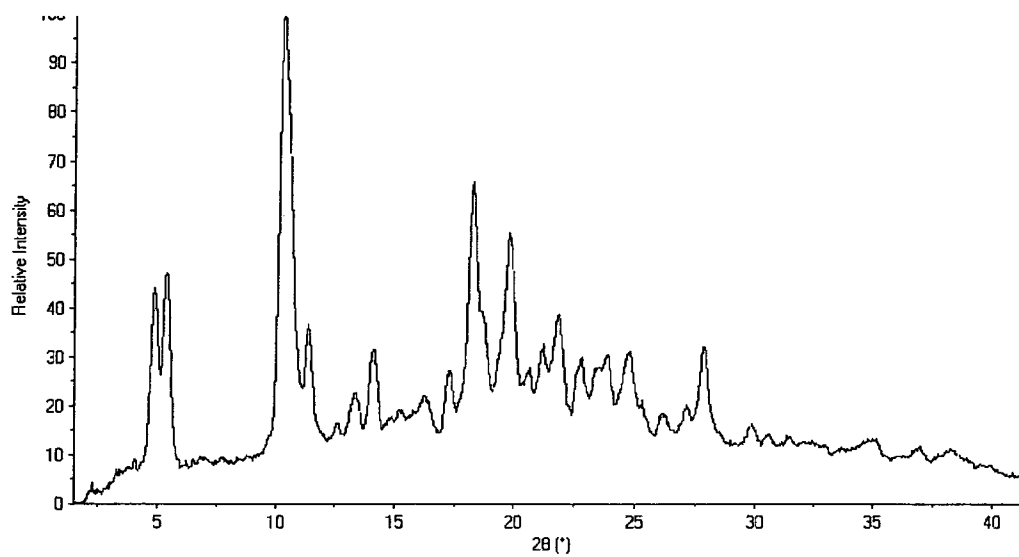
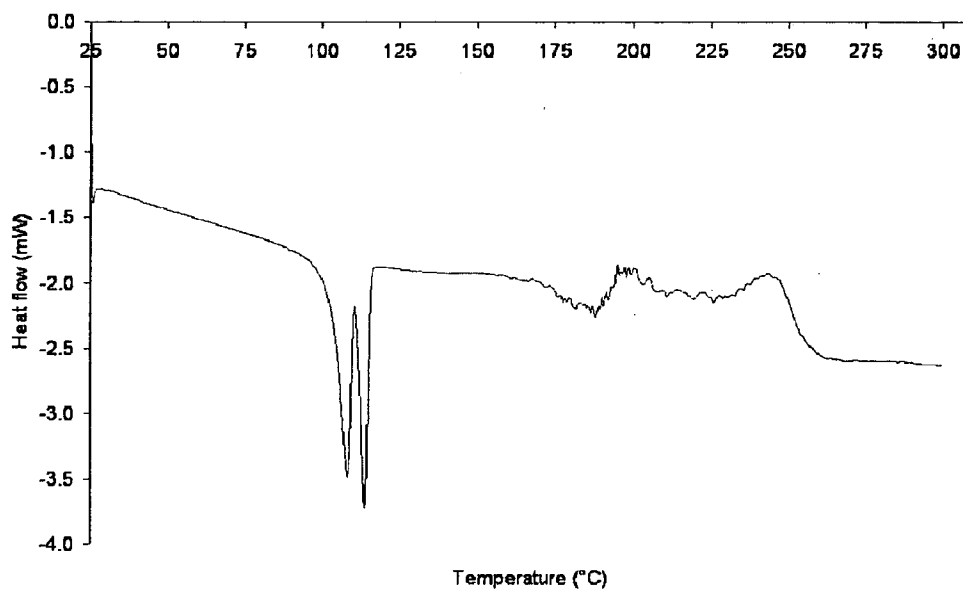
35 54. Use of one or more selected from the group consisting of
ULT-4, ULT-5, ULT-6, ULT-7, ULT-8, ULT-10, ULT-11, ULT-12, ULT-
13, ULT-14, ULT-15, ULT-16, ULT-17, ULT-18, ULT-19, ULT-20, ULT-
21 and ULT-22 as a medicament.

40 55. Use of one or more selected from the group consisting of
ULT-4, ULT-5, ULT-6, ULT-7, ULT-8, ULT-10, ULT-11, ULT-12, ULT-
13, ULT-14, ULT-15, ULT-16, ULT-17, ULT-18, ULT-19, ULT-20, ULT-

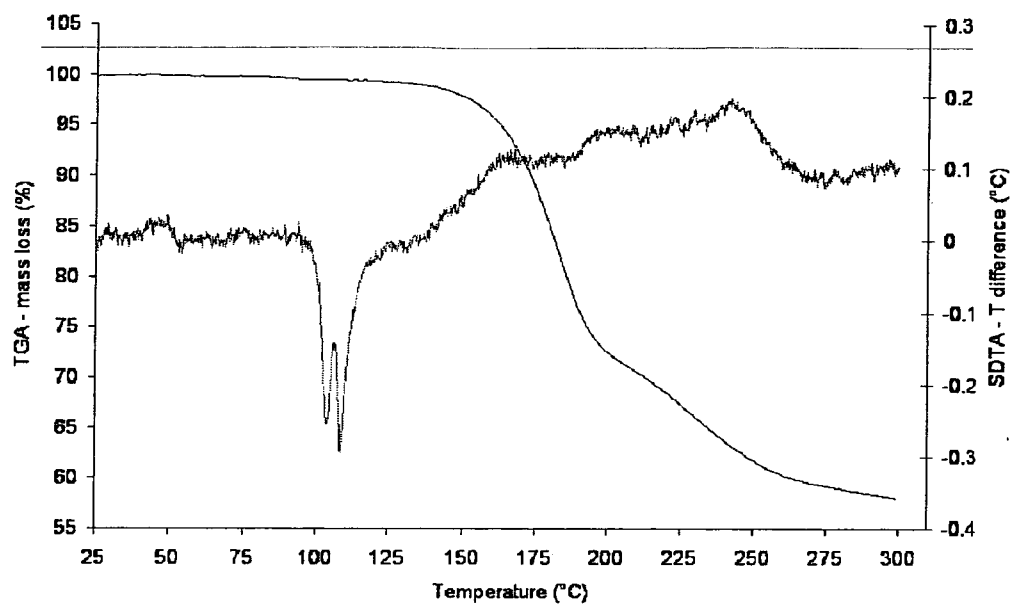
5 21 and **ULT-22** in the preparation⁷³ of a medicament for the treatment of HIV.

56. Use of one or more selected from the group consisting of
10 **ULT-4, ULT-5, ULT-6, ULT-7, ULT-8, ULT-10, ULT-11, ULT-12, ULT-13, ULT-14, ULT-15, ULT-16, ULT-17, ULT-18, ULT-19, ULT-20, ULT-21** and **ULT-22** in the treatment of HIV.

57. Use of one or more selected from the group consisting of
15 **ULT-4, ULT-5, ULT-6, ULT-7, ULT-8, ULT-10, ULT-11, ULT-12, ULT-13, ULT-14, ULT-15, ULT-16, ULT-17, ULT-18, ULT-19, ULT-20, ULT-21** and **ULT-22** in combination with another pharmaceutical ingredient, preferably an anti HIV agent, preferably Efavirenz and/or Emtricitabine

FIG 1A Tenofovir DF **ULT-4**FIG 1B Tenofovir DF **ULT-4**

H02_K4
DSC (10°C/min)
Onset 1: 96.2°C
Endotherm 1: 108.9°C
Onset 2: 111.2°C
Endotherm 1: 114.3°C

FIG 1C Tenofovir DF **ULT-4**

H02_C1
TGA (10°C/min)
Mass loss <1.2% for T<140°C

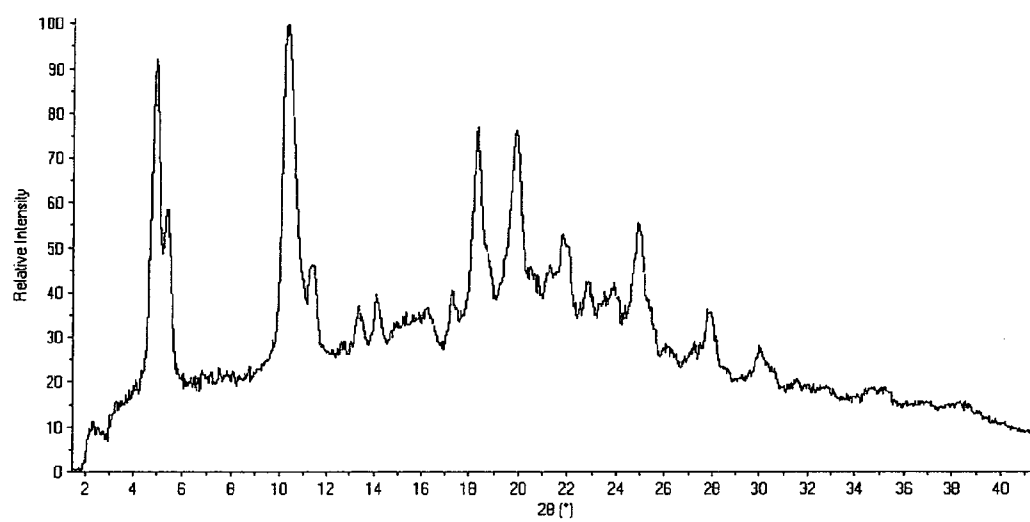
FIG 2A Tenofovir DF **ULT-5**

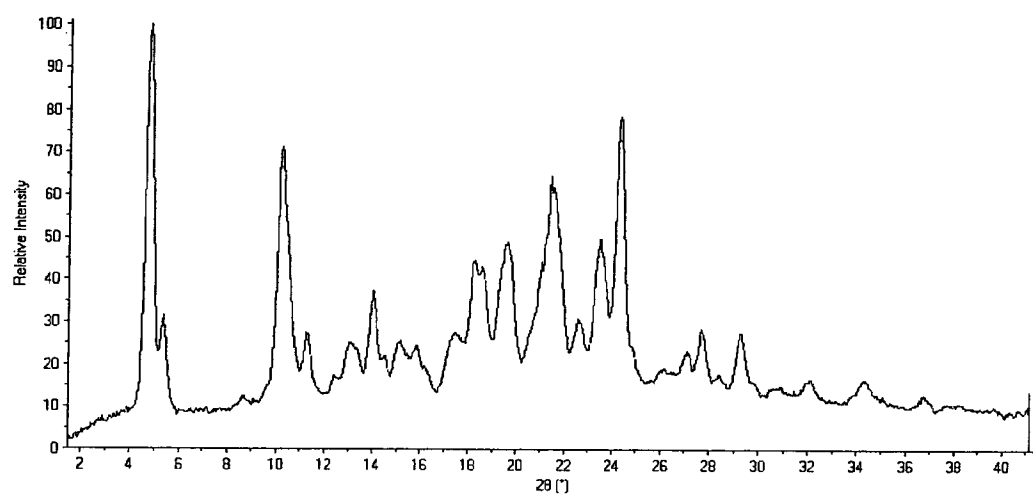
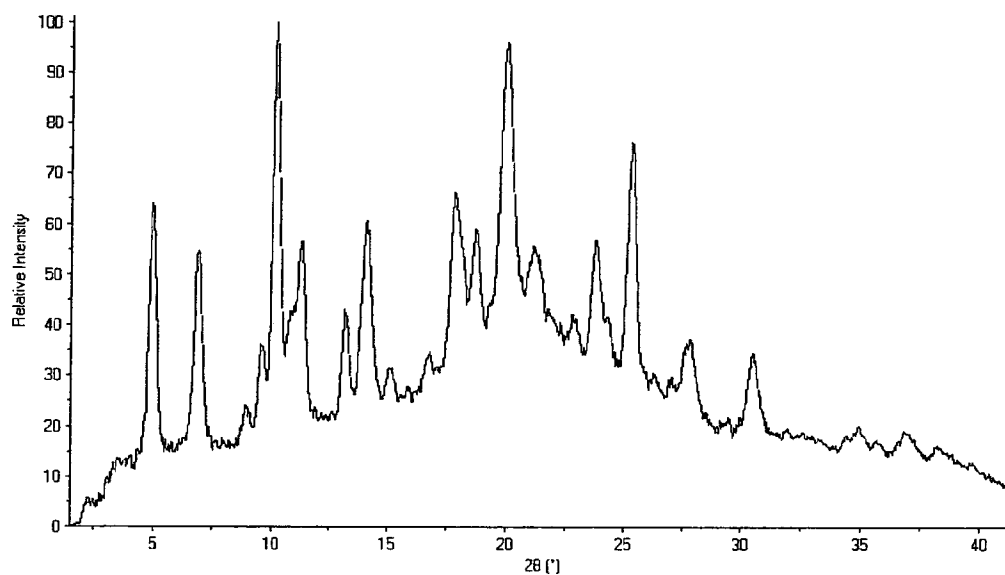
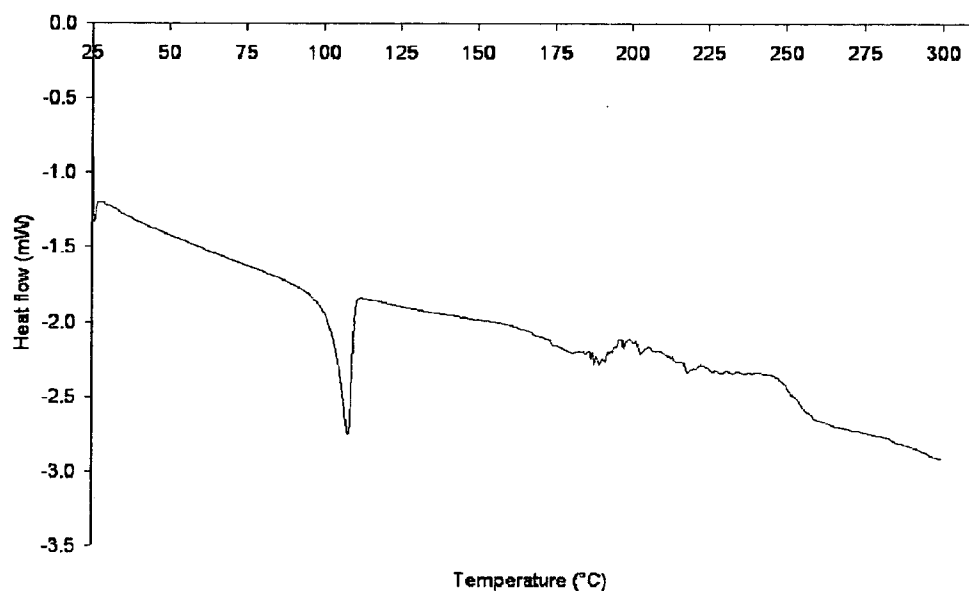
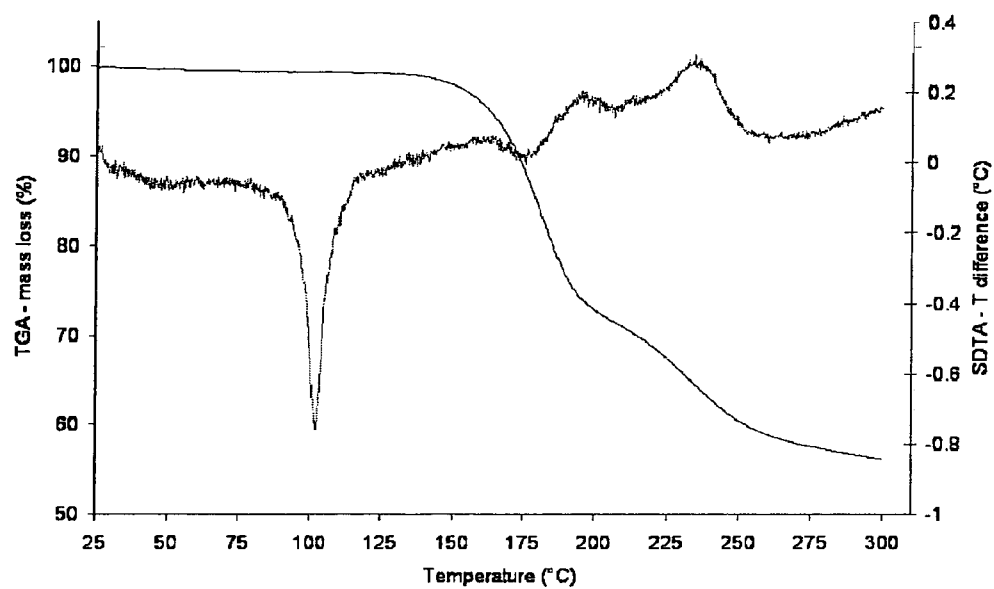
FIG 3A Tenofovir DF **ULT-6**

FIG 4A Tenofovir DF **ULT-7**FIG 4B Tenofovir DF **ULT-7**

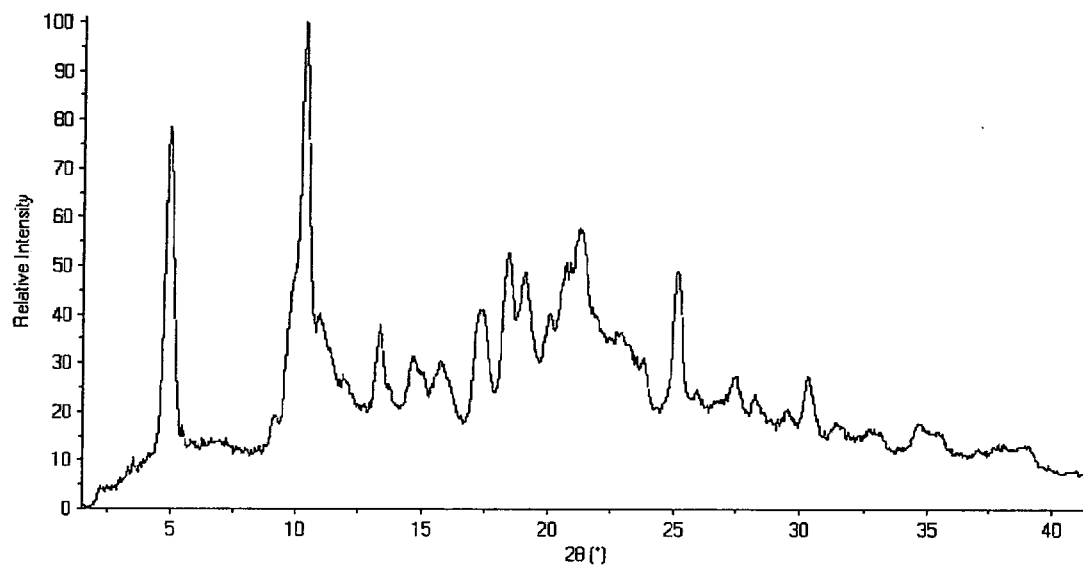
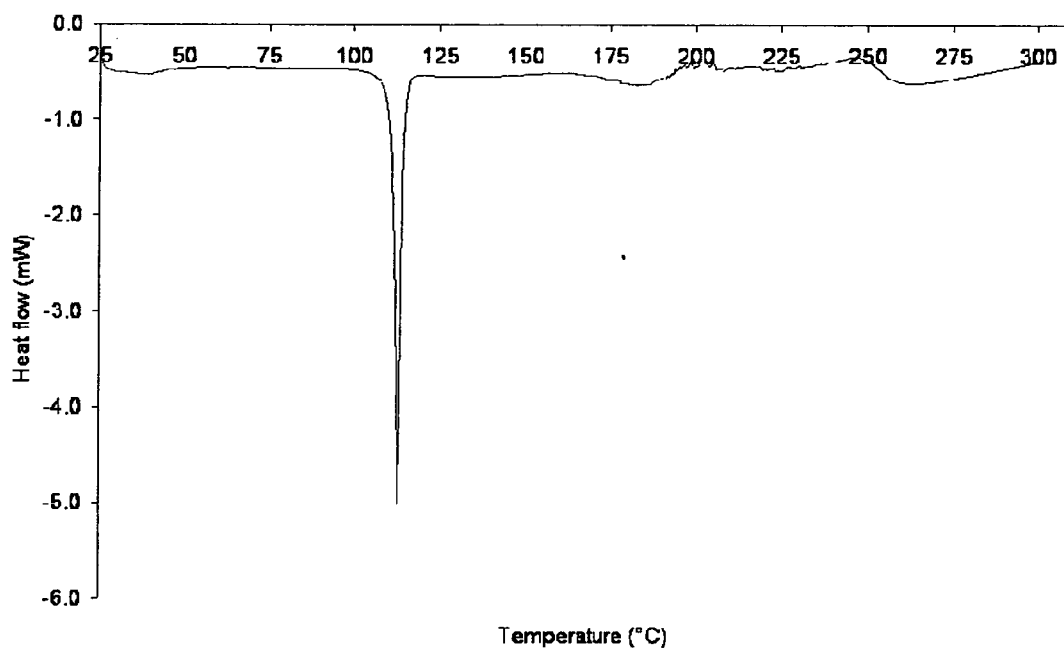
H02_F4
DSC (10°C/min)
Onset 1: 98.4°C
Endotherm 1: 108.4°C

FIG 4C Tenofovir DF **ULT-7**

H02_B4

TGA (10°C/min)

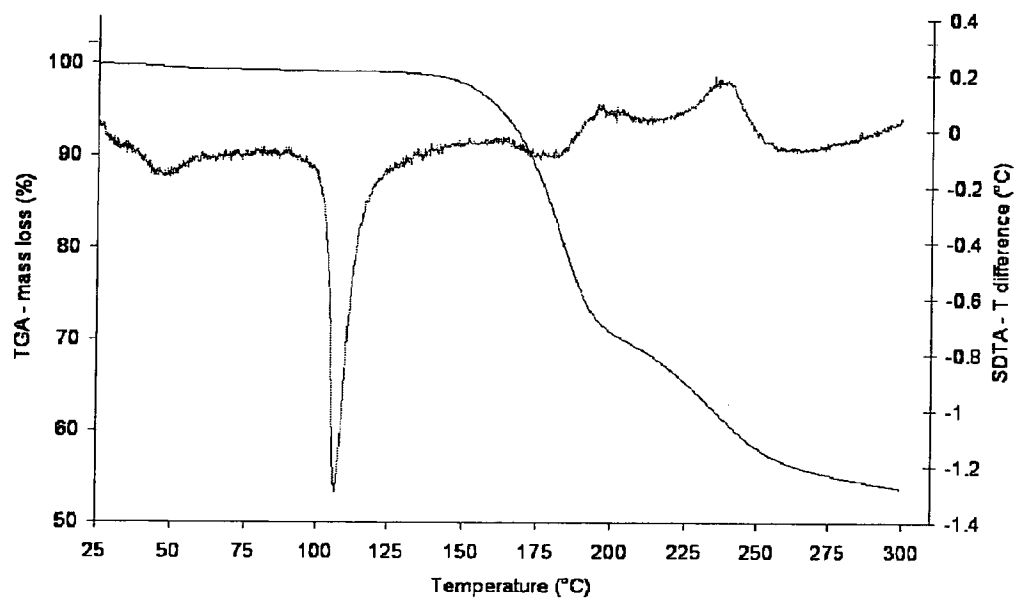
Mass loss <1% for T<130°C

FIG 5A Tenofovir DF **ULT-8**FIG 5B Tenofovir DF **ULT-8**

DSC (10°C/min)

Onset 1: 104.8°C

Endotherm 1: 113.0°C

FIG 5C Tenofovir DF **ULT-8**

TGA (10°C/min)

Mass loss <1% for T<120°C

anhydrous

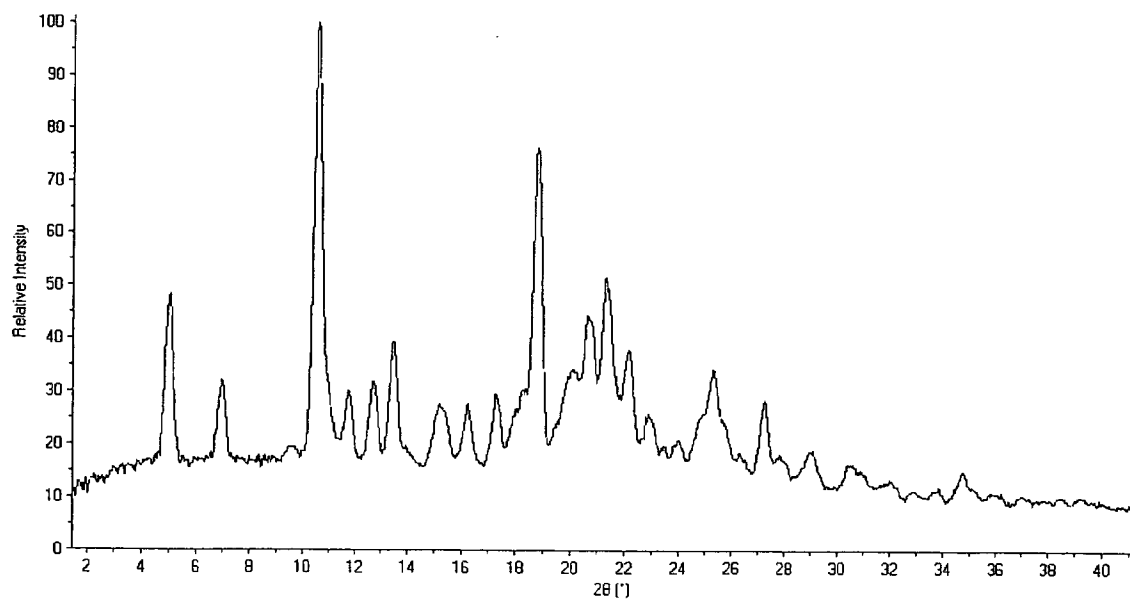
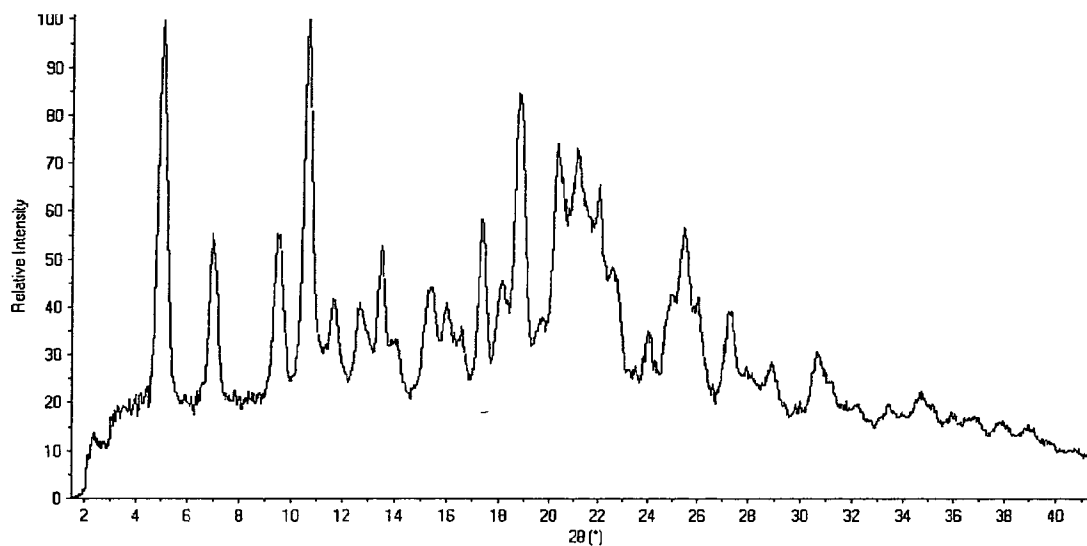
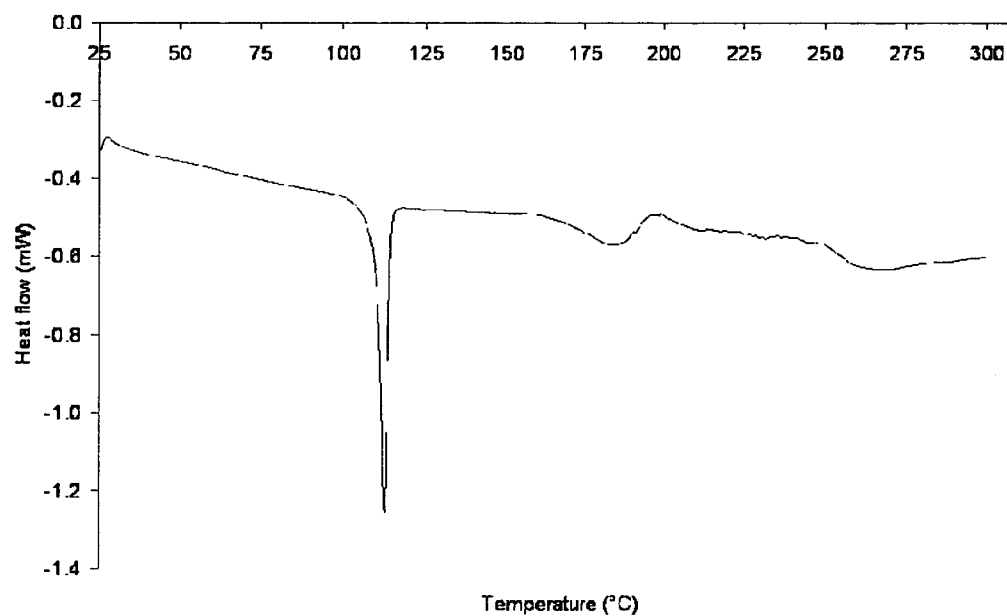
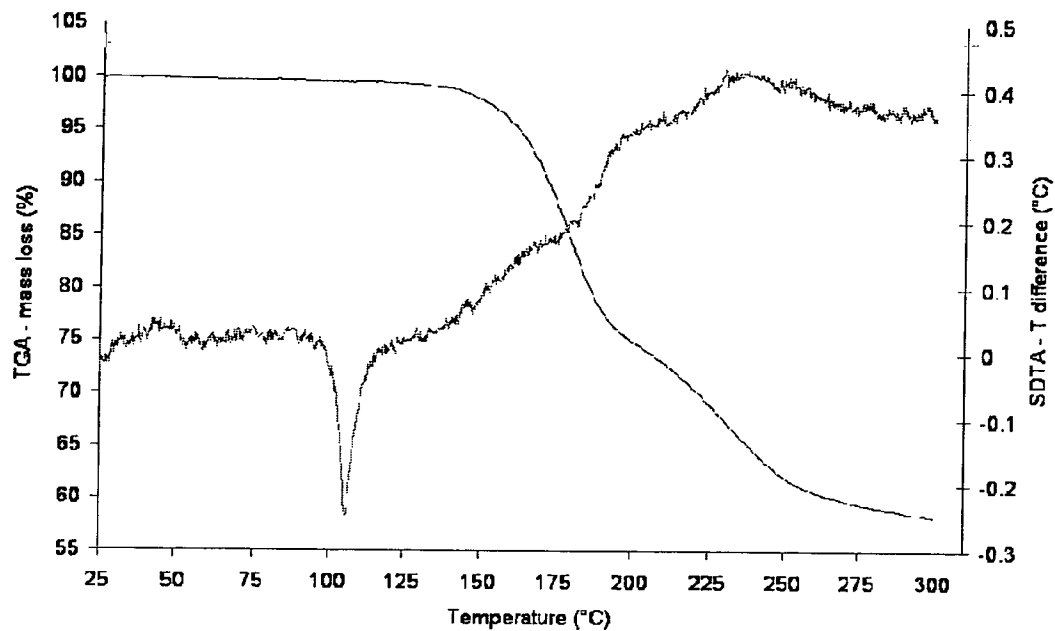
FIG 7A Tenofovir DF **ULT-10**

FIG 8A Tenofovir DF **ULT-11**FIG 8B Tenofovir DF **ULT-11**

H03_F6
DSC (10°C/min)
Onset 1: 104.5°C
Endotherm 1: 112.8°C

FIG 8C Tenofovir DF **ULT-11**

H02_A3
TGA (10°C/min)
Mass loss <0.7% for T<130°C

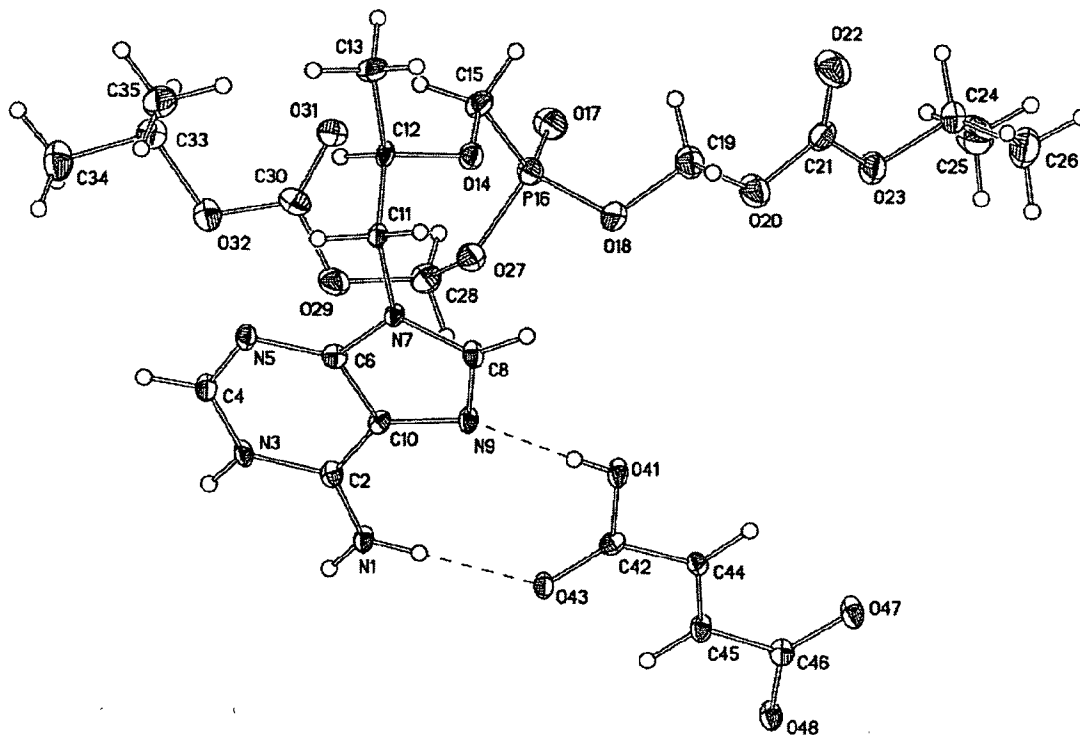
FIG 8D Tenofovir DF **ULT-11**

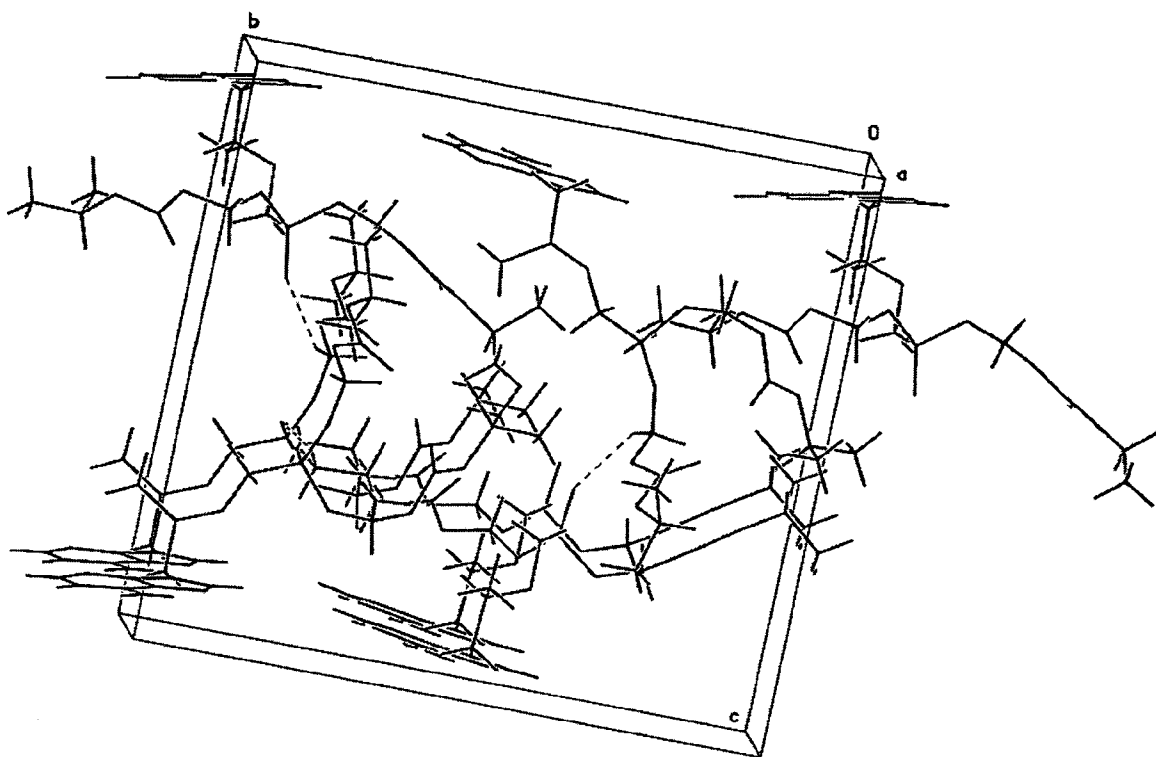
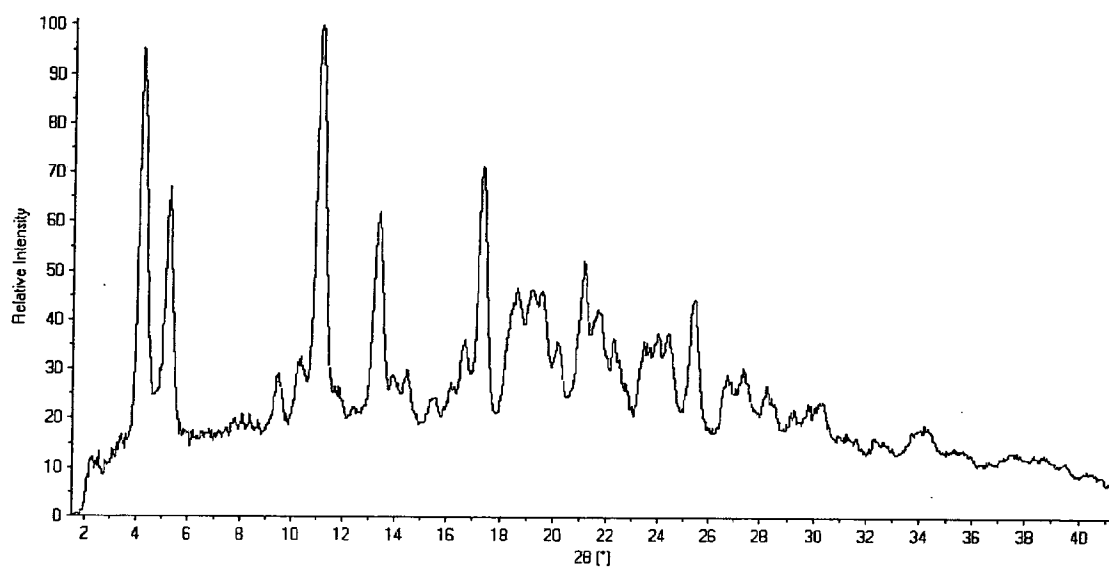
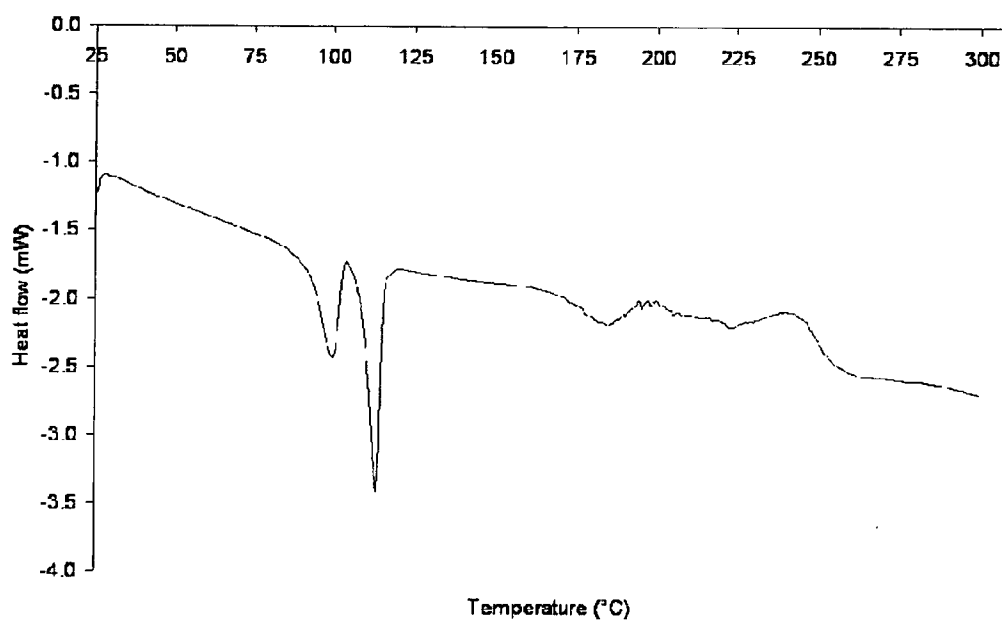
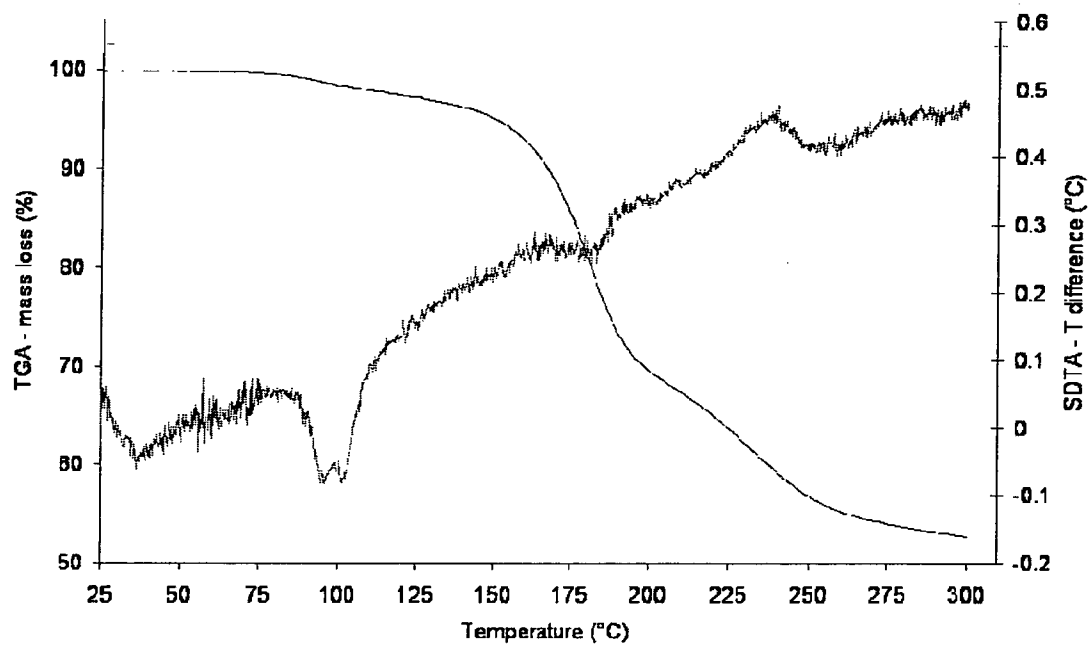
FIG 8E Tenofovir DF **ULT-11**

FIG 9A Tenofovir DF **ULT-12**FIG 9B Tenofovir DF **ULT-12**

H03_L5
DSC (10°C/min)
Onset 1: 90.0°C
Endotherm 1: 100.4°C
Onset 2: 107.9°C
Endotherm 2: 113.7°C

FIG 9C Tenofovir DF **ULT-12**

H03_E8

TGA (10°C/min)

Mass loss ~2.5% for T < 120°C (solvate)

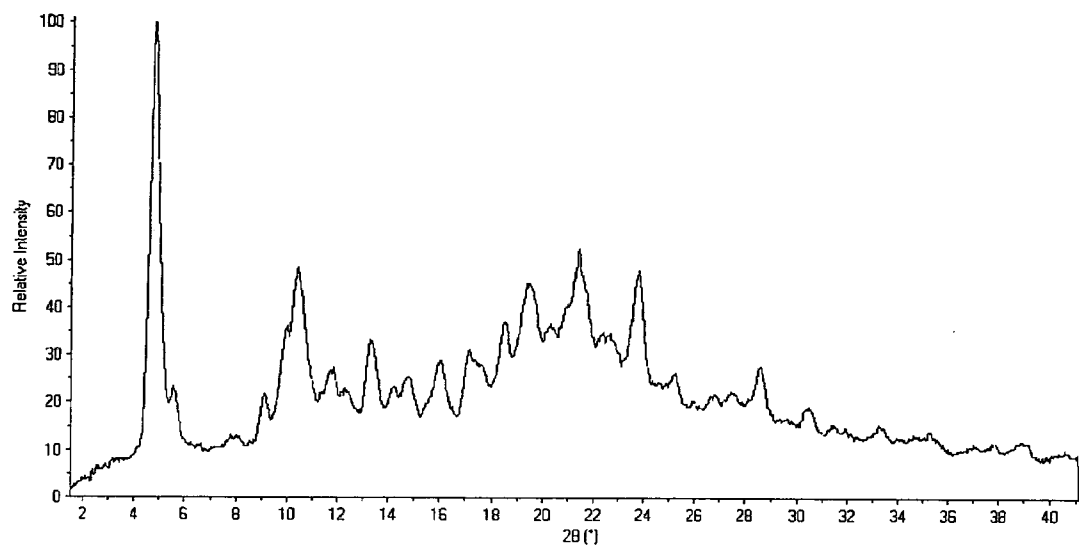
FIG 10A Tenofovir DF **ULT-13**

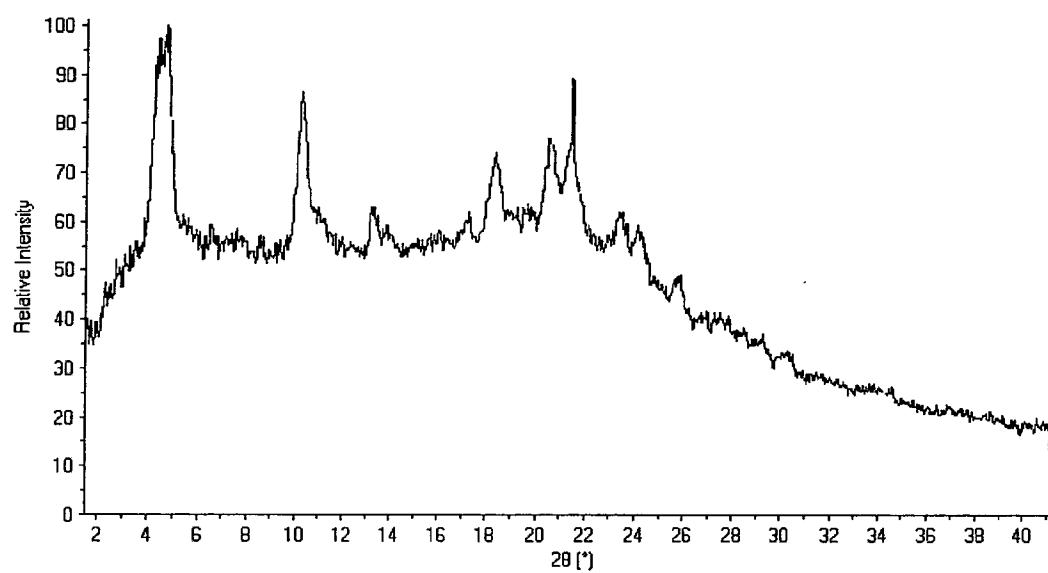
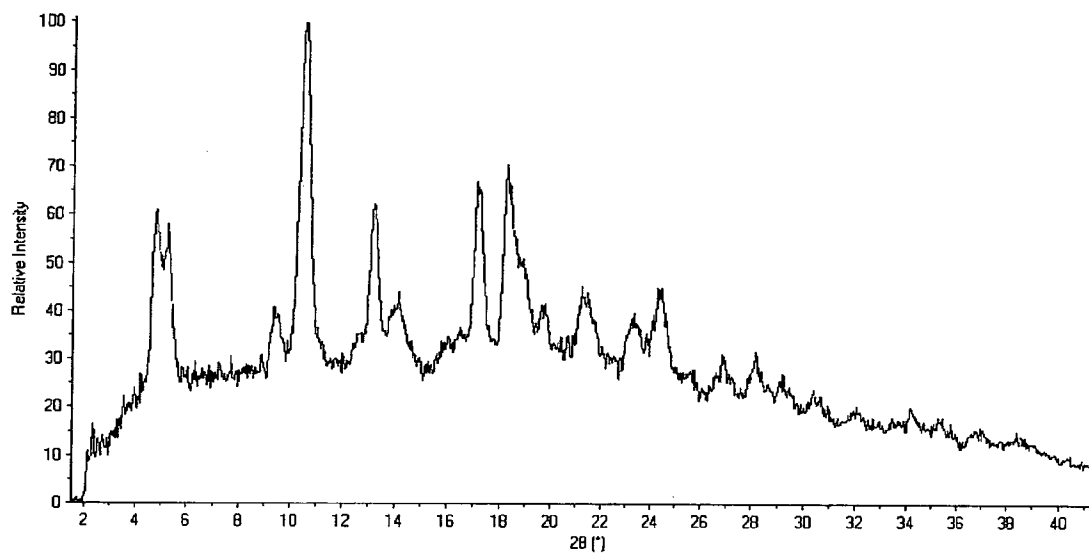
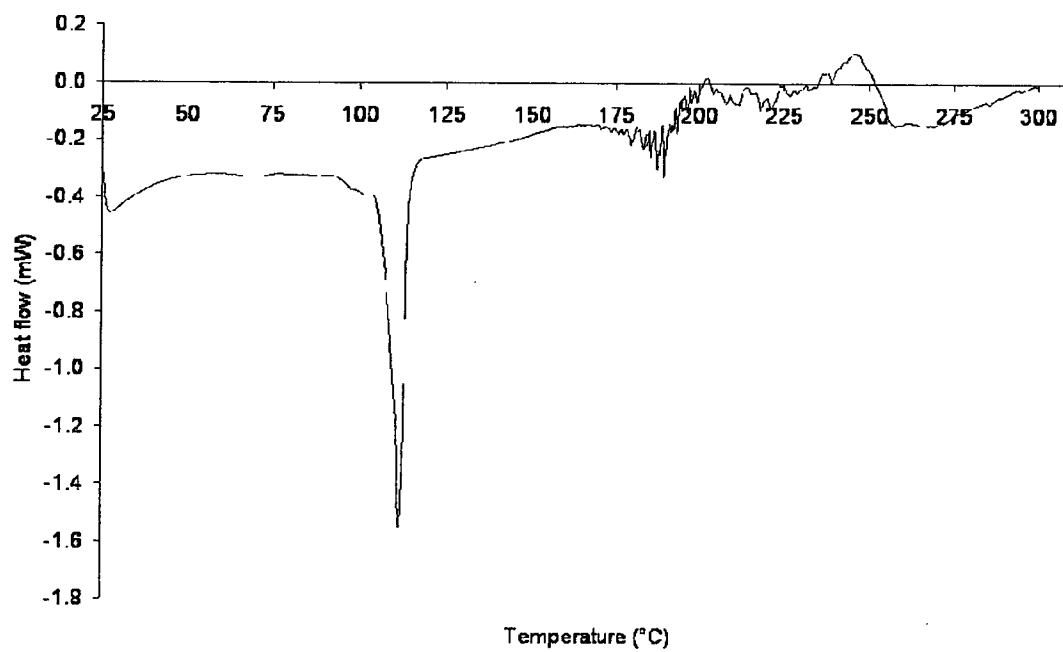
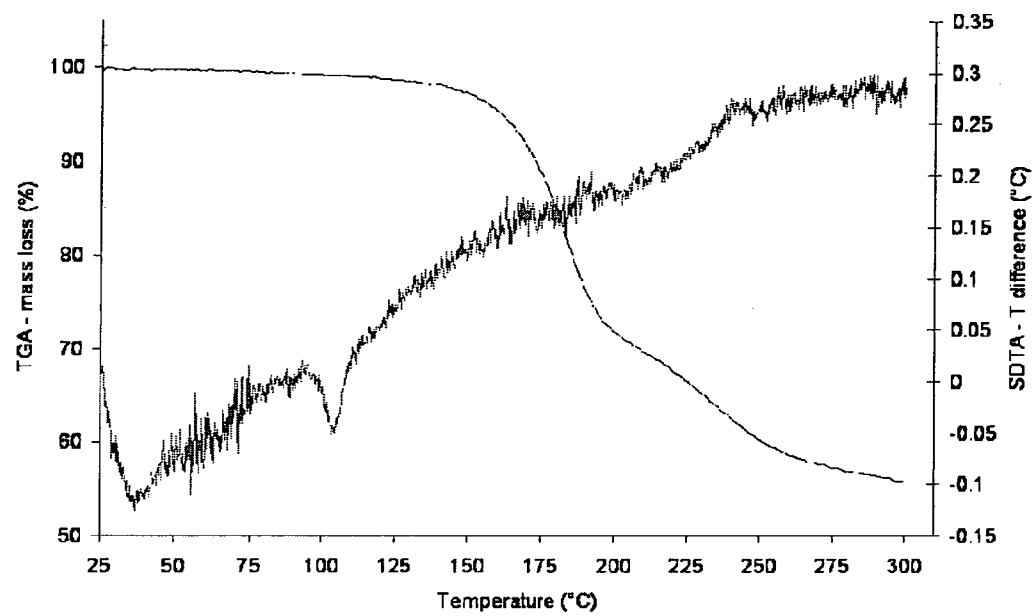
FIG 11A Tenofovir DF **ULT-14**

FIG 12A Tenofovir DF **ULT-15**FIG 12B Tenofovir DF **ULT-15**

_K3
DSC (10°C/min)
Onset 1: 61.3°C
Endotherm 1: 69.8°C
Onset 1: 92.8°C
Endotherm 1: 97.8°C
Onset 3: 104.8°C
Endotherm 3 (MAIN): 111.8°C

FIG 12C Tenofovir DF **ULT-15**

004_K3

TGA (10°C/min)

Mass loss ~1.3% for T<120°C

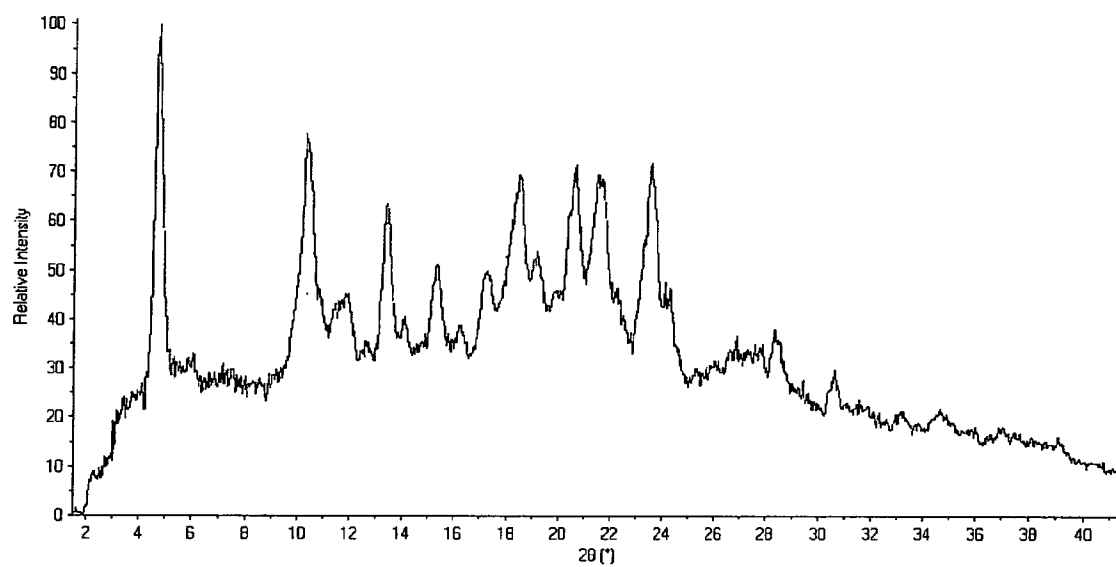
FIG 13A Tenofovir DF **ULT-16**

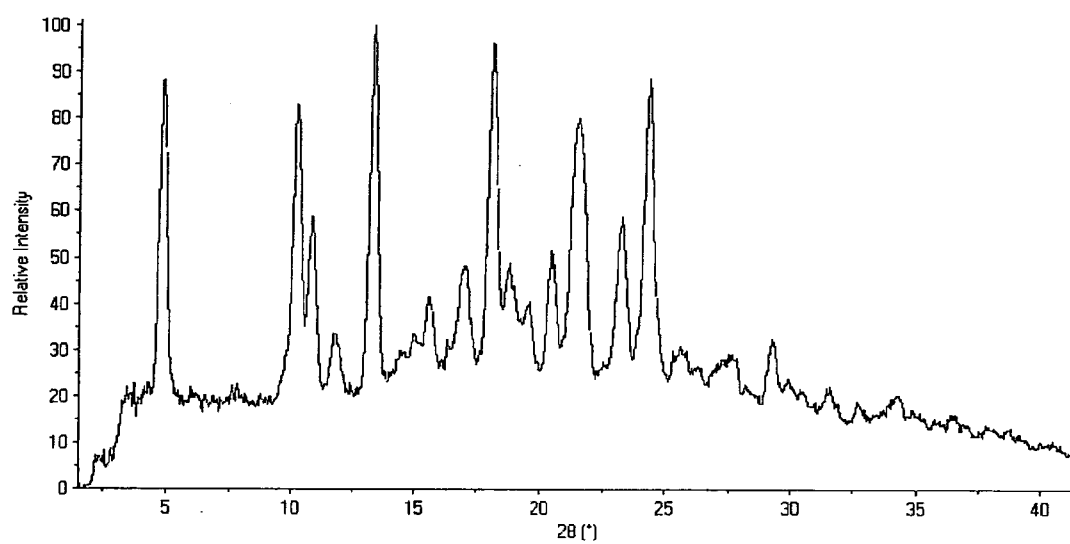
FIG 14A Tenofovir DF **ULT-17**

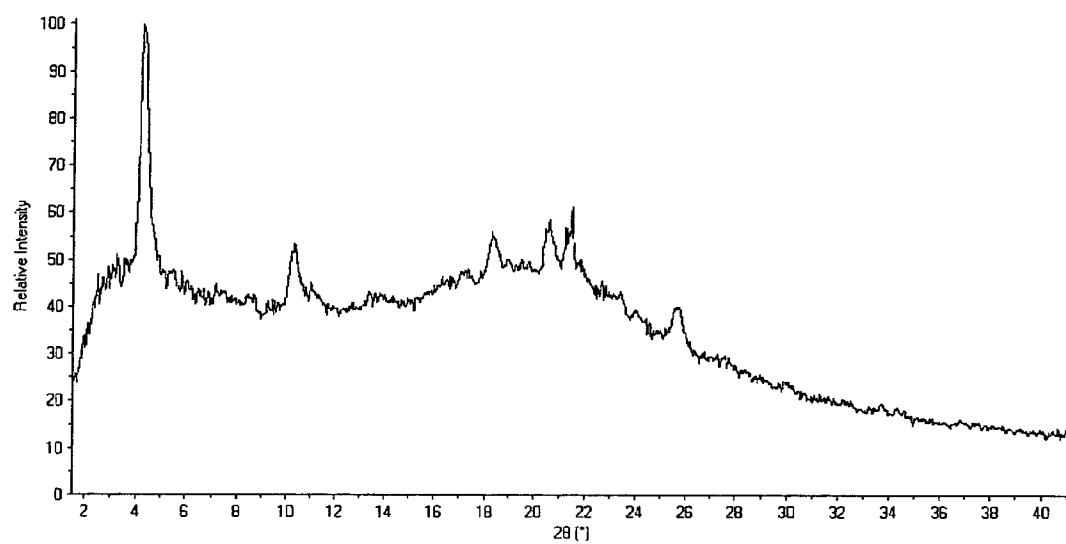
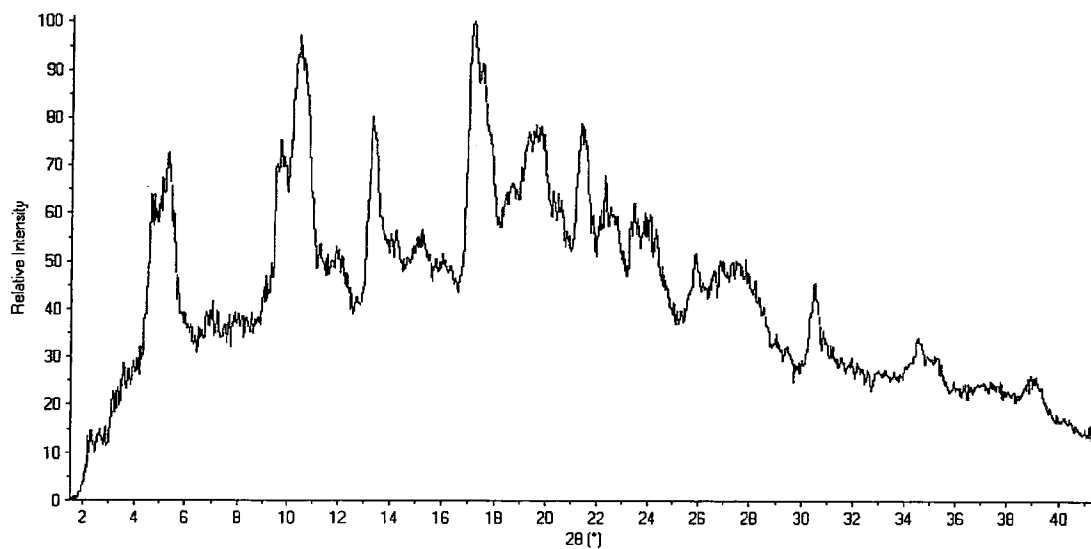
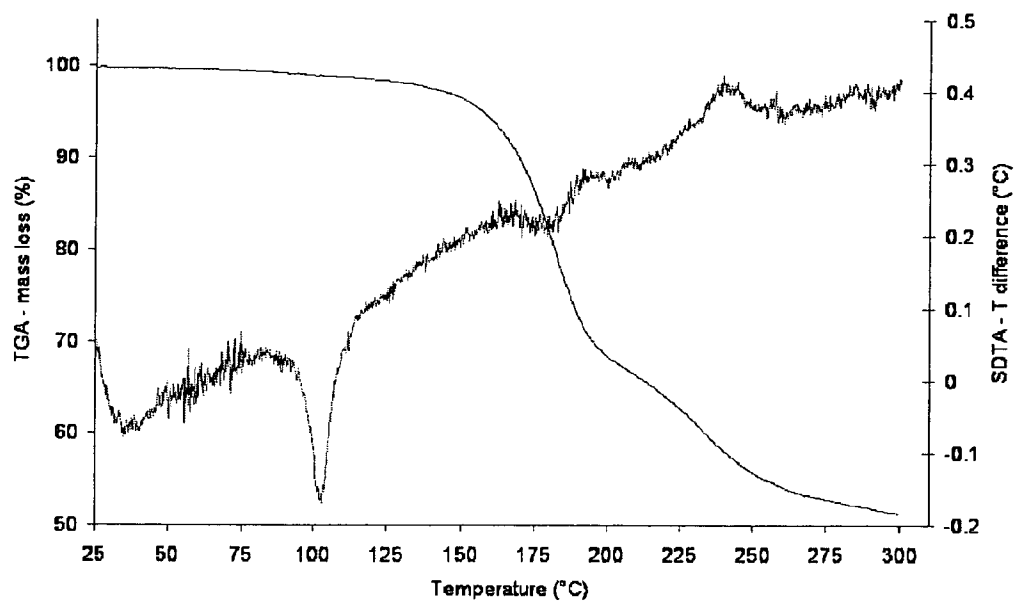
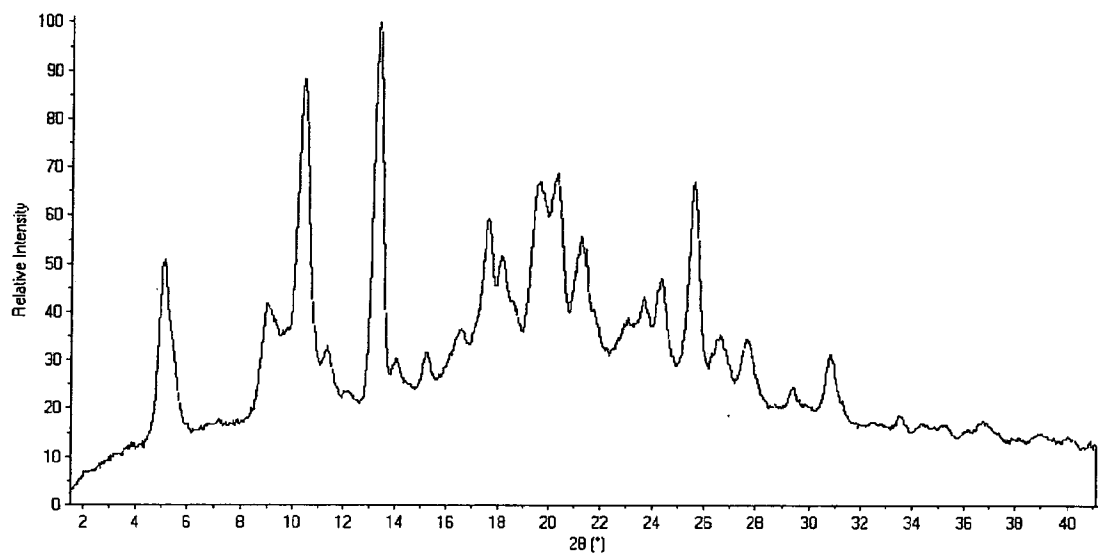
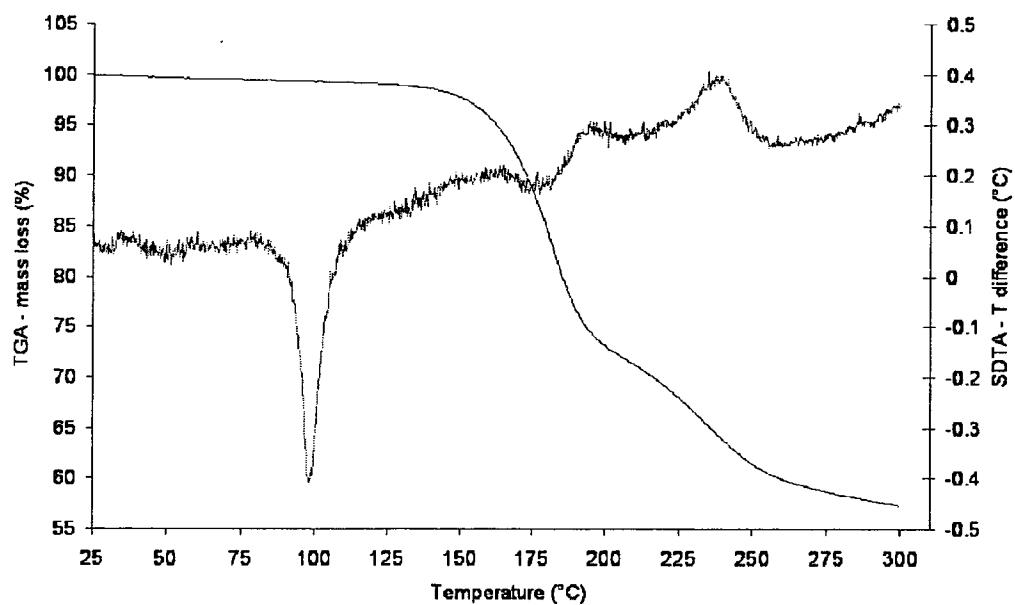
FIG 15A Tenofovir DF **ULT-18**

FIG 16A Tenofovir DF **ULT-19**FIG 16C Tenofovir DF **ULT-19**

003_K2

TGA (10°C/min)

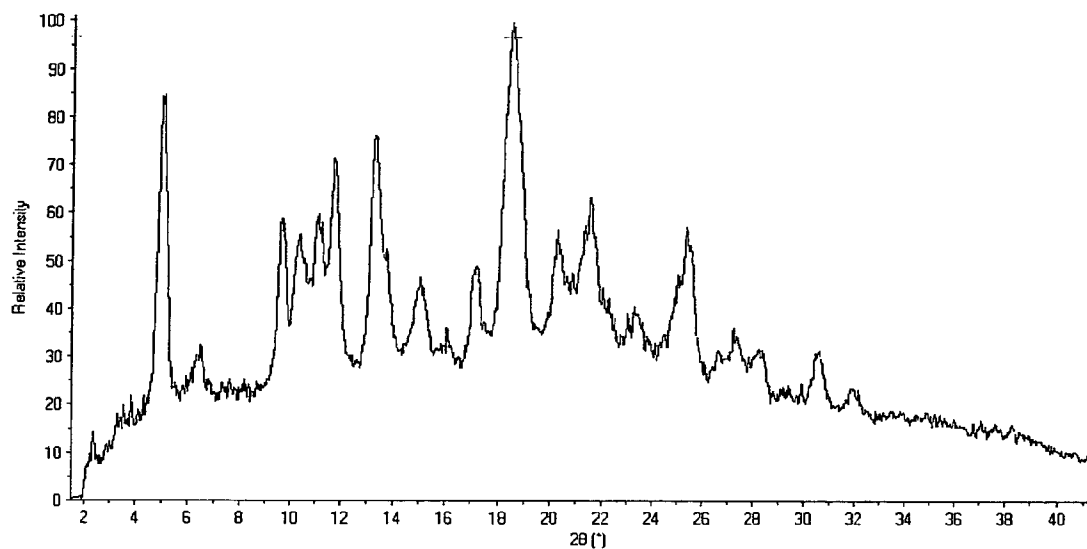
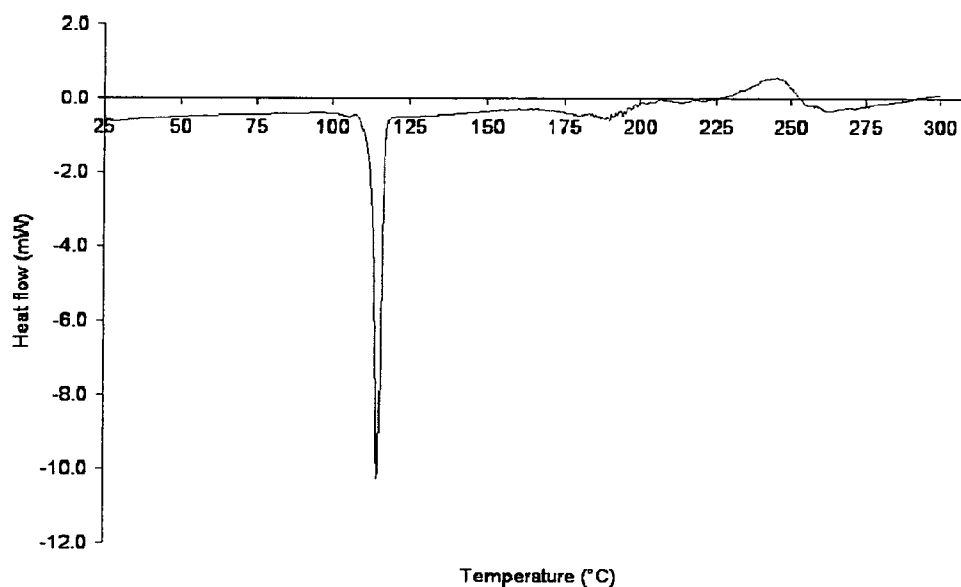
Mass loss ~1.8% for T<130°C

FIG 17A Tenofovir DF **ULT-20**FIG 17C Tenofovir DF **ULT-20**

H02_A4

TGA (10°C/min)

Mass loss ~1.1% for T<130°C anhydrous

FIG 18A Tenofovir DF **ULT-21**FIG 18B Tenofovir DF **ULT-21**

Form V (A13_J7)

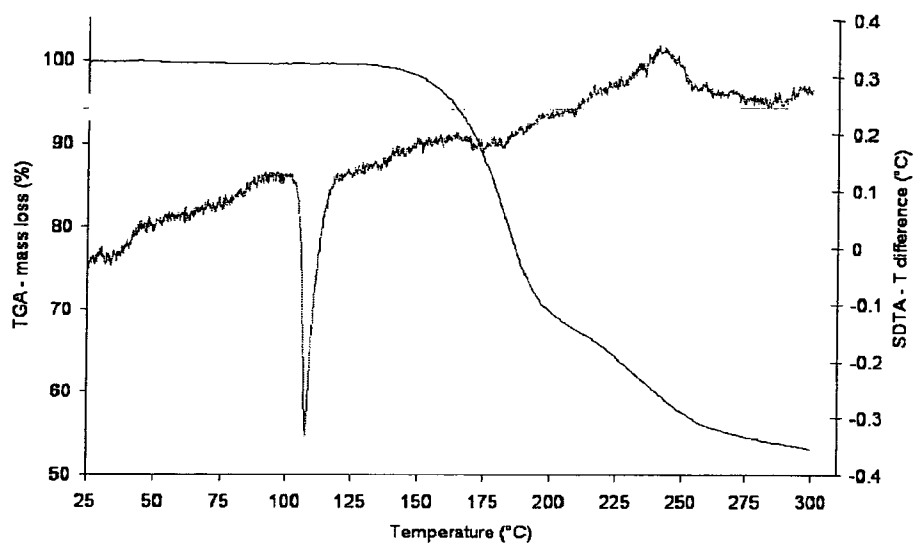
Endotherm 1 (adjacent to the main endotherm)

Onset temp: 100.8°C, Peak temp: 105.6°C

Endotherm 2 (main endotherm)

Onset temp: 107.6, Peak temp: 114.7°C

FIG 18C Tenofovir DF **ULT-21**



Form V (A13_K7)

Mass loss <0.5% for T<130°C anhydrous

FIG 19 Tenofovir DF **ULT-22**

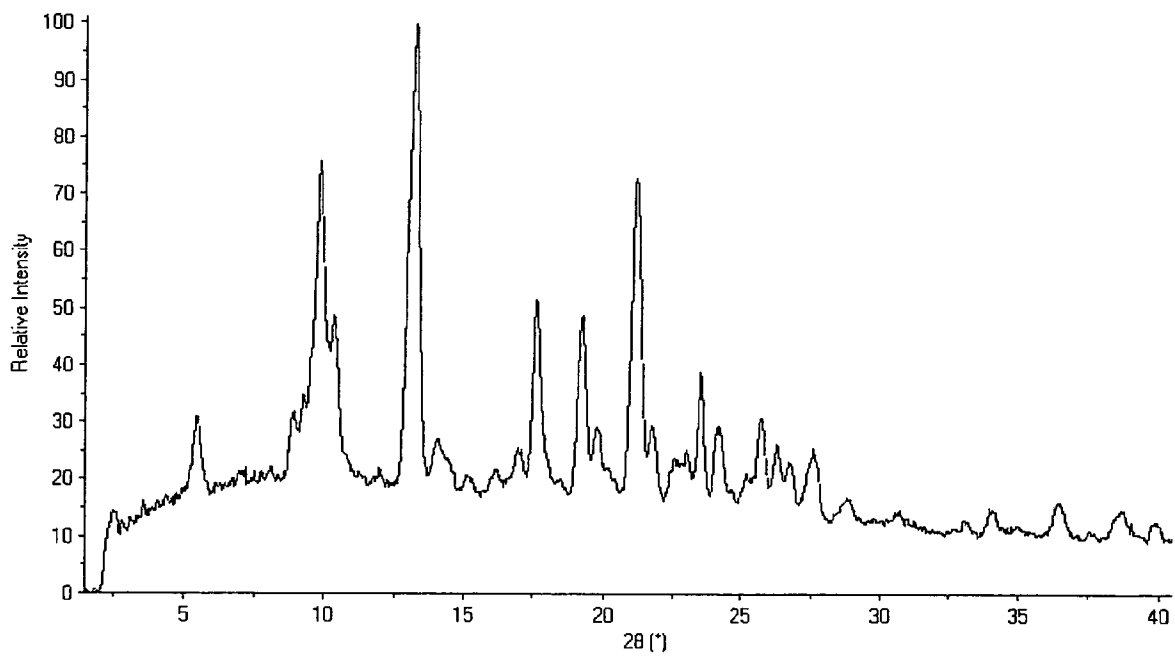


Table I:

Form	Solvent 1	Solvent 2	% solvent 1
ULT-4 A1	1,4-Dioxane	Methanol	50
ULT-4 A1	1-Hexanol	-	-
ULT-4 A1	2-Nitropropane	-	-
ULT-4 A1	Butyronitrile	-	-
ULT-4 A1	1-Methoxy-2-propanol	-	-
ULT-4 A1	Ethylacetate	-	-
ULT-4 A1	2-Methoxyethanol	-	-
ULT-4 A1	1,4-Dioxane	2-Butanone	50
ULT-4 A1	1-Nitropropane	-	-
ULT-4 A1	Butyronitrile	-	-
ULT-4 A1	1-Octanol	Acetone	50
ULT-4 A1	2-Methoxyethanol	-	-
ULT-4 A1	1,4-Dioxane	Tetrahydrofuran	50
ULT-4 A1	1,4-Dioxane	Acetonitrile	50
ULT-4 A1	1,4-Dioxane	Water	50
ULT-4 A1	2-Nitropropane	-	-
ULT-4 A1	Butyronitrile	-	-
ULT-4 A1	2-Nitropropane	-	-
ULT-4 A1	1-Methoxy-2-propanol	-	-

Form	Solvent 1		Solvent 2	% solvent 1
ULT-4	A1	2-Methoxyethanol	-	-
ULT-4	A1	2-Methoxyethanol	-	-
ULT-4	A1	1-Nitropropane	-	-
ULT-4	A1	1-Nitropropane	-	-
ULT-4	A1	1-Butanol	-	-
ULT-4	A1	2-Methoxyethanol	-	-
ULT-4	A1	1-Nitropropane	-	-
ULT-4	A1	Butyronitrile	-	-
ULT-4	A1	2-Nitropropane	-	-
ULT-4	A1	2-Methoxyethanol	-	-
ULT-4	A1	1-Nitropropane	-	-
ULT-4	A1	Butyronitrile	-	-
ULT-4	A1	1-Propanol	-	-
ULT-4	A1	N,N-Dimethylacetamide	-	-
ULT-4	A1	Butyronitrile	-	-
ULT-4	A1	1-Octanol	Tetrahydrofuran	50
ULT-4	A1	Isopropyl acetate	-	-
ULT-4	A1	Butyronitrile	-	-
ULT-4	A1	2-Pentanol	-	-
ULT-4	A1	2-Nitropropane	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-4 A1	2-Nitropropane	-	-
ULT-4 A1	Butyronitrile	-	-
ULT-4 A1	2-Nitropropane	-	-
ULT-4 A1	Butyronitrile	-	-
ULT-4 A1	Methyl acetate	-	-
ULT-4 A1	2-Methoxyethanol	-	-
ULT-4 A1	1-Nitropropane	-	-
ULT-4 A1	1-Nitropropane	-	-
ULT-4 A1	1,2-Dimethoxyethane	Tetrahydrofuran	50
ULT-4 A1	1,4-Dioxane	Acetone	50
ULT-4 A1	Ethyl formate	-	-
ULT-4 A1	1,2-Dimethoxyethane	-	-
ULT-4 A1	2-Nitropropane	-	-
ULT-4 A1	2-Nitropropane	-	-
ULT-4 A1	Methyl acetate	-	-
ULT-4 A1	Tetrahydrofuran	-	-
ULT-4 A1	N,N-Dimethylacetamide	-	-
ULT-4 A1	1-Butanol	-	-
ULT-4 A1	2-Methoxyethanol	-	-
ULT-4 A1	1,4-Dioxane	Tetrahydrofuran	50

Form	Solvent 1		Solvent 2	% solvent 1
ULT-4	A1	Acetone	-	-
ULT-4	A1	Methyl acetate	-	-
ULT-4	A1	Acetonitrile	Water	50
ULT-4	A1	1-Butanol	-	-
ULT-4	A1	1,4-Dioxane	Water	50
ULT-4	A1	Methyl propionate	-	-
ULT-4	A1	Butyronitrile	-	-
ULT-4	A1	Butyronitrile	-	-
ULT-4	A1	2-Nitropropane	-	-
ULT-4	A1	2-Propanol	-	-
ULT-4	A1	1-Nitropropane	-	-
ULT-4	A1	Acetonitrile	N-Methyl Pyrrolidone	50
ULT-4	A1	2-Methoxyethanol	-	-
ULT-4	A1	1-Propanol	-	-
ULT-4	A1	Methyl propionate	-	-
ULT-4	A1	2-Nitropropane	-	-
ULT-4	A1	1-Methoxy-2-propanol	-	-
ULT-4	A1	Butyronitrile	-	-
ULT-4	A1	Methyl acetate	-	-
ULT-4	A1	1-Nitropropane	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-4	A1	Butyronitrile	-
ULT-4	A1	2-Nitropropane	-
ULT-4	A1	2-Nitropropane	-
ULT-4	A1	Butyronitrile	-
ULT-4	A1	2-Nitropropane	-
ULT-4	A1	Methyl acetate	-
ULT-4	A1	1-Nitropropane	-
ULT-4	A1	Methyl acetate	-
ULT-4	A1	Methyl propionate	-
ULT-4	A1	Methyl propionate	-
ULT-4	A1	2-Nitropropane	-
ULT-4	A1	1,4-Dioxane	Water
ULT-4	A1	1-Propanol	-
ULT-4	A1	1,4-Dioxane	Water
ULT-4	A1	2-Nitropropane	-
ULT-4	A1	1,4-Dioxane	50
ULT-4	A1	2-Propanol	-
ULT-4	A1	1-Propanol	-
ULT-4	A1	Methyl acetate	-
ULT-4	A1	1-Methoxy-2-propanol	-

Form		Solvent 1	Solvent 2	% solvent 1
ULT-4	A1	1,2-Diethoxyethane	-	-
ULT-4	A1	Butyronitrile	-	-
ULT-4	A1	Methyl butyrate	-	-
ULT-4	A1	Butyronitrile	-	-
ULT-4	A1	Butyronitrile	-	-
ULT-4	A1	2-Methoxyethanol	-	-
ULT-6	A4	2-Nitropropane	-	-
ULT-6	A4	2-Methoxyethanol	-	-
ULT-6	A4	1,4-Dioxane	Water	50
ULT-6	A4	1-Nitropropane	-	-
ULT-6	A4	Acetonitrile	N-Methyl Pyrrolidone	50
ULT-6	A4	2-Butanone	N-Methyl Pyrrolidone	50
ULT-6	A4	1-Nitropropane	-	-
ULT-6	A4	N-Methyl Pyrrolidone	Water	50
ULT-6	A4	2-Nitropropane	-	-
ULT-6	A4	1-Nitropropane	-	-
ULT-6	A4	Methyl acetate	-	-
ULT-6	A4	1-Octanol	2-Butanone	50
ULT-6	A4	2-Methoxyethanol	-	-
ULT-6	A4	1,4-Dioxane	Water	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-6 A4	Tetrahydropyran	-	-
ULT-6 A4	1-Octanol	Tetrahydrofuran	50
ULT-6 A4	1,4-Dioxane	Water	50
ULT-6 A4	1,4-Dioxane	Acetone	50
ULT-6 A4	1,4-Dioxane	2-Butanone	50
ULT-6 A4	1,2-Diethoxyethane	-	-
ULT-6 A4	1-Nitropropane	-	-
ULT-6 A4	1-Nitropropane	-	-
ULT-6 A4	2-Methoxyethanol	-	-
ULT-6 A4	1-Nitropropane	-	-
ULT-8 C	2-Butanone	Acetonitrile	50
ULT-8 C	1,2-Dimethoxyethane	Acetone	50
ULT-8 C	1,2-Dimethoxyethane	Acetonitrile	50
ULT-8 C	2-Propanol	-	-
ULT-8 C	2-Propanol	-	-
ULT-8 C	Acetone	Acetonitrile	50
ULT-8 C	1-Propanol	-	-
ULT-8 C	Dimethylcarbonate	-	-
ULT-8 C	Nitromethane	-	-
ULT-8 C	2-Butanone	Acetone	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-8 C	Tetrahydrofuran	-	-
ULT-8 C	1,4-Dioxane	Acetone	50
ULT-8 C	Water	-	-
ULT-8 C	2-Butanone	Tetrahydrofuran	50
ULT-8 C	1,2-Dimethoxyethane	Acetonitrile	50
ULT-8 C	1,4-Dioxane	Tetrahydrofuran	50
ULT-8 C	tert-Butanol	-	-
ULT-8 C	1,4-Dioxane	Tetrahydrofuran	50
ULT-8 C	Acetone	Tetrahydrofuran	50
ULT-8 C	2-Butanone	Tetrahydrofuran	50
ULT-8 C	tert-Butanol	-	-
ULT-8 C	2-Butanone	Acetonitrile	50
ULT-8 C	Propionitrile	-	-
ULT-8 C	2-Butanone	Acetone	50
ULT-8 C	1,2-Dimethoxyethane	Acetonitrile	50
ULT-8 C	1,2-Dimethoxyethane	2-Butanone	50
ULT-8 C	1,2-Dimethoxyethane	1,4-Dioxane	50
ULT-8 C	Tetrahydropyran	-	-
ULT-8 C	1,4-Dioxane	-	-
ULT-8 C	1,4-Dioxane	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-8 C	Acetone	Acetonitrile	50
ULT-8 C	Acetonitrile	Tetrahydrofuran	50
ULT-8 C	Acetonitrile	Tetrahydrofuran	50
ULT-8 C	1,4-Dioxane	2-Butanone	50
ULT-8 C	Ethylacetate	-	-
ULT-8 C	Acetone	Acetonitrile	50
ULT-8 C	1,4-Dioxane	-	-
ULT-8 C	Methyl propionate	-	-
ULT-8 C	Diethylene glycol dimethylether	-	-
ULT-8 C	2-Butanone	Acetone	50
ULT-8 C	Acetone	-	-
ULT-8 C	1,4-Dioxane	Tetrahydrofuran	50
ULT-8 C	1,2-Dimethoxyethane	1,4-Dioxane	50
ULT-8 C	2-Propanol	-	-
ULT-8 C	Cyclopentanone	-	-
ULT-8 C	4-Hydroxy-4-methyl-2-pentanone	-	-
ULT-8 C	Methoxyethyl acetate	-	-
ULT-8 C	1,2-Dimethoxyethane	Acetone	50
ULT-8 C	Nitroethane	-	-
ULT-8 C	1,4-Dioxane	2-Butanone	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-8 C	Nitromethane	-	-
ULT-8 C	1-Propanol	-	-
ULT-8 C	Acetonitrile	Tetrahydrofuran	50
ULT-8 C	1,4-Dioxane	Tetrahydrofuran	50
ULT-8 C	1,4-Dioxane	-	-
ULT-8 C	1-Methoxy-2-propanol	-	-
ULT-8 C	1,2-Dimethoxyethane	1,4-Dioxane	50
ULT-8 C	Acetone	Tetrahydrofuran	50
ULT-8 C	1,2-Dimethoxyethane	Acetonitrile	50
ULT-8 C	1-Octanol	2-Butanone	50
ULT-8 C	4-Hydroxy-4-methyl-2-pentanone	-	-
ULT-8 C	2-Butanone	Acetonitrile	50
ULT-8 C	2-Nitropropane	-	-
ULT-8 C	1,2-Dimethoxyethane	2-Butanone	50
ULT-8 C	Ethylene glycol monobutyl ether	-	-
ULT-8 C	1,4-Dioxane	Acetonitrile	50
ULT-8 C	Tetrahydrofuran	-	-
ULT-8 C	Ethyl formate	-	-
ULT-8 C	Acetonitrile	N-Methyl Pyrrolidone	50
ULT-8 C	1-Octanol	Acetonitrile	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-8 C	1,4-Dioxane	-	-
ULT-8 C	Acetone	-	-
ULT-8 C	Nitroethane	-	-
ULT-8 C	Acetone	Acetonitrile	50
ULT-8 C	Cyclopentanone	-	-
ULT-8 C	1,2-Dimethoxyethane	2-Butanone	50
ULT-8 C	Ethylene glycol monobutyl ether	-	-
ULT-8 C	2-Butanone	Acetone	50
ULT-8 C	2-Butanone	Nitrobenzene	50
ULT-8 C	1,2-Dimethoxyethane	1,4-Dioxane	50
ULT-8 C	1,2-Dimethoxyethane	N-Methyl Pyrrolidone	50
ULT-8 C	Cyclopentanone	-	-
ULT-8 C	1,4-Dioxane	-	-
ULT-8 C	1-Methoxy-2-propanol	-	-
ULT-8 C	Methoxyethyl acetate	-	-
ULT-8 C	2,2,2-Trifluoroethanol	-	-
ULT-8 C	2-Butanone	Acetone	50
ULT-8 C	1,4-Dioxane	Acetone	50
ULT-8 C	Diethylene glycol dimethylether	-	-
ULT-8 C	Propionitrile	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-8 C	1,2-Dimethoxyethane	Acetonitrile	50
ULT-8 C	2-Butanone	Nitrobenzene	50
ULT-8 C	2-Pentanol	-	-
ULT-8 C	1-Propanol	-	-
ULT-8 C	tert-Butanol	-	-
ULT-8 C	1,2-Dimethoxyethane	Acetone	50
ULT-8 C	1,4-Dioxane	-	-
ULT-8 C	Tetrahydrofuran	-	-
ULT-8 C	1,4-Dioxane	Nitrobenzene	50
ULT-8 C	2-Butanone	-	-
ULT-8 C	4-Hydroxy-4-methyl-2-pentanol	-	-
ULT-8 C	Nitroethane	-	-
ULT-8 C	tert-Butanol	-	-
ULT-8 C	1,2-Dimethoxyethane	1,4-Dioxane	50
ULT-8 C	Methoxyethyl acetate	-	-
ULT-8 C	Acetonitrile	-	-
ULT-8 C	1,4-Dioxane	Acetonitrile	50
ULT-8 C	1,2-Dimethoxyethane	1,4-Dioxane	50
ULT-8 C	Dimethylcarbonate	-	-
ULT-8 C	(R) - (-) -2-Octanol	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-8 C	1-Propanol	-	-
ULT-8 C	2-Butanone	Acetonitrile	50
ULT-8 C	Tetrahydrofuran	-	-
ULT-8 C	1,2-Dimethoxyethane	Tetrahydrofuran	50
ULT-8 C	1,2-Dimethoxyethane	Acetonitrile	50
ULT-8 C	1-Propanol	-	-
ULT-8 C	2-Butanone	-	-
ULT-8 C	Acetone	Tetrahydrofuran	50
ULT-8 C	1,4-Dioxane	Methanol	50
ULT-8 C	Propionitrile	-	-
ULT-8 C	2-Butanone	Acetonitrile	50
ULT-8 C	2-Propanol	-	-
ULT-8 C	Diethylene glycol dimethylether	-	-
ULT-8 C	Methyl propionate	-	-
ULT-8 C	2-Methoxyethanol	-	-
ULT-8 C	2-Propanol	-	-
ULT-8 C	1,2-Dimethoxyethane	Nitrobenzene	50
ULT-8 C	1,4-Dioxane	Nitrobenzene	50
ULT-8 C	N,N-Dimethylacetamide	-	-
ULT-8 C	Propyl acetate	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-8 C	Acetone	Acetonitrile	50
ULT-8 C	Acetone	Tetrahydrofuran	50
ULT-8 C	Cyclopentanone	-	-
ULT-8 C	2-Pentanol	-	-
ULT-8 C	Nitroethane	-	-
ULT-8 C	Cyclopentanol	-	-
ULT-8 C	1-Propanol	-	-
ULT-8 C	1,2-Dimethoxyethane	Nitrobenzene	50
ULT-8 C	1,2-Dimethoxyethane	Acetone	50
ULT-8 C	Acetone	Nitrobenzene	50
ULT-8 C	2-Hexanol	-	-
ULT-8 C	Methoxyethyl acetate	-	-
ULT-8 C	Tetrahydrofuran	-	-
ULT-8 C	1,2-Dimethoxyethane	1-Octanol	50
ULT-8 C	Cyclopentanone	-	-
ULT-8 C	Methoxyethyl acetate	-	-
ULT-8 C	2-Butanone	Nitrobenzene	50
ULT-8 C	Cyclopentanone	-	-
ULT-8 C	Tetrahydrofuran	-	-
ULT-8 C	Nitroethane	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-8 C	Acetonitrile	Nitrobenzene	50
ULT-8 C	1-Octanol	Acetonitrile	50
ULT-8 C	1,4-Dioxane	Acetone	50
ULT-8 C	Nitroethane	-	-
ULT-8 C	1,2-Dimethoxyethane	Acetone	50
ULT-8 C	Acetone	N-Methyl Pyrrolidone	50
ULT-8 C	Propionitrile	-	-
ULT-8 C	2-Butanone	Acetonitrile	50
ULT-8 C	1-Methoxy-2-propanol	-	-
ULT-8 C	Acetone	Acetonitrile	50
ULT-8 C	1-Propanol	-	-
ULT-8 C	Dimethylcarbonate	-	-
ULT-8 C	tert-Butanol	-	-
ULT-8 C	2-Butanone	Tetrahydrofuran	50
ULT-8 C	N,N-Dimethylacetamide	-	-
ULT-8 C	Water	-	-
ULT-8 C	2-Methoxyethanol	-	-
ULT-8 C	1-Nitropropane	-	-
ULT-8 C	1-Butanol	-	-
ULT-8 C	1,4-Dioxane	2-Butanone	50

Form		Solvent 1	Solvent 2	% solvent 1
ULT-8	C	Diethylene glycol dimethylether	-	-
ULT-8	C	Methoxyethyl acetate	-	-
ULT-8	C	Acetonitrile	Tetrahydrofuran	50
ULT-8	C	N,N-Dimethylformamide	-	-
ULT-8	C	2-Methoxyethanol	-	-
ULT-8	C	2-Butanone	Tetrahydrofuran	50
ULT-8	C	2-Methoxyethanol	-	-
ULT-8	C	2-Butanone	Nitrobenzene	50
ULT-8	C	2-Ethoxyethanol	-	-
ULT-8	C	Diethylene glycol dimethylether	-	-
ULT-8	C	Tetrahydrofuran	-	-
ULT-8	C	Acetone	Nitrobenzene	50
ULT-8	C	Tetrahydrofurfurylalcohol	-	-
ULT-8	C	1-Methoxy-2-propanol	-	-
ULT-8	C	1,2-Dimethoxyethane	Acetone	50
ULT-8	C	Propionitrile	-	-
ULT-8	C	Nitromethane	-	-
ULT-8	C	Diethylene glycol dimethylether	-	-
ULT-8	C	2-Butanone	Acetone	50
ULT-8	C	1,2-Dimethoxyethane	Acetonitrile	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-8 C	1,2-Dimethoxyethane	Acetone	50
ULT-8 C	2-Butanone	Acetonitrile	50
ULT-8 C	N-Methyl Pyrrolidone	Water	50
ULT-8 C	Acetonitrile	Nitrobenzene	50
ULT-8 C	Cyclopentanone	-	-
ULT-8 C	Acetone	Tetrahydrofuran	50
ULT-8 C	N,N-Dimethylacetamide	-	-
ULT-8 C	Acetonitrile	-	-
ULT-8 C	1-Methoxy-2-propanol	-	-
ULT-8 C	1,2-Dimethoxyethane	Acetonitrile	50
ULT-8 C	1,4-Dioxane	-	-
ULT-8 C	1,4-Dioxane	-	-
ULT-8 C	Cyclopentanol	-	-
ULT-8 C	2-Propanol	-	-
ULT-8 C	2-Pentanol	-	-
ULT-8 C	1-Propanol	-	-
ULT-8 C	Acetone	N-Methyl Pyrrolidone	50
ULT-8 C	Diethylene glycol dimethylether	-	-
ULT-8 C	Ethylacetate	-	-
ULT-8 C	1,2-Dimethoxyethane	2-Butanone	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-8 C	2-Butanone	-	-
ULT-8 C	1,2-Dimethoxyethane	1,4-Dioxane	50
ULT-8 C	1,2-Dimethoxyethane	1,4-Dioxane	50
ULT-8 C	2-Butanone	Acetone	50
ULT-8 C	Tetrahydrofuran	-	-
ULT-8 C	1,4-Dioxane	Acetone	50
ULT-8 C	1,4-Dioxane	Acetonitrile	50
ULT-8 C	Acetone	Tetrahydrofuran	50
ULT-8 C	1,2-Dimethoxyethane	Acetonitrile	50
ULT-8 C	1,2-Dimethoxyethane	2-Butanone	50
ULT-8 C	Propionitrile	-	-
ULT-8 C	Tetrahydrofurfurylalcohol	-	-
ULT-8 C	1,2-Dimethoxyethane	Tetrahydrofuran	50
ULT-8 C	2-Butanone	Acetonitrile	50
ULT-8 C	Tetrahydrofuran	-	-
ULT-8 C	1-Butanol	-	-
ULT-8 C	1-Methoxy-2-propanol	-	-
ULT-8 C	Ethylene glycol monobutyl ether	-	-
ULT-8 C	1-Octanol	Acetonitrile	50
ULT-8 C	2-Butanone	Tetrahydrofuran	50

Form		Solvent 1	Solvent 2	% solvent 1
ULT-8	C	Ethylene glycol monobutyl ether	-	-
ULT-8	C	Ethylene glycol monobutyl ether	-	-
ULT-8	C	1,4-Dioxane	-	-
ULT-8	C	1-Nitropropane	-	-
ULT-8	C	1,4-Dioxane	Tetrahydrofuran	50
ULT-8	C	Dimethylcarbonate	-	-
ULT-8	C	1,4-Dioxane	2-Butanone	50
ULT-8	C	2-Ethoxyethyl acetate	-	-
ULT-8	C	Acetone	Tetrahydrofuran	50
ULT-8	C	1,2-Dimethoxyethane	Acetonitrile	50
ULT-8	C	2-Butanone	Acetone	50
ULT-8	C	Diethylene glycol dimethylether	-	-
ULT-8	C	1,2-Dimethoxyethane	1,4-Dioxane	50
ULT-8	C	Nitromethane	-	-
ULT-8	C	2-Butanone	Methanol	50
ULT-8	C	Acetonitrile	Tetrahydrofuran	50
ULT-8	C	Acetonitrile	Tetrahydrofuran	50
ULT-8	C	Acetone	Tetrahydrofuran	50
ULT-8	C	Acetone	Acetonitrile	50
ULT-8	C	2-Butanone	Acetone	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-8 C	Acetone	-	-
ULT-8 C	Tetrahydropyran	-	-
ULT-8 C	Cyclopentanone	-	-
ULT-10 F	1,2-Dimethoxyethane	-	-
ULT-10 F	Methanol	Water	50
ULT-10 F	Methyl propionate	-	-
ULT-10 F	2-Butanone	Acetone	50
ULT-10 F	Acetonitrile	Tetrahydrofuran	50
ULT-10 F	Tetrahydrofuran	-	-
ULT-10 F	1,2-Dimethoxyethane	1,4-Dioxane	50
ULT-10 F	Water	-	-
ULT-10 F	Acetone	Methanol	50
ULT-10 F	1,2-Dimethoxyethane	Acetone	50
ULT-10 F	2,2,2-Trifluoroethanol	-	-
ULT-10 F	Water	-	-
ULT-10 F	1,2-Dimethoxyethane	Tetrahydrofuran	50
ULT-10 F	Propyl acetate	-	-
ULT-10 F	1,4-Dioxane	2-Butanone	50
ULT-10 F	Acetone	-	-
ULT-10 F	1,4-Dioxane	Acetonitrile	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-10 F	1-Hexanol	-	-
ULT-10 F	1,4-Dioxane	-	-
ULT-10 F	1,2-Dimethoxyethane	Acetone	50
ULT-10 F	Methanol	Water	50
ULT-10 F	2-Butanone	Methanol	50
ULT-10 F	1,2-Dimethoxyethane	Tetrahydrofuran	50
ULT-10 F	1-Hexanol	-	-
ULT-10 F	Ethylene glycol monobutyl ether	-	-
ULT-10 F	1,2-Dimethoxyethane	2-Butanone	50
ULT-10 F	Methyl-4-2-Pentanol	-	-
ULT-10 F	Water	-	-
ULT-10 F	2-Butanone	Acetonitrile	50
ULT-10 F	1,2-Dimethoxyethane	Acetone	50
ULT-10 F	2-Butanone	Methanol	50
ULT-10 F	Acetone	Tetrahydrofuran	50
ULT-10 F	Methanol	Water	50
ULT-10 F	1,2-Dimethoxyethane	2-Butanone	50
ULT-10 F	Acetone	Methanol	50
ULT-10 F	Acetone	Acetonitrile	50
ULT-10 F	Water	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-10 F	(R) - (-) -2-Octanol	-	-
ULT-10 F	1,4-Dioxane	Acetone	50
ULT-10 F	Acetonitrile	Tetrahydrofuran	50
ULT-10 F	1,2-Dimethoxyethane	-	-
ULT-10 F	1-Heptanol	-	-
ULT-10 F	2,2,2-Trifluoroethanol	-	-
ULT-10 F	1,4-Dioxane	Acetonitrile	50
ULT-10 F	1,4-Dioxane	Acetonitrile	50
ULT-10 F	1,4-Dioxane	Tetrahydrofuran	50
ULT-10 F	tert-Butanol	-	-
ULT-10 F	1-Heptanol	-	-
ULT-10 F	1,4-Dioxane	Nitrobenzene	50
ULT-10 F	Acetone	Methanol	50
ULT-10 F	2,2,2-Trifluoroethanol	-	-
ULT-10 F	1,4-Dioxane	2-Butanone	50
ULT-10 F	2-Butanone	Methanol	50
ULT-10 F	1,2-Dimethoxyethane	Acetonitrile	50
ULT-10 F	2-Butanone	Methanol	50
ULT-10 F	Diethylene glycol dimethylether	-	-
ULT-10 F	1,4-Dioxane	2-Butanone	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-10 F	Acetone	-	-
ULT-10 F	Tetrahydrofuran	-	-
ULT-10 F	1,2-Dimethoxyethane	Acetone	50
ULT-10 F	Nitromethane	-	-
ULT-10 F	Cyclopentanone	-	-
ULT-10 F	1,4-Dioxane	1-Octanol	50
ULT-10 F	1-Octanol	Acetonitrile	50
ULT-10 F	Acetonitrile	Tetrahydrofuran	50
ULT-10 F	(R)-(-)-2-Octanol	-	-
ULT-10 F	Acetonitrile	Nitrobenzene	50
ULT-10 F	Methoxyethyl acetate	-	-
ULT-10 F	1,2-Dimethoxyethane	Nitrobenzene	50
ULT-10 F	1,4-Dioxane	Nitrobenzene	50
ULT-10 F	1,2-Diethoxyethane	-	-
ULT-10 F	1-Octanol	2-Butanone	50
ULT-10 F	Acetonitrile	Water	50
ULT-10 F	Water	-	-
ULT-10 F	1,2-Dimethoxyethane	Acetonitrile	50
ULT-10 F	Acetonitrile	-	-
ULT-10 F	Water	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-10	F	2-Butanone	Tetrahydrofuran
ULT-10	F	Propyl acetate	-
ULT-10	F	Acetone	Tetrahydrofuran
ULT-10	F	Ethylacetate	-
ULT-10	F	Water	-
ULT-10	F	Methanol	-
ULT-10	F	1,2-Dimethoxyethane	Methanol
ULT-10	F	1,2-Dimethoxyethane	1,4-Dioxane
ULT-10	F	Acetone	Methanol
ULT-10	F	tert-Butanol	-
ULT-10	F	Water	-
ULT-10	F	tert-Butanol	-
ULT-10	F	2-Butanone	Tetrahydrofuran
ULT-10	F	2-Hexanol	-
ULT-10	F	2-Butanone	Acetonitrile
ULT-10	F	tert-Butanol	-
ULT-10	F	1,2-Diethoxyethane	-
ULT-10	F	2-Butanone	-
ULT-10	F	Acetonitrile	-
ULT-10	F	Acetonitrile	Tetrahydrofuran

Form	Solvent 1	Solvent 2	% solvent 1
ULT-10 F	1,2-Dimethoxyethane	2-Butanone	50
ULT-10 F	Ethyl formate	-	-
ULT-10 F	Nitromethane	-	-
ULT-10 F	2-Butanone	Acetonitrile	50
ULT-10 F	Methyl butyrate	-	-
ULT-10 F	Acetone	Acetonitrile	50
ULT-10 F	2-Propanol	-	-
ULT-10 F	1,2-Dimethoxyethane	1-Octanol	50
ULT-10 F	Ethyl formate	-	-
ULT-10 F	1,2-Dimethoxyethane	Nitrobenzene	50
ULT-10 F	1-Hexanol	-	-
ULT-10 F	1-Heptanol	-	-
ULT-10 F	1,2-Dimethoxyethane	Nitrobenzene	50
ULT-10 F	tert-Butanol	-	-
ULT-10 F	2-Propanol	-	-
ULT-10 F	1-Octanol	2-Butanone	50
ULT-10 F	1,2-Dimethoxyethane	Nitrobenzene	50
ULT-10 F	Ethylene glycol monobutyl ether	-	-
ULT-10 F	Water	-	-
ULT-10 F	Water	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-10 F	Propylene glycol methyl ether acetate	-	-
ULT-10 F	1,4-Dioxane	Nitrobenzene	50
ULT-10 F	1,4-Dioxane	Water	50
ULT-10 F	Acetone	Nitrobenzene	50
ULT-10 F	Cyclopentanol	-	-
ULT-10 F	1-Heptanol	-	-
ULT-10 F	2-Hexanol	-	-
ULT-10 F	Propylene glycol methyl ether acetate	-	-
ULT-11 F1	Ethylacetate	-	-
ULT-11 F1	Acetonitrile	-	-
ULT-11 F1	2-Butanone	Acetonitrile	50
ULT-11 F1	Propionitrile	-	-
ULT-11 F1	2-Butanone	-	-
ULT-11 F1	1,2-Dimethoxyethane	2-Butanone	50
ULT-11 F1	1,4-Dioxane	Acetonitrile	50
ULT-11 F1	Acetone	Methanol	50
ULT-11 F1	Ethyl formate	-	-
ULT-11 F1	Acetone	Methanol	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-11 F1	Acetone	Acetonitrile	50
ULT-11 F1	Methoxyethyl acetate	-	-
ULT-11 F1	2-Pentanol	-	-
ULT-11 F1	Dimethylcarbonate	-	-
ULT-11 F1	(R)-(-)-2-Octanol	-	-
ULT-11 F1	Dimethylcarbonate	-	-
ULT-11 F1	Nitromethane	-	-
ULT-11 F1	Acetone	-	-
ULT-11 F1	2-Butanone	Acetone	50
ULT-11 F1	Acetonitrile	-	-
ULT-11 F1	Propyl acetate	-	-
ULT-11 F1	1,4-Dioxane	Methanol	50
ULT-11 F1	Ethylacetate	-	-
ULT-11 F1	2-Hexanol	-	-
ULT-11 F1	N,N-Dimethylformamide	-	-
ULT-11 F1	2-Hexanol	-	-
ULT-11 F1	2-Butanone	Acetone	50
ULT-11 F1	4-Hydroxy-4-methyl-2-pentanol	-	-
ULT-11 F1	1-Octanol	Acetone	50
ULT-11 F1	2-Butanone	Nitrobenzene	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-11 F1	2-Butanone	-	-
ULT-11 F1	Diethylene glycol dimethylether	-	-
ULT-11 F1	Acetone	-	-
ULT-11 F1	2,2,2-Trifluoroethanol	-	-
ULT-11 F1	1-Hexanol	-	-
ULT-11 F1	Methyl-4-2-Pentanol	-	-
ULT-11 F1	1,2-Dimethoxyethane	Acetonitrile	50
ULT-11 F1	Nitromethane	-	-
ULT-11 F1	N,N-Dimethylformamide	-	-
ULT-11 F1	2-Hexanol	-	-
ULT-11 F1	1,2-Dimethoxyethane	Acetonitrile	50
ULT-11 F1	tert-Butanol	-	-
ULT-11 F1	2-Ethoxyethanol	-	-
ULT-11 F1	Acetone	Acetonitrile	50
ULT-11 F1	1,2-Dimethoxyethane	1,4-Dioxane	50
ULT-11 F1	Acetonitrile	Nitrobenzene	50
ULT-11 F1	2-Hexanol	-	-
ULT-11 F1	Nitromethane	-	-
ULT-11 F1	1,2-Dimethoxyethane	Acetone	50
ULT-11 F1	2-Butanone	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-11 F1	1-Heptanol	-	-
ULT-11 F1	Ethyl formate	-	-
ULT-11 F1	Methanol	Water	50
ULT-11 F1	tert-Butanol	-	-
ULT-11 F1	1-Methoxy-2-propanol	-	-
ULT-11 F1	Diethylene glycol dimethylether	-	-
ULT-11 F1	2-Butanone	Nitrobenzene	50
ULT-11 F1	2-Butanone	Acetonitrile	50
ULT-11 F1	Methyl-4-2-Pentanol	-	-
ULT-11 F1	Nitroethane	-	-
ULT-11 F1	Methyl-4-2-Pentanol	-	-
ULT-11 F1	2-Hexanol	-	-
ULT-11 F1	1,2-Dimethoxyethane	Acetone	50
ULT-11 F1	Nitromethane	-	-
ULT-11 F1	Nitroethane	-	-
ULT-11 F1	2-Butanone	-	-
ULT-11 F1	Methyl-4-2-Pentanol	-	-
ULT-11 F1	Ethylacetate	-	-
ULT-11 F1	2-Pentanol	-	-
ULT-11 F1	2-Pentanol	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-11 F1	1-Heptanol	-	-
ULT-11 F1	2-Ethoxyethyl acetate	-	-
ULT-11 F1	Propionitrile	-	-
ULT-11 F1	1-Hexanol	-	-
ULT-11 F1	Acetone	Tetrahydrofuran	50
ULT-11 F1	Propylene glycol methyl ether acetate	-	-
ULT-11 F1	1-Octanol	2-Butanone	50
ULT-11 F1	Acetone	Acetonitrile	50
ULT-11 F1	Dimethylcarbonate	-	-
ULT-11 F1	1,4-Dioxane	2-Butanone	50
ULT-11 F1	Ethyl formate	-	-
ULT-11 F1	Methyl-4-2-Pentanol	-	-
ULT-11 F1	2-Butanone	Acetone	50
ULT-11 F1	Methanol	Water	50
ULT-11 F1	2-Butanone	-	-
ULT-11 F1	Ethyl formate	-	-
ULT-11 F1	tert-Butanol	-	-
ULT-11 F1	2-Butanone	Tetrahydrofuran	50
ULT-11 F1	Ethyl formate	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-11 F1	Methoxyethyl acetate	-	-
ULT-11 F1	1,2-Dimethoxyethane	Acetonitrile	50
ULT-11 F1	2-Butanone	Acetonitrile	50
ULT-11 F1	1,2-Dimethoxyethane	Tetrahydrofuran	50
ULT-11 F1	Ethylacetate	-	-
ULT-11 F1	Propionitrile	-	-
ULT-11 F1	2-Pentanol	-	-
ULT-11 F1	2-Butanone	Acetone	50
ULT-11 F1	1,2-Dimethoxyethane	2-Butanone	50
ULT-11 F1	2-Hexanol	-	-
ULT-11 F1	Methyl-4-2-Pentanol	-	-
ULT-11 F1	Ethyl formate	-	-
ULT-11 F1	1-Hexanol	-	-
ULT-11 F1	1-Hexanol	-	-
ULT-11 F1	Methyl-4-2-Pentanol	-	-
ULT-11 F1	1-Heptanol	-	-
ULT-11 F1	1-Hexanol	-	-
ULT-11 F1	Ethylene glycol monobutyl ether	-	-
ULT-11 F1	Acetone	-	-
ULT-11 F1	2-Ethoxyethyl acetate	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-11 F1	Methanol	Water	50
ULT-11 F1	1-Methoxy-2-propanol	-	-
ULT-11 F1	(R)-(-)-2-Octanol	-	-
ULT-11 F1	Methanol	Water	50
ULT-11 F1	Ethyl formate	-	-
ULT-11 F1	Acetonitrile	Tetrahydrofuran	50
ULT-11 F1	2-Hexanol	-	-
ULT-11 F1	Propylene glycol methyl ether acetate	-	-
ULT-11 F1	1,4-Dioxane	Acetone	50
ULT-11 F1	Nitroethane	-	-
ULT-11 F1	Acetonitrile	Water	50
ULT-11 F1	Tetrahydropyran	-	-
ULT-11 F1	Isobutanol	-	-
ULT-11 F1	Water	-	-
ULT-11 F1	Acetone	-	-
ULT-11 F1	1,4-Dioxane	Nitrobenzene	50
ULT-11 F1	2-Pentanol	-	-
ULT-11 F1	2-Ethoxyethanol	-	-
ULT-11 F1	Acetonitrile	Tetrahydrofuran	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-11 F1	2-Pentanol	-	-
ULT-11 F1	1-Hexanol	-	-
ULT-11 F1	2-Hexanol	-	-
ULT-11 F1	1-Heptanol	-	-
ULT-11 F1	Ethylene glycol monobutyl ether	-	-
ULT-11 F1	2-Butanone	-	-
ULT-11 F1	2-Butanone	Nitrobenzene	50
ULT-11 F1	Tetrahydropyran	-	-
ULT-11 F1	Methanol	Water	50
ULT-11 F1	2-Butanone	-	-
ULT-11 F1	Propylene glycol methyl ether acetate	-	-
ULT-11 F1	2-Hexanol	-	-
ULT-11 F1	4-Hydroxy-4-methyl-2-pentanone	-	-
ULT-11 F1	1,2-Dimethoxyethane	2-Butanone	50
ULT-11 F1	Acetone	Acetonitrile	50
ULT-11 F1	Acetone	Nitrobenzene	50
ULT-11 F1	Ethylacetate	-	-
ULT-11 F1	Ethylene glycol monobutyl ether	-	-
ULT-11 F1	2-Butanone	Acetonitrile	50

Form	Solvent 1		Solvent 2	% solvent 1
ULT-11 F1	Water		-	-
ULT-11 F1	Acetone		Acetonitrile	50
ULT-11 F1	Dimethylcarbonate		-	-
ULT-11 F1	2-Butanone		Acetonitrile	50
ULT-11 F1	1,2-Dimethoxyethane		Acetone	50
ULT-11 F1	1-Hexanol		-	-
ULT-11 F1	Propylene glycol methyl ether acetate		-	-
ULT-11 F1	2-Pentanol		-	-
ULT-11 F1	Nitroethane		-	-
ULT-11 F1	Acetone		-	-
ULT-11 F1	2,2,2-Trifluoroethanol		-	-
ULT-11 F1	Methyl-4-2-Pentanol		-	-
ULT-11 F1	2-Hexanol		-	-
ULT-11 F1	2-Butanone		-	-
ULT-11 F1	Dimethylcarbonate		-	-
ULT-11 F1	Diethylene glycol dimethylether		-	-
ULT-11 F1	(R)-(-)-2-Octanol		-	-
ULT-11 F1	1,2-Diethoxyethane		-	-
ULT-11 F1	2-Butanone		Acetone	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-11 F1	2-Hexanol	-	-
ULT-11 F1	(R) - (-) - 2-Octanol	-	-
ULT-11 F1	Propylene glycol methyl ether acetate	-	-
ULT-11 F1	2-Ethoxyethanol	-	-
ULT-11 F1	1,4-Dioxane	Acetonitrile	50
ULT-11 F1	Acetone	Acetonitrile	50
ULT-11 F1	Acetonitrile	Tetrahydrofuran	50
ULT-11 F1	Water	-	-
ULT-11 F1	1,2-Dimethoxyethane	Acetone	50
ULT-11 F1	Nitromethane	-	-
ULT-11 F1	1,4-Dioxane	Acetone	50
ULT-11 F1	1,4-Dioxane	-	-
ULT-11 F1	Propionitrile	-	-
ULT-11 F1	2-Butanone	Acetone	50
ULT-11 F1	Ethylacetate	-	-
ULT-11 F1	2-Hexanol	-	-
ULT-11 F1	1,2-Dimethoxyethane	Acetonitrile	50
ULT-11 F1	Methyl-4-2-Pentanol	-	-
ULT-11 F1	N,N-Dimethylacetamide	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-11	F1	1,4-Dioxane	50
ULT-11	F1	1-Octanol	50
ULT-11	F1	Nitromethane	-
ULT-11	F1	2-Butanone	50
ULT-11	F1	1-Hexanol	-
ULT-11	F1	Acetone	-
ULT-11	F1	1-Octanol	50
ULT-11	F1	Nitromethane	-
ULT-11	F1	1,2-Dimethoxyethane	50
ULT-11	F1	1,2-Dimethoxyethane	50
ULT-11	F1	2-Butanone	50
ULT-11	F1	Ethylacetate	-
ULT-11	F1	Propionitrile	-
ULT-11	F1	Methyl-4-2-Pentanol	-
ULT-11	F1	Cyclopentanol	-
ULT-11	F1	1-Heptanol	-
ULT-11	F1	Ethylacetate	-
ULT-11	F1	Dimethylcarbonate	-
ULT-11	F1	Acetonitrile	-
ULT-11	F1	Dimethylcarbonate	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-11 F1	Methyl propionate	-	-
ULT-11 F1	Tetrahydropyran	-	-
ULT-11 F1	Methanol	Water	50
ULT-11 F1	Acetone	Acetonitrile	50
ULT-11 F1	1,4-Dioxane	-	-
ULT-11 F1	1,2-Dimethoxyethane	Nitrobenzene	50
ULT-11 F1	2-Ethoxyethyl acetate	-	-
ULT-11 F1	Acetonitrile	Water	50
ULT-11 F1	Acetonitrile	Tetrahydrofuran	50
ULT-11 F1	Water	-	-
ULT-11 F1	N,N-Dimethylacetamide	-	-
ULT-11 F1	Methyl-4-2-Pentanol	-	-
ULT-11 F1	Methanol	Water	50
ULT-11 F1	2-Butanone	-	-
ULT-11 F1	Methyl-4-2-Pentanol	-	-
ULT-11 F1	2-Hexanol	-	-
ULT-11 F1	Acetone	Nitrobenzene	50
ULT-11 F1	2-Pentanol	-	-
ULT-11 F1	2-Pentanol	-	-
ULT-11 F1	Ethyl formate	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-11 F1	Methyl-4-2-Pentanol	-	-
ULT-11 F1	1,2-Dimethoxyethane	1,4-Dioxane	50
ULT-11 F1	1,4-Dioxane	Tetrahydrofuran	50
ULT-11 F1	1-Hexanol	-	-
ULT-11 F1	Ethanol	-	-
ULT-11 F1	Acetonitrile	-	-
ULT-11 F1	Ethanol	-	-
ULT-11 F1	Propyl acetate	-	-
ULT-11 F1	Ethyl formate	-	-
ULT-11 F1	Ethyl formate	-	-
ULT-11 F1	1,4-Dioxane	Acetonitrile	50
ULT-11 F1	2-Butanone	Acetone	50
ULT-11 F1	2-Hexanol	-	-
ULT-11 F1	Ethyl formate	-	-
ULT-11 F1	Acetone	Acetonitrile	50
ULT-11 F1	1,4-Dioxane	Tetrahydrofuran	50
ULT-11 F1	Acetone	Acetonitrile	50
ULT-11 F1	1-Heptanol	-	-
ULT-11 F1	1,2-Dimethoxyethane	Acetone	50
ULT-11 F1	Dimethylcarbonate	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-11 F1	2-Butanone	Acetonitrile	50
ULT-11 F1	1,4-Dioxane	2-Butanone	50
ULT-11 F1	Propionitrile	-	-
ULT-11 F1	Methanol	Water	50
ULT-11 F1	Propionitrile	-	-
ULT-11 F1	Methanol	Water	50
ULT-11 F1	Ethylacetate	-	-
ULT-11 F1	1,2-Dimethoxyethane	Acetonitrile	50
ULT-11 F1	2-Pentanol	-	-
ULT-11 F1	2-Butanone	-	-
ULT-11 F1	Methyl-4-2-Pentanol	-	-
ULT-11 F1	1,2-Dimethoxyethane	1-Octanol	50
ULT-11 F1	Dimethylcarbonate	-	-
ULT-11 F1	Methyl-4-2-Pentanol	-	-
ULT-11 F1	Nitromethane	-	-
ULT-11 F1	1-Octanol	Acetonitrile	50
ULT-11 F1	1,2-Dimethoxyethane	-	-
ULT-11 F1	Acetone	Acetonitrile	50
ULT-11 F1	2-Butanone	Acetone	50
ULT-11 F1	Acetone	Acetonitrile	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-11	F1	1,4-Dioxane	Acetonitrile
ULT-11	F1	Nitroethane	-
ULT-11	F1	2-Butanone	Acetonitrile
ULT-11	F1	Dimethylcarbonate	-
ULT-11	F1	Acetone	-
ULT-11	F1	2-Pentanol	-
ULT-11	F1	1-Hexanol	-
ULT-11	F1	Acetonitrile	-
ULT-11	F1	Propionitrile	-
ULT-11	F1	Ethylacetate	-
ULT-11	F1	Tetrahydropyran	-
ULT-11	F1	1,4-Dioxane	2-Butanone
ULT-11	F1	Methanol	Water
ULT-11	F1	2-Pentanol	-
ULT-11	F1	Methanol	Water
ULT-11	F1	2-Ethoxyethanol	-
ULT-11	F1	2-Butanone	-
ULT-11	F1	Acetonitrile	Water
ULT-11	F1	1,2-Dimethoxyethane	2-Butanone
ULT-12	H	Cyclohexanol	-

[illegible]

Form	Solvent 1	Solvent 2	% solvent 1
ULT-13 K	Nitroethane	-	-
ULT-13 K	1,4-Dioxane	Nitrobenzene	50
ULT-13 K	Acetonitrile	Nitrobenzene	50
ULT-13 K	Methoxyethyl acetate	-	-
ULT-13 K	2-Ethoxyethanol	-	-
ULT-13 K	1,2-Dimethoxyethane	1-Octanol	50
ULT-13 K	Diethylene glycol dimethylether	-	-
ULT-13 K	Cyclopentanol	-	-
ULT-13 K	N,N-Dimethylformamide	-	-
ULT-13 K	Acetonitrile	Nitrobenzene	50
ULT-13 K	2-Butanone	Nitrobenzene	50
ULT-13 K	1-Octanol	Tetrahydrofuran	50
ULT-13 K	Acetone	Nitrobenzene	50
ULT-13 K	Ethylene glycol monobutyl ether	-	-
ULT-13 K	1-Octanol	Acetone	50
ULT-13 K	2-Butanone	Nitrobenzene	50
ULT-13 K	Cyclopentanol	-	-
ULT-13 K	Dimethylcarbonate	-	-
ULT-13 K	2-Ethoxyethyl acetate	-	-
ULT-13 K	N-Methyl Pyrrolidone	Tetrahydrofuran	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-13 K	N-Methyl Pyrrolidone	Water	50
ULT-13 K	Methoxyethyl acetate	-	-
ULT-13 K	2-Ethoxyethyl acetate	-	-
ULT-13 K	Propylene glycol methyl ether acetate	-	-
ULT-13 K	N,N-Dimethylformamide	-	-
ULT-13 K	N,N-Dimethylformamide	-	-
ULT-13 K	1,2-Dimethoxyethane	Nitrobenzene	50
ULT-13 K	2-Ethoxyethyl acetate	-	-
ULT-13 K	Acetonitrile	Nitrobenzene	50
ULT-13 K	4-Hydroxy-4-methyl-2-pentanone	-	-
ULT-13 K	Acetonitrile	Nitrobenzene	50
ULT-13 K	1,4-Dioxane	Nitrobenzene	50
ULT-13 K	1-Octanol	2-Butanone	50
ULT-13 K	4-Hydroxy-4-methyl-2-pentanone	-	-
ULT-13 K	N,N-Dimethylformamide	-	-
ULT-13 K	1,4-Dioxane	Nitrobenzene	50
ULT-13 K	Acetonitrile	Nitrobenzene	50
ULT-13 K	2-Ethoxyethanol	-	-
ULT-13 K	Cyclopentanol	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-13 K	Acetone	Nitrobenzene	50
ULT-13 K	Diethylene glycol dimethylether	-	-
ULT-13 K	2-Butanone	Nitrobenzene	50
ULT-13 K	N,N-Dimethylacetamide	-	-
ULT-13 K	1-Octanol	2-Butanone	50
ULT-13 K	Acetonitrile	Nitrobenzene	50
ULT-13 K	Acetone	Nitrobenzene	50
ULT-13 K	1,2-Dimethoxyethane	Nitrobenzene	50
ULT-13 K	Dimethylcarbonate	-	-
ULT-13 K	Ethylene glycol monobutyl ether	-	-
ULT-13 K	1,2-Dimethoxyethane	Nitrobenzene	50
ULT-13 K	N,N-Dimethylformamide	-	-
ULT-13 K	2-Butanone	Nitrobenzene	50
ULT-13 K	Ethylene glycol monobutyl ether	-	-
ULT-13 K	2-Butanone	Nitrobenzene	50
ULT-13 K	Cyclopentanol	-	-
ULT-13 K	4-Hydroxy-4-methyl-2-pentanone	-	-
ULT-13 K	N,N-Dimethylformamide	-	-
ULT-13 K	Acetone	Nitrobenzene	50
ULT-13 K	N,N-Dimethylacetamide	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-13 K	1,4-Dioxane	Nitrobenzene	50
ULT-13 K	Acetonitrile	Nitrobenzene	50
ULT-13 K	2-Ethoxyethyl acetate	-	-
ULT-13 K	Nitroethane	-	-
ULT-13 K	N,N-Dimethylacetamide	-	-
ULT-13 K	1,4-Dioxane	Nitrobenzene	50
ULT-13 K	2-Ethoxyethyl acetate	-	-
ULT-13 K	1,2-Dimethoxyethane	Nitrobenzene	50
ULT-13 K	Methoxyethyl acetate	-	-
ULT-13 K	Cyclopentanol	-	-
ULT-13 K	2-Ethoxyethyl acetate	-	-
ULT-13 K	N,N-Dimethylformamide	-	-
ULT-13 K	Propylene glycol methyl ether acetate	-	-
ULT-13 K	1-Octanol	2-Butanone	50
ULT-13 K	Acetonitrile	Nitrobenzene	50
ULT-13 K	1-Octanol	Acetone	50
ULT-13 K	1,2-Dimethoxyethane	Nitrobenzene	50
ULT-13 K	Nitroethane	-	-
ULT-13 K	2-Butanone	Nitrobenzene	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-13 K	1-Octanol	Acetone	50
ULT-13 K	Tetrahydropyran	-	-
ULT-13 K	2-Butanone	Tetrahydrofuran	50
ULT-13 K	1,4-Dioxane	1-Octanol	50
ULT-13 K	1,4-Dioxane	1-Octanol	50
ULT-13 K	1-Octanol	2-Butanone	50
ULT-13 K	Cyclopentanol	-	-
ULT-13 K	2-Pentanol	-	-
ULT-13 K	1-Nitropropane	-	-
ULT-13 K	2-Ethoxyethanol	-	-
ULT-13 K	2-Pentanol	-	-
ULT-13 K	Nitroethane	-	-
ULT-13 K	1,2-Dimethoxyethane	1-Octanol	50
ULT-13 K	1,2-Dimethoxyethane	1-Octanol	50
ULT-13 K	1-Butanol	-	-
ULT-13 K	Nitroethane	-	-
ULT-13 K	Butyronitrile	-	-
ULT-13 K	1-Nitropropane	-	-
ULT-13 K	4-Hydroxy-4-methyl-2-pentanone	-	-
ULT-13 K	2-Butanone	Nitrobenzene	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-13 K	Cyclopentanol	-	-
ULT-13 K	N,N-Dimethylformamide	-	-
ULT-13 K	1-Octanol	Tetrahydrofuran	50
ULT-13 K	N-Methyl Pyrrolidone	Tetrahydrofuran	50
ULT-13 K	1,4-Dioxane	1-Octanol	50
ULT-13 K	1-Octanol	Acetone	50
ULT-13 K	2-Ethoxyethanol	-	-
ULT-13 K	Cyclopentanol	-	-
ULT-13 K	Furfuryl alcohol	-	-
ULT-13 K	Ethylacetate	-	-
ULT-13 K	1-Octanol	Tetrahydrofuran	50
ULT-13 K	2-Ethoxyethyl acetate	-	-
ULT-13 K	Acetonitrile	Nitrobenzene	50
ULT-13 K	Ethylene glycol monobutyl ether	-	-
ULT-13 K	1,2-Dimethoxyethane	Nitrobenzene	50
ULT-13 K	Nitroethane	-	-
ULT-13 K	1,4-Dioxane	Nitrobenzene	50
ULT-13 K	N,N-Dimethylacetamide	-	-
ULT-13 K	2-Ethoxyethyl acetate	-	-
ULT-13 K	1,2-Dimethoxyethane	Nitrobenzene	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-13 K	Acetonitrile	Nitrobenzene	50
ULT-13 K	Methoxyethyl acetate	-	-
ULT-13 K	Cyclopentanone	-	-
ULT-13 K	2-Ethoxyethyl acetate	-	-
ULT-13 K	2-Butanone	Nitrobenzene	50
ULT-13 K	1,4-Dioxane	Nitrobenzene	50
ULT-13 K	N,N-Dimethylformamide	-	-
ULT-13 K	2-Butanone	Nitrobenzene	50
ULT-13 K	Acetone	Nitrobenzene	50
ULT-13 K	Diethylene glycol dimethylether	-	-
ULT-13 K	Cyclopentanol	-	-
ULT-13 K	Cyclopentanol	-	-
ULT-13 K	Acetone	Nitrobenzene	50
ULT-13 K	2-Ethoxyethanol	-	-
ULT-13 K	Cyclopentanone	-	-
ULT-13 K	Methoxyethyl acetate	-	-
ULT-13 K	Acetonitrile	Nitrobenzene	50
ULT-13 K	N,N-Dimethylformamide	-	-
ULT-13 K	4-Hydroxy-4-methyl-2-pentanone	-	-
ULT-13 K	1-Methoxy-2-propanol	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-13 K	Cyclopentanol	-	-
ULT-13 K	Cyclopentanol	-	-
ULT-13 K	2-Butanone	Nitrobenzene	50
ULT-13 K	Acetone	N-Methyl Pyrrolidone	50
ULT-13 K	N,N-Dimethylformamide	-	-
ULT-13 K	2-Ethoxyethyl acetate	-	-
ULT-13 K	Acetone	Nitrobenzene	50
ULT-13 K	Methoxyethyl acetate	-	-
ULT-13 K	Isobutanol	-	-
ULT-13 K	Methoxyethyl acetate	-	-
ULT-13 K	Acetonitrile	Nitrobenzene	50
ULT-13 K	2-Ethoxyethyl acetate	-	-
ULT-13 K	N,N-Dimethylacetamide	-	-
ULT-13 K	Diethylene glycol dimethylether	-	-
ULT-13 K	1,2-Dimethoxyethane	N-Methyl Pyrrolidone	50
ULT-13 K	Acetone	Nitrobenzene	50
ULT-13 K	Cyclopentanol	-	-
ULT-13 K	Cyclopentanol	-	-
ULT-13 K	N-Methyl Pyrrolidone	Water	50
ULT-13 K	Acetone	N-Methyl Pyrrolidone	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-13 K	2-Butanone	Nitrobenzene	50
ULT-13 K	2-Ethoxyethyl acetate	-	-
ULT-13 K	Acetonitrile	N-Methyl Pyrrolidone	50
ULT-14 L	Tetrahydropyran	-	-
ULT-14 L	Tetrahydropyran	-	-
ULT-14 L	Tetrahydropyran	-	-
ULT-14 L	Tetrahydropyran	-	-
ULT-14 L	Tetrahydropyran	-	-
ULT-14 L	Tetrahydropyran	-	-
ULT-14 L	Tetrahydropyran	-	-
ULT-14 L	Tetrahydropyran	-	-
ULT-14 L	Tetrahydropyran	-	-
ULT-14 L	Tetrahydropyran	-	-
ULT-14 L	Tetrahydropyran	-	-
ULT-14 L	Tetrahydropyran	-	-
ULT-14 L	Tetrahydropyran	-	-
ULT-14 L	Tetrahydropyran	-	-
ULT-14 L	Tetrahydropyran	-	-
ULT-14 L	Tetrahydropyran	-	-
ULT-14 L	Tetrahydropyran	-	-
ULT-15 Q	1,2-Dimethoxyethane	N-Methyl Pyrrolidone	50
ULT-15 Q	Nitrobenzene	Tetrahydrofuran	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-15 Q	Acetonitrile	N-Methyl Pyrrolidone	50
ULT-15 Q	1,4-Dioxane	N-Methyl Pyrrolidone	50
ULT-15 Q	Acetone	N-Methyl Pyrrolidone	50
ULT-15 Q	N-Methyl Pyrrolidone	Tetrahydrofuran	50
ULT-15 Q	N-Methyl Pyrrolidone	Tetrahydrofuran	50
ULT-15 Q	1,4-Dioxane	N-Methyl Pyrrolidone	50
ULT-15 Q	Nitrobenzene	Tetrahydrofuran	50
ULT-15 Q	N-Methyl Pyrrolidone	Tetrahydrofuran	50
ULT-15 Q	Acetonitrile	N-Methyl Pyrrolidone	50
ULT-15 Q	1,2-Dimethoxyethane	N-Methyl Pyrrolidone	50
ULT-15 Q	1,4-Dioxane	N-Methyl Pyrrolidone	50
ULT-15 Q	2-Butanone	N-Methyl Pyrrolidone	50
ULT-15 Q	2-Butanone	N-Methyl Pyrrolidone	50
ULT-15 Q	1,4-Dioxane	N-Methyl Pyrrolidone	50
ULT-15 Q	2-Butanone	N-Methyl Pyrrolidone	50
ULT-15 Q	1,4-Dioxane	N-Methyl Pyrrolidone	50
ULT-15 Q	Acetonitrile	N-Methyl Pyrrolidone	50
ULT-15 Q	Acetone	N-Methyl Pyrrolidone	50
ULT-15 Q	1,2-Dimethoxyethane	N-Methyl Pyrrolidone	50
ULT-15 Q	Acetonitrile	N-Methyl Pyrrolidone	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-15 Q	2-Butanone	N-Methyl Pyrrolidone	50
ULT-15 Q	N-Methyl Pyrrolidone	Tetrahydrofuran	50
ULT-15 Q	1,2-Dimethoxyethane	N-Methyl Pyrrolidone	50
ULT-15 Q	Acetone	N-Methyl Pyrrolidone	50
ULT-15 Q	N-Methyl Pyrrolidone	Tetrahydrofuran	50
ULT-15 Q	2-Butanone	N-Methyl Pyrrolidone	50
ULT-15 Q	2-Butanone	N-Methyl Pyrrolidone	50
ULT-15 Q	Nitrobenzene	Tetrahydrofuran	50
ULT-15 Q	Acetonitrile	N-Methyl Pyrrolidone	50
ULT-15 Q	Acetonitrile	N-Methyl Pyrrolidone	50
ULT-15 Q	Acetone	N-Methyl Pyrrolidone	50
ULT-15 Q	2-Butanone	N-Methyl Pyrrolidone	50
ULT-15 Q	1,2-Dimethoxyethane	N-Methyl Pyrrolidone	50
ULT-15 Q	Acetonitrile	N-Methyl Pyrrolidone	50
ULT-15 Q	1,2-Dimethoxyethane	N-Methyl Pyrrolidone	50
ULT-15 Q	Nitrobenzene	Tetrahydrofuran	50
ULT-15 Q	1,4-Dioxane	N-Methyl Pyrrolidone	50
ULT-15 Q	Nitrobenzene	Tetrahydrofuran	50
ULT-15 Q	N-Methyl Pyrrolidone	Tetrahydrofuran	50
ULT-15 Q	Acetonitrile	N-Methyl Pyrrolidone	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-15 Q	1,2-Dimethoxyethane	N-Methyl Pyrrolidone	50
ULT-15 Q	Acetonitrile	N-Methyl Pyrrolidone	50
ULT-15 Q	N-Methyl Pyrrolidone	Tetrahydrofuran	50
ULT-15 Q	2-Butanone	N-Methyl Pyrrolidone	50
ULT-15 Q	1,2-Dimethoxyethane	N-Methyl Pyrrolidone	50
ULT-15 Q	1,2-Dimethoxyethane	N-Methyl Pyrrolidone	50
ULT-15 Q	N-Methyl Pyrrolidone	Water	50
ULT-15 Q	1,4-Dioxane	N-Methyl Pyrrolidone	50
ULT-15 Q	Acetone	N-Methyl Pyrrolidone	50
ULT-15 Q	1,2-Dimethoxyethane	N-Methyl Pyrrolidone	50
ULT-15 Q	Nitrobenzene	Tetrahydrofuran	50
ULT-15 Q	Acetone	N-Methyl Pyrrolidone	50
ULT-15 Q	Acetonitrile	N-Methyl Pyrrolidone	50
ULT-15 Q	Nitrobenzene	Tetrahydrofuran	50
ULT-15 Q	1,4-Dioxane	N-Methyl Pyrrolidone	50
ULT-15 Q	1,4-Dioxane	N-Methyl Pyrrolidone	50
ULT-15 Q	1,2-Dimethoxyethane	N-Methyl Pyrrolidone	50
ULT-15 Q	2-Butanone	N-Methyl Pyrrolidone	50
ULT-15 Q	1,4-Dioxane	N-Methyl Pyrrolidone	50
ULT-15 Q	Acetone	N-Methyl Pyrrolidone	50

Form	Solvent 1	Solvent 2	% solvent 1
ULT-16 R	2-Methoxyethanol	-	-
ULT-16 R	1-Butanol	-	-
ULT-16 R	1,4-Dioxane	N-Methyl Pyrrolidone	50
ULT-16 R	1,4-Dioxane	N-Methyl Pyrrolidone	50
ULT-16 R	1,4-Dioxane	N-Methyl Pyrrolidone	50
ULT-16 R	Acetone	N-Methyl Pyrrolidone	50
ULT-16 R	Nitrobenzene	Tetrahydrofuran	50
ULT-16 R	Furfuryl alcohol	-	-
ULT-16 R	Furfuryl alcohol	-	-
ULT-16 R	Acetonitrile	N-Methyl Pyrrolidone	50
ULT-16 R	Tetrahydrofurfurylalcohol	-	-
ULT-16 R	2-Butanone	N-Methyl Pyrrolidone	50
ULT-16 R	1-Octanol	Tetrahydrofuran	50
ULT-16 R	1-Octanol	Tetrahydrofuran	50
ULT-16 R	Acetonitrile	N-Methyl Pyrrolidone	50
ULT-16 R	Cyclohexanol	-	-
ULT-16 R	1,2-Dimethoxyethane	N-Methyl Pyrrolidone	50
ULT-16 R	Acetone	N-Methyl Pyrrolidone	50
ULT-17 S	N-Methyl Pyrrolidone	Water	50
ULT-18 T	2-Ethoxyethyl acetate	-	-

Form	Solvent 1	Solvent 2	% solvent 1
ULT-18 T	2-Ethoxyethyl acetate	-	-

Table II

Form	solvent 1	Solvent 2	(mg/mL) Stock Concentration	Evaporation Time (hrs)
ULT-4	A1 1,2-Dimethoxyethane	Tetrahydrofuran	366,5	21,5
ULT-4	A1 1,2-Dimethoxyethane	1,4-Dioxane	358,5	70,5
ULT-4	A1 N,N-Dimethylacetamide	-	360,5	111,4
ULT-4	A1 1,2-Dimethoxyethane	Acetone	359	21,5
ULT-4	A1 1-Propanol	-	237,3	70,5
ULT-4	A1 1,4-Dioxane	Acetonitrile	361,5	70,5
ULT-4	A1 1,4-Dioxane	-	358	21,5
ULT-4	A1 1,2-Dimethoxyethane	Tetrahydrofuran	366,5	70,5
ULT-4	A1 1,2-Dimethoxyethane	1,4-Dioxane	361,5	21,5
ULT-4	A1 1-Propanol	-	237,3	21,5
ULT-4	A1 Methoxy-2-1-Propanol	-	357	21,5
ULT-4	A1 Acetone	Tetrahydrofuran	361	21,5
ULT-4	A1 1,2-Dimethoxyethane	1,4-Dioxane	361,5	70,5
ULT-4	A1 1,2-Dimethoxyethane	1,4-Dioxane	361,5	21,5
ULT-4	A1 1,4-Dioxane	Acetonitrile	361,5	70,5
ULT-4	A1 Methyl propionate	-	360	111,4
ULT-4	A1 1,4-Dioxane	Acetone	354,5	70,5
ULT-4	A1 Methyl propionate	-	360	111,4

Form	solvent 1	Solvent 2	(mg/mL) Stock Concentration	Evaporation Time (hrs)
ULT-4	A1 1,2-Dimethoxyethane	1,4-Dioxane	358,5	70,5
ULT-5	A3 Tetrahydrofuran	-	359,5	70,5
ULT-5	A3 1,2-Dimethoxyethane	Acetone	359	70,5
ULT-5	A3 N,N-Dimethylacetamide	-	360,5	111,4
ULT-5	A3 Methyl propionate	-	360	111,4
ULT-5	A3 1,2-Dimethoxyethane	Acetone	359	70,5
ULT-5	A3 Tetrahydrofuran	-	359,5	21,5
ULT-5	A3 Methyl propionate	-	360	111,4
ULT-6	A4 N,N-Dimethylacetamide	-	367	167,1
ULT-6	A4 N,N-Dimethylacetamide	-	367	167,1
ULT-6	A4 Nitromethane	-	72,5	160,3
ULT-6	A4 1,4-Dioxane	Acetonitrile	361,5	21,5
ULT-6	A4 1,4-Dioxane	Acetone	354,5	21,5
ULT-6	A4 N,N-Dimethylacetamide	-	360,5	111,4
ULT-6	A4 N,N-Dimethylacetamide	-	360,5	111,4
ULT-6	A4 1,4-Dioxane	Tetrahydrofuran	357,5	21,5
ULT-6	A4 1,4-Dioxane	Tetrahydrofuran	357,5	21,5
ULT-7	B1 Methanol	1,4-Dioxane	364	21,5
ULT-7	B1 Methanol	1,4-Dioxane	364	21,5

Form	solvent 1	Solvent 2	(mg/mL) Stock Concentration	Evaporation Time (hrs)
ULT-7	B1 1,4-Dioxane	Methanol	356, 5	21, 5
ULT-7	B1 Methanol	1,4-Dioxane	364	70, 5
ULT-7	B1 1,4-Dioxane	Methanol	356, 5	70, 5
ULT-7	B1 1,4-Dioxane	Methanol	356, 5	21, 5
ULT-7	B1 Methanol	1,4-Dioxane	364	70, 5
ULT-8	C 1,4-Dioxane	Methanol	359	15, 1
ULT-8	C (R) - (-) - 2-Octanol	-	70, 8	15, 1
ULT-8	C 1,4-Dioxane	Tetrahydrofuran	355, 5	15, 1
ULT-8	C 1,2-Dimethoxyethane	Acetone	357, 5	15, 1
ULT-8	C Acetonitrile	-	102, 6	15, 1
ULT-8	C 1,4-Dioxane	Acetonitrile	355, 5	15, 1
ULT-8	C N,N-Dimethylformamide	-	358	111, 4
ULT-8	C N,N-Dimethylformamide	-	359, 5	167, 1
ULT-8	C Water	-	71, 1	15, 1
ULT-8	C 1,2-Dimethoxyethane	1,4-Dioxane	356	15, 1
ULT-8	C 1,2-Dimethoxyethane	1,4-Dioxane	356	15, 1
ULT-8	C 1,4-Dioxane	-	363	0
ULT-8	C 1,4-Dioxane	Methanol	359	15, 1
ULT-8	C 1,2-Dimethoxyethane	-	364	15, 1

Form	solvent 1	Solvent 2	(mg/mL) Stock Concentration	Evaporation Time (hrs)
ULT-8	C	Tetrahydrofuran	359,5	15,1
ULT-8	C	Isobutanol	181,5	15,1
ULT-8	C	1,2-Dimethoxyethane	357,5	15,1
ULT-8	C	Isopropyl acetate	73,7	15,1
ULT-8	C	1,2-Dimethoxyethane	356,5	15,1
ULT-8	C	2-Butanone	362,5	15,1
ULT-8	C	1,4-Dioxane	355,5	15,1
ULT-8	C	Water	71,1	15,1
ULT-8	C	Methanol	364,5	15,1
ULT-8	C	Isobutanol	181,5	15,1
ULT-8	C	1,4-Dioxane	355,5	15,1
ULT-8	C	Acetonitrile	102,6	15,1
ULT-8	C	tert-Butanol	355	15,1
ULT-8	C	1,2-Dimethoxyethane	356,5	15,1
ULT-8	C	1,4-Dioxane	354	15,1
ULT-8	C	Acetone	361,5	15,1
ULT-8	C	tert-Butanol	355	15,1
ULT-8	C	Cyclopentanone	361,5	15,1
ULT-8	C	(R) - (-) -2-Octanol	70,8	15,1

Form	solvent 1	Solvent 2	(mg/mL) Stock Concentration	Evaporation Time (hrs)
ULT-8	C 1,2-Dimethoxyethane	1,4-Dioxane	359	15,1
ULT-8	C Tetrahydrofuran	-	359,5	15,1
ULT-8	C Acetonitrile	-	70,9	70,5
ULT-8	C Acetone	Tetrahydrofuran	361,5	15,1
ULT-8	C Cyclopentanone	-	361,5	15,1
ULT-8	C 1-Nitropropane	-	71,8	167,1
ULT-8	C Methanol	1,4-Dioxane	364,5	15,1
ULT-8	C Acetonitrile	-	70,9	21,5
ULT-8	C 1,4-Dioxane	-	363	15,1
ULT-8	C 1,2-Dimethoxyethane	1,4-Dioxane	359	15,1
ULT-8	C Cyclopentanone	-	357,5	21,5
ULT-8	C 1,4-Dioxane	-	358	70,5
ULT-8	C 2-Ethoxyethyl acetate	-	119,7	160,3
ULT-8	C 1,4-Dioxane	Tetrahydrofuran	357,5	70,5
ULT-8	C N,N-Dimethylformamide	-	358	111,4
ULT-8	C 1,2-Dimethoxyethane	-	364	15,1
ULT-8	C 1,4-Dioxane	-	358	70,5
ULT-8	C 1,4-Dioxane	Tetrahydrofuran	357,5	70,5
ULT-8	C 2-Ethoxyethyl acetate	-	119,7	160,3

Form	solvent 1	Solvent 2	(mg/mL) Stock Concentration	Evaporation Time (hrs)
ULT-8	C	1,4-Dioxane	354	15,1
ULT-8	C	2-Ethoxyethyl acetate	119,7	111,4
ULT-9	D	2-Ethoxyethyl acetate	119	70,5
ULT-9	D	2-Methyl-4-pentanol	89,6	70,5
ULT-9	D	2-Ethoxyethyl acetate	119	70,5
ULT-9	D	2-Propanol	238,3	15,1
ULT-10	F	Water	72,2	21,5
ULT-10	F	2-Nitropropane	72,7	167,1
ULT-10	F	Water	72,2	70,5
ULT-11	F1	Isopropyl acetate	72,2	21,5
ULT-11	F1	Water	72,2	70,5
ULT-11	F1	(R)-(-)-2-Octanol	71,9	0
ULT-11	F1	Isopropyl acetate	73,7	257
ULT-11	F1	(R)-(-)-2-Octanol	70,9	0
ULT-11	F1	(R)-(-)-2-Octanol	70,9	0
ULT-11	F1	Water	72,2	21,5
ULT-11	F1	Cyclopentanone	357,5	70,5
ULT-11	F1	Nitromethane	70,9	167,1
ULT-12	H	Isobutanol	179,5	70,5

Form	solvent 1	Solvent 2	(mg/mL) Stock Concentration	Evaporation Time (hrs)
ULT-12	H Cyclopentanol	-	181	70,5
ULT-12	H Cyclopentanol	-	181	70,5
ULT-12	H Cyclopentanol	-	181	167,1
ULT-12	H Isobutanol	-	179,5	70,5
ULT-13	K N,N-Dimethylformamide	-	358	111,4
ULT-13	K Acetone	Tetrahydrofuran	361	167,1
ULT-13	K N,N-Dimethylformamide	-	359,5	167,1
ULT-13	K N,N-Dimethylformamide	-	359,5	21,5
ULT-13	K 1,2-Diethoxyethane	-	71,4	257
ULT-13	K N,N-Dimethylformamide	-	358	111,4
ULT-17	S 1,2-Diethoxyethane	-	71,3	21,5
ULT-17	S 1,2-Diethoxyethane	-	71,3	70,5
ULT-19	U 1,2-Dimethoxyethane	Methanol	361,5	70,5
ULT-19	U Acetone	Methanol	362,5	70,5
ULT-19	U Ethanol	-	287,6	21,5
ULT-19	U 1,2-Dimethoxyethane	Methanol	361,5	21,5
ULT-19	U Acetone	Methanol	362,5	21,5
ULT-19	U 1,2-Dimethoxyethane	Methanol	361,5	21,5
ULT-19	U 1,2-Dimethoxyethane	Methanol	355	15,1

Form	solvent 1	Solvent 2	(mg/mL) Stock Concentration	Evaporation Time (hrs)
ULT-19	U 1,4-Dioxane	Methanol	359	15,1
ULT-19	U Acetone	Methanol	370	15,1
ULT-19	U Acetone	Methanol	362,5	21,5
ULT-19	U Ethanol	-	287,6	21,5

Table III

Form	Solvent 1	(mg/mL) Stock Concentration	Anti solvent	Anti solvent - Solvent Ratio (x:1)
ULT-5	A3 1,2-Dimethoxyethane	36, 3	Toluene	2
ULT-5	A3 1,4-Dioxane	45, 4	Amyl ether	1
ULT-5	A3 Water	16, 9	Chloroform	4
ULT-6	A4 Water	16, 9	Chloroform	4
ULT-6	A4 Water	16, 9	Dichloromethane	4
ULT-6	A4 N-Methyl Pyrrolidone	504, 6	Nitromethane	2
ULT-6	A4 N-Methyl Pyrrolidone	504, 6	Dichloromethane	2
ULT-8	C 1,4-Dioxane	45, 4	Butyl benzene	1
ULT-8	C 1,2-Dimethoxyethane	36, 3	Toluene	1
ULT-8	C 1,4-Dioxane	45, 4	Nitromethane	4
ULT-8	C 1,4-Dioxane	45, 4	Hexafluorobenzene	1
ULT-8	C 1,4-Dioxane	45, 4	Toluene	1
ULT-8	C 1,4-Dioxane	45, 4	Butyl benzene	1
ULT-10	F 1,2-Dimethoxyethane	36, 3	Chloroform	1
ULT-10	F 1,2-Dimethoxyethane	36, 3	Hexafluorobenzene	1
ULT-11	F1 Acetonitrile	13, 5	Toluene	4
ULT-11	F1 Tetrahydrofuran	66, 8	Dichloromethane	4

Form	Solvent 1	(mg/mL) Stock Concentration	Anti solvent	Anti solvent - Solvent Ratio (x:1)
ULT-11	F1 Acetonitrile	13,5	Cyclohexane	4
ULT-11	F1 Water	16,9	Hexafluorobenzene	4
ULT-11	F1 Acetonitrile	13,5	1,2-Dichloroethane	4
ULT-11	F1 Acetonitrile	13,5	n-Heptane	4
ULT-11	F1 Water	16,9	tert-Butyl methyl ether	4
ULT-11	F1 Tetrahydrofuran	66,8	1,2-Dichloroethane	4
ULT-11	F1 Acetonitrile	13,5	Nitromethane	4
ULT-11	F1 2-Butanone	36,4	Dichloromethane	4
ULT-11	F1 tert-Butyl methyl ether	100,2	Acetone	4
ULT-11	F1 2-Butanone	36,4	Nitromethane	4
ULT-11	F1 Water	16,9	Hexafluorobenzene	4
ULT-11	F1 Acetonitrile	13,5	Chloroform	4
ULT-11	F1 2-Butanone	36,4	tert-Butyl methyl ether	4
ULT-11	F1 Tetrahydrofuran	66,8	Nitromethane	4
ULT-11	F1 Water	16,9	1,2-Dichloroethane	4
ULT-11	F1 2-Butanone	36,4	Chloroform	4
ULT-11	F1 1,2-Dimethoxyethane	36,3	Dichloromethane	4
ULT-11	F1 1,4-Dioxane	45,4	Dichloromethane	4

Form	Solvent 1	(mg/mL) Stock Concentration	Anti solvent	Anti solvent - Solvent Ratio (x:1)
ULT-11	F1 Acetonitrile	13, 5	tert-Butyl methyl ether	4
ULT-11	F1 2-Butanone	36, 4	Chloroform	4
ULT-11	F1 1,2-Dimethoxyethane	36, 3	Nitromethane	4
ULT-11	F1 2-Butanone	36, 4	Nitromethane	4
ULT-11	F1 2-Butanone	36, 4	Dichloromethane	4
ULT-11	F1 Acetonitrile	13, 5	Dichloromethane	4
ULT-11	F1 2-Butanone	36, 4	tert-Butyl methyl ether	4
ULT-11	F1 2-Butanone	36, 4	1,2-Dichloroethane	4
ULT-11	F1 1,4-Dioxane	45, 4	n-Heptane	1
ULT-11	F1 1,4-Dioxane	45, 4	2,6-Dimethyl-4-heptanone	2
ULT-11	F1 1,2-Dimethoxyethane	36, 3	1,2-Dichloroethane	4
ULT-11	F1 Acetonitrile	13, 5	Cyclohexane	4
ULT-11	F1 1,4-Dioxane	45, 4	tert-Butyl methyl ether	4
ULT-11	F1 Acetonitrile	13, 5	n-Heptane	4
ULT-11	F1 1,4-Dioxane	45, 4	Cyclohexane	1
ULT-11	F1 1,2-Dimethoxyethane	36, 3	Dichloromethane	4
ULT-11	F1 1,4-Dioxane	45, 4	Dichloromethane	4
ULT-11	F1 Methanol	101	n-Heptane	1

Form	Solvent 1	(mg/mL) Stock Concentration	Anti solvent	Anti solvent - Solvent Ratio (x:1)
ULT-11	F1 1,4-Dioxane	45,4	Chloroform	4
ULT-11	F1 Tetrahydrofuran	66,8	Chloroform	4
ULT-11	F1 2-Butanone	36,4	1,2-Dichloroethane	4
ULT-11	F1 1,4-Dioxane	45,4	1,2-Dichloroethane	4
ULT-11	F1 1,2-Dimethoxyethane	36,3	Nitromethane	4
ULT-11	F1 Tetrahydrofuran	66,8	Dichloromethane	4
ULT-11	F1 1,4-Dioxane	45,4	Toluene	1
ULT-11	F1 Acetonitrile	13,5	Toluene	4
ULT-11	F1 1,4-Dioxane	45,4	Amyl ether	1
ULT-11	F1 Tetrahydrofuran	66,8	1,2-Dichloroethane	2
ULT-11	F1 Acetonitrile	13,5	1,2-Dichloroethane	4
ULT-11	F1 1,2-Dimethoxyethane	36,3	1,2-Dichloroethane	4
ULT-11	F1 Acetonitrile	13,5	Nitromethane	4
ULT-16	R N-Methyl Pyrrolidone	504,6	Nitromethane	4
ULT-16	R N-Methyl Pyrrolidone	504,6	Dichloromethane	4
ULT-20	V Tetrahydrofuran	66,8	Chloroform	4

INTERNATIONAL SEARCH REPORT

International application No

PCT/NL2008/000129

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D473/34 C07F9/6561 A61K31/52 A61P31/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D C07F A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	WO 2007/013086 A (HETERO DRUGS LTD [IN]; PARTHASARADHI REDDY BANDI [IN]; RATHNAKAR REDDY) 1 February 2007 (2007-02-01) the whole document	1-57
X	US 5 935 946 A (MUNGER JR JOHN D [US] ET AL) 10 August 1999 (1999-08-10) cited in the application the whole document	1-57



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/NL2008/000129

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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