Supplementary Material for:

In Silico Screening of Molecular Imprinting Prepolymerization Systems: Oseltamivir Selective Polymers through Full-system Molecular Dynamics-based Studies

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Table of Contents

Elemental Analysis

CHN analysis of molecularly imprinted polymers (MIPs) and corresponding reference polymers(REFs)	Table S1	S3

Fourier Transform Infrared spectroscopy (FT-IR spectroscopy)

Molecularly imprinted polymers (MIPs) and corresponding reference polymers (REFs) prepared in acetonitrile and chloroform.

4-vinylpyridine (4VP)	Figure S1	S4
Acrylamide (ACA)	Figure S2	S4
2-hydroxyethyl methacrylate (HEMA)	Figure S3	S4
Methacrylric acid (MAA)	Figure S4	S5
2-(Trifluoromethyl)acrylic acid (TFMAA)	Figure S5	S5

Scanning Electron Microscopy (SEM)

SEM images of molecularly imprinted polymers (MIPs) and corresponding reference polymers (REFs) prepared in acetonitrile, chloroform.

4-vinylpyridine (4VP)	Figure S6	S6
Acryl amide (ACA)	Figure S7	S6
2-hydroxyethyl methacrylate (HEMA)	Figure S8	S6
Methacrylic acid (MAA)	Figure S9	S7
2-(Trifluoromethyl)acrylic acid (TFMAA)	Figure S10	S7

SEM images of molecularly imprinted polymers (MIPs) and corresponding reference polymers (REFs) prepared in methanol.

2-hydroxyethyl methacrylate (HEMA)	Figure S11	S7
2-(Trifluoromethyl)acrylic acid (TFMAA)	Figure S11	S7

BET (Brunauer–Emmett–Teller analysis)

BET surface area analysis of molecularly imprinted polymers (MIPs) and corresponding non-imprinted reference polymers (REFs) Table S2 S8

Laser Diffraction Analysis (size determination studies)

Graphical presentation of size determination studies on Molecularly Imprinted Polymers (MIPs) and corresponding reference polymers (REFs) prepared in acetonitrile and chloroform.

4-vinylpyridine (4VP) Figure S12 S9
Acryl amide (ACA) Figure S13 S10
2-hydroxyethyl methacrylate (HEMA) Figure S14 S11
Methacrylic acid (MAA) Figure S15 S12
2-(Trifluoromethyl)acrylic acid (TFMAA) Figure S16 S13

Tabulated presentation of size determination studies on Molecularly Imprinted Polymers (MIPs) and corresponding reference polymers Table S3 S14

Competitive binding studies

Competitive binding studies of methacrylic acid based molecularly imprinted polymer prepared in acetonitrile or chloroform and evaluated in acetonitrile, toluene or buffer.

Results from competitive binding studies Figure S17 S15

Elemental Analysis (CHN)

Table S1. CHN analysis results

Polymer[a]	Calculated Mass %[b]			Found Mass %[c]		
	C	**N**	**H**	**C**	**N**	**H**
4VP-CF-REF	62.5	2.1	7.1	60.3	1.9	7.3
4VP-CF-MIP	62.8	2.3	7.2	61.3	1.7	7.3
4VP-ACN-REF	62.5	2.0	7.1	60.6	1.8	7.1
4VP-ACN-MIP	62.8	2.2	7.2	61.0	1.7	7.2
ACA-CF-REF	59.8	2.1	7.1	57.8	2.1	7.2
ACA-CF-MIP	60.2	2.3	7.2	57.3	1.6	7.2
ACA-ACN-REF	59.9	2.1	7.1	58.4	1.8	7.2
ACA-ACN-MIP	60.2	2.3	7.2	57.8	2.0	7.2
HEM-CF-REF	59.9	0.7	7.2	57.5	< 0.3	7.4
HEM-CF-MIP	60.2	0.9	7.3	58.3	< 0.3	7.4
HEM-ACN-REF	59.9	0.7	7.2	58.5	< 0.3	7.3
HEM-ACN-MIP	60.2	0.9	7.3	58.2	< 0.3	7.3
MAA-CF-REF	60.1	0.7	7.1	58.0	< 0.3	7.3
MAA-CF-MIP	60.5	1.0	7.2	58.0	< 0.3	7.2
MAA-ACN-REF	60.2	0.7	7.1	58.0	< 0.3	7.2
MAA-ACN-MIP	60.5	0.9	7.2	58.0	< 0.3	7.2
TFM-CF-REF	57.1	0.7	6.5	57.5	< 0.3	7.1
TFM-CF-MIP	57.5	0.9	6.6	56.9	< 0.3	6.8
TFM-ACN-REF	57.2	0.7	6.5	56.2	< 0.3	6.8
TFM-ACN-MIP	57.5	0.9	6.6	55.8	< 0.3	6.8

[a] CHN analysis of reference- (REF) and molecularly imprinted polymers (MIPs) prepared in acetonitrile (ACN) and chloroform ($CHCl_3$). The following data designated Calculated and Found, are the mass percentage of carbon, hydrogen and nitrogen present in the molecularly imprinted polymers. The data designated: [b] Calculated have been that have been computed manually and the data designated [c] Found are results of CHN analysis.

Fourier Transfom Infrared Spectroscopy (FT-IR)
FT-IR spectra of Molecularly Imprinted Polymers (MIPs,) synthesized in acetonitrile (left images) and chloroform (right images). The continuous lines show spectra of molecularly imprinted polymers and the dashed lines show the spectra of corresponding reference polymers.

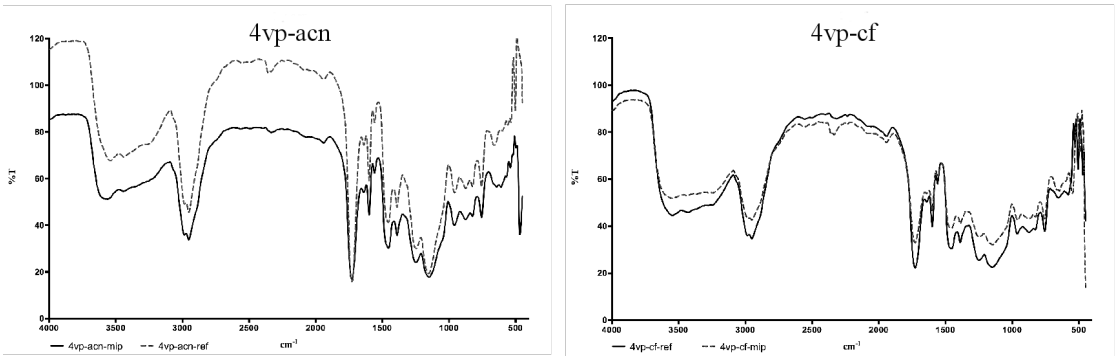

Figure S1. FT-IR spectra of 4-vinylpyridine polymers (4VP) produced in acetonitrile (left, 4vp-acn) and in chloroform (right, 4vp-cf). The continuous lines show spectra of molecularly imprinted polymers and the dashed lines show the spectra of corresponding reference polymers.

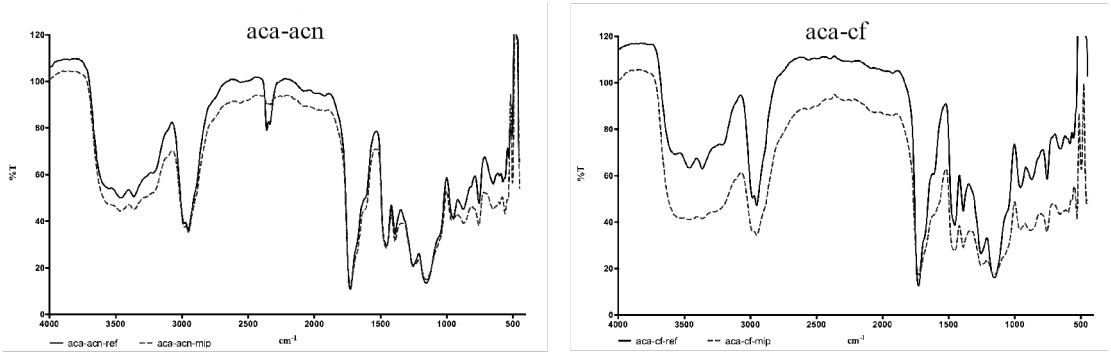

Figure S2. FT-IR spectra of acrylamide polymers (ACA) produced in acetonitrile (left, aca-acn) and in chloroform (right aca-cf). The continuous lines show spectra of molecularly imprinted polymers and the dashed lines show the spectra of corresponding reference polymers.

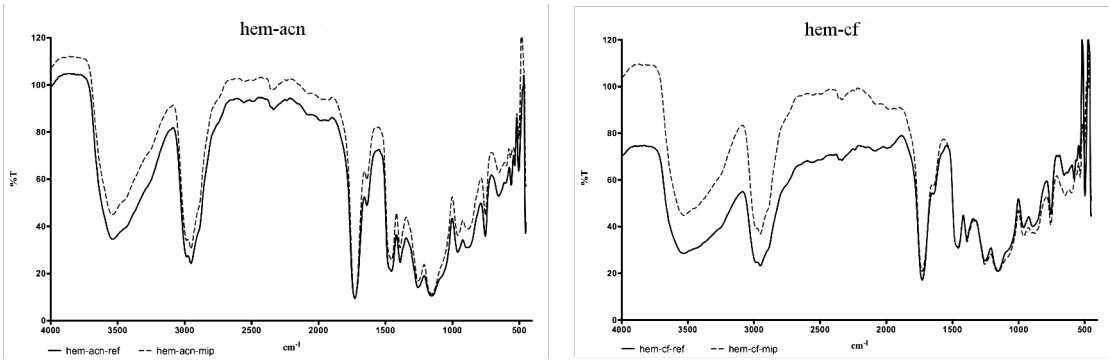

Figure S3. FT-IR spectra of 2-hydroxyethyl methacrylate polymers (HEMA) produced in acetonitrile (left, hem-acn) and in chloroform (right, hem-cf). The continuous lines show spectra of molecularly imprinted polymers and the dashed lines show the spectra of corresponding reference polymers.

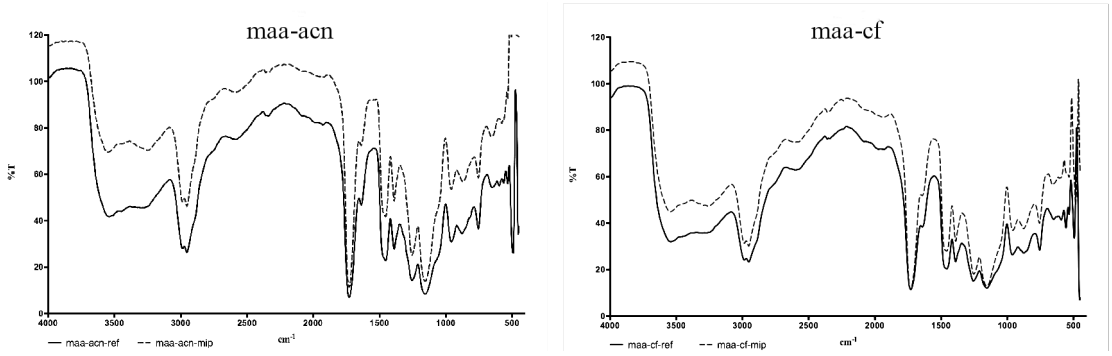

Figure S4. FT-IR spectra of methacrylic acid polymers (MAA) produced in acetonitrile (left, maa-acn) and in chloroform (right, maa-cf). The continuous lines show spectra of molecularly imprinted polymers and the dashed lines show the spectra of corresponding reference polymers.

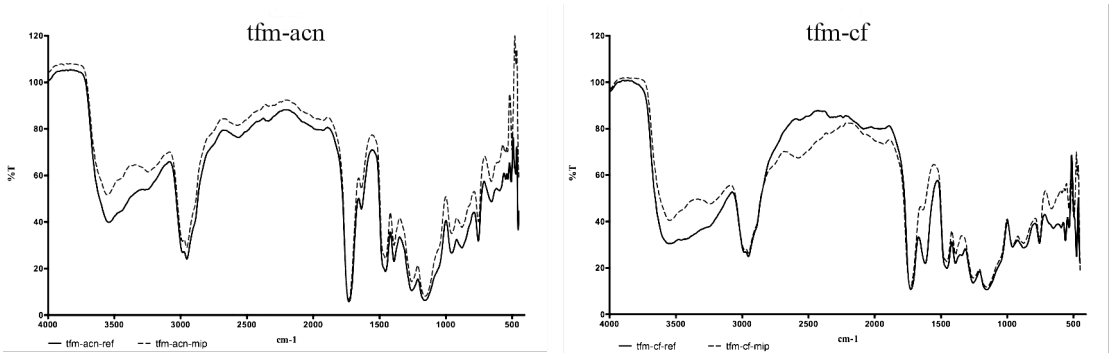

Figure S5. FT-IR spectra of 2-(trifluoromethyl)acrylic acid polymers (TFMAA) produced in acetonitrile (left, tfm-acn) and chloroform (right, tfm-cf). The continuous lines show spectra of molecularly imprinted polymers and the dashed lines show the spectra of corresponding reference polymers.

SEM

Scanning Electron Microscopy images of 25-63 μm reference (REF) and molecularly imprinted polymers (MIP) synthesized with different functional monomers, using acetonitrile (ACN), chloroform ($CHCl_3$) or methanol (MeOH) as porogens during polymer synthesis.

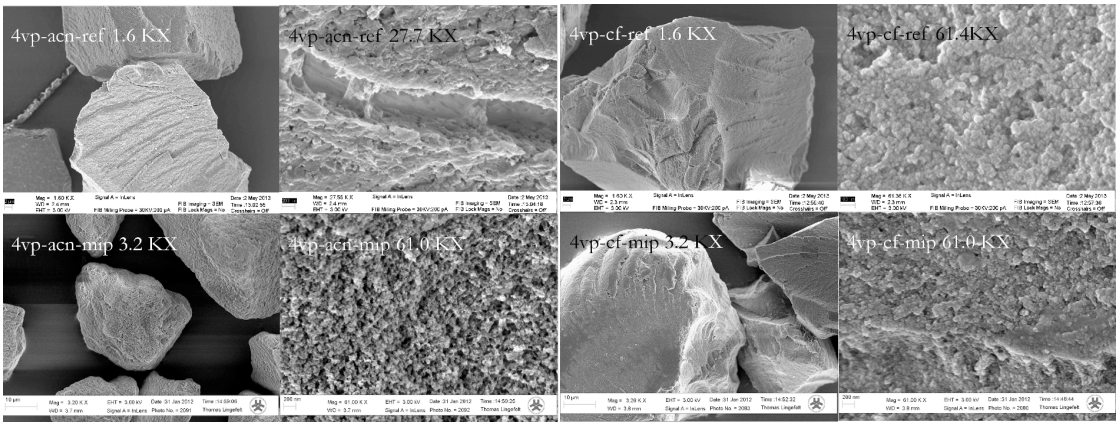

Figure S6. SEM images of polymers produced with 4-vinylpyridine (4VP) as functional monomer prepared in ACN (left) and $CHCl_3$ (right) as porogen. Upper left, REF polymer magnified 1.6 and 27.7 KX. Lower left, MIP magnified 3.2 and 61.0 KX. The REF polymer prepared in ACN shows smoother surface with less pores compared to the MIP. Upper right, REF polymer magnified 1.6 and 61.4 KX and lower right, MIP magnified 3.2 and 61.0 KX. The polymers prepared in chloroform show much smoother surface with fewer pores in comparison to the polymers prepared in acetonitrile.

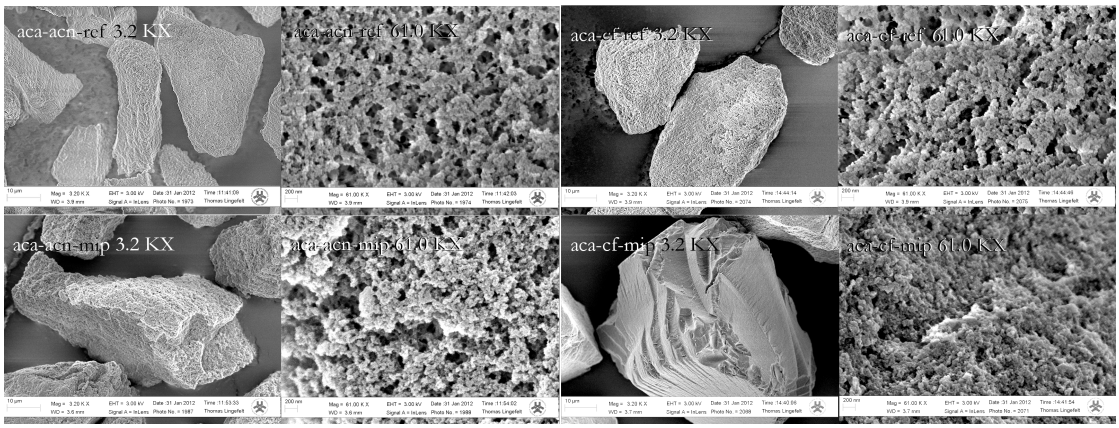

Figure S7. SEM images of polymers with acrylamide (ACA) as functional monomer prepared in ACN (left) and $CHCl_3$ (right) as porogen. Upper left, REF polymer magnified 3.2 and 61.0 KX and lower left, MIP with 3.2 and 61.0 KX magnification. Upper right REF polymer with 3.2 and 61.0 KX magnification and lower right MIP with 3.2 and 61.0 KX magnification. Polymers prepared in ACN show more porous structures than corresponding polymers prepared in $CHCl_3$.

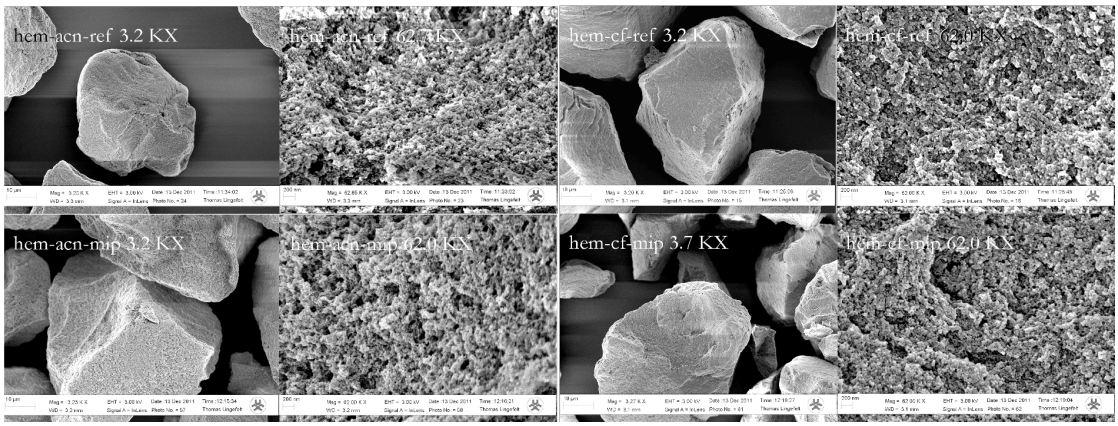

Figure S8. SEM images of polymers with 2-hydroxyethyl methacrylate (HEMA) as functional monomer produced in ACN (left) and $CHCl_3$ (right). Upper left, REF polymer, magnified 3.2 and 62.7 KX and lower left MIP with 3.2 and 62.0 KX magnification. Upper right, REF polymer magnified 3.2 and 61.0 KX and lower right, MIP with 3.7 and 62.0 KX magnification. Polymers prepared in ACN show more porous structures than polymers prepared in $CHCl_3$.

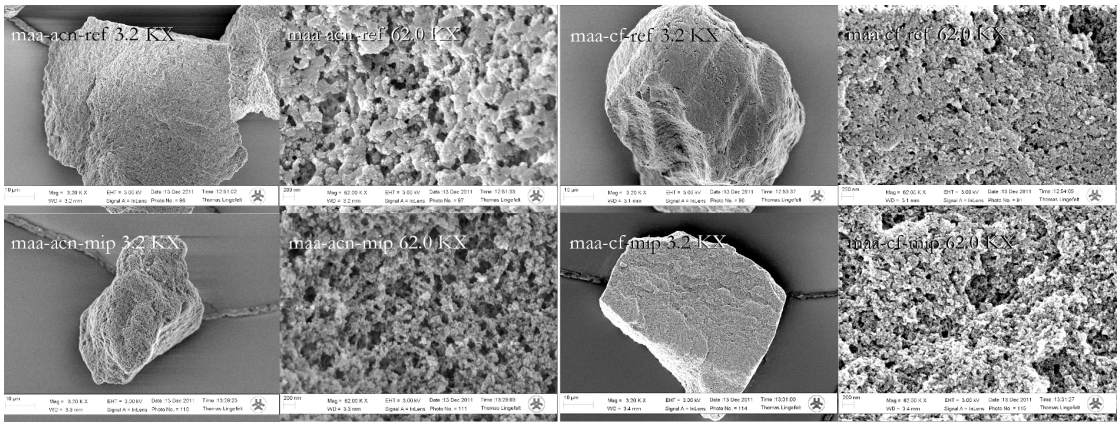

Figure S9. SEM images of polymers with methacrylic acid (MAA) as functional monomer. Upper left, REF polymer prepared in ACN, magnified 3.2 and 62.0 KX and lower left, MIP prepared in ACN with 3.2 and 62.0 KX magnification. Upper right, REF polymer, prepared in $CHCl_3$, magnified 3.2 and 62.0 KX and lower right MIP prepared in $CHCl_3$ with 3.2 and 62.0 KX magnification. Polymers prepared in ACN show more porous structure than corresponding polymers prepared in $CHCl_3$.

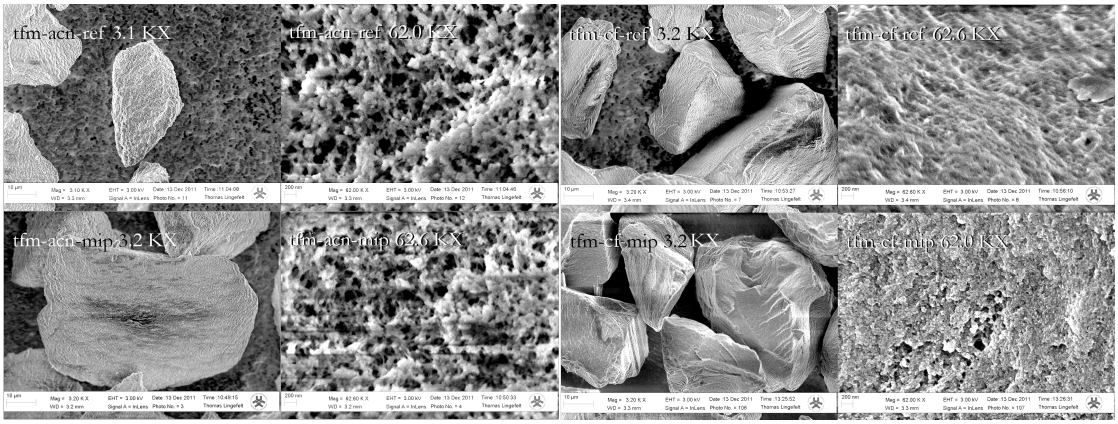

Figure S10. SEM images of polymers with 2-(Trifluoromethyl)acrylic acid (tfm) as functional monomer prepared in ACN (left) and $CHCl_3$ (right). Upper left, REF polymer with 3.1 and 63.0 KX magnification. Lower left MIP magnified 3.2 and 62.7 KX. Upper right, REF polymer magnified 3.2 and 62.6 KX. Lower right, MIP with 3.2 and 62.0 KX magnification. Polymers prepared in $CHCl_3$ show much lower degree of porosity than the polymers prepared in ACN.

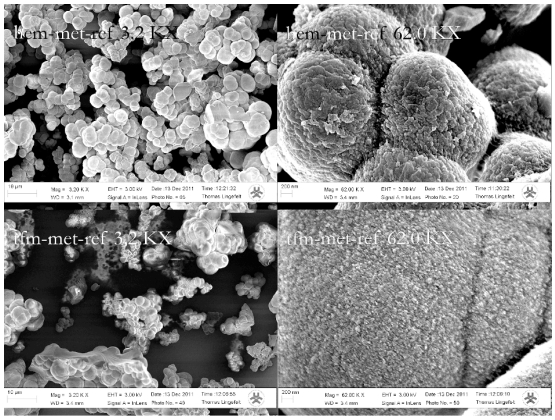

Figure S11. SEM images of REF polymers prepared in MeOH. Upper images show the REF polymer with 2-hydroxyethyl methacrylate (HEMA) as functional monomer with magnifications of 3.2 and 62.0 KX. The lower images show the REF polymer with 2-(trifluoromethyl)acrylic acid (TFMAA**)** as the functional monomer with magnifications of 3.2 and 62.0 KX. The polymer particles show spherical shapes with sizes in nano- to few micro-meter, where the μm size particles are often ligated nm sized particles.

BET (Brunauer–Emmett–Teller surface area analysis)

Table S2. Results of surface area and pore diameter analysis of molecularly imprinted polymer and their counterpart reference system, synthesized in acetonitrile and chloroform.

Polymer systems[a] 25-63µm	$CHCl_3$[b]				ACN			
	Av. Pore Diam. (Å)		BET Surface Area (m^2/g)		Av. Pore Diam. (Å)		BET Surface Area (m^2/g)	
	MIP[c]	REF	MIP	REF	MIP	REF	MIP	REF
4VP	161.8	74.3	1.6	1.7	155.7	230.9	241.0	89.6
ACA	131.0	136.9	2.6	242.1	79.0	103.0	175.0	246.6
HEMA	78.1	88.8	52.0	1.6	74.5	84.3	320.5	261.5
MAA	61.3	42.9	322.6	179.7	114.2	99.0	338.0	227.8
TFMAA	30.0	33.9	121.1	346.4	76.1	76.5	442.6	349.9

[a] Functional monomer used in polymer system abbreviated as 4VP = 4-vinyl pyridine, ACA= acrylamide, HEMA = hydroxyethyl methacrylicate, MAA = methacrylic acid, TFMAA = 2-(trifluoromethyl)acrylic acid. [b] Polymers were produced using either chloroform ($CHCl_{3)}$ or acetonitrile (ACN) as porogen during synthesis. [c] Polymers were synthesized in the presence of oseltamivir as template, MIP = molecularly imprinted polymer or as reference polymers, REF = non-imprinted polymer, identical to the MIPs but in absence of the template oseltamivir.

Laser Diffraction Analysis

Size distribution of reference (REF) and molecularly imprinted polymers (MIPs) synthesized with different functional monomers, using acetonitrile (ACN) or chloroform ($CHCl_3$) as solvents.

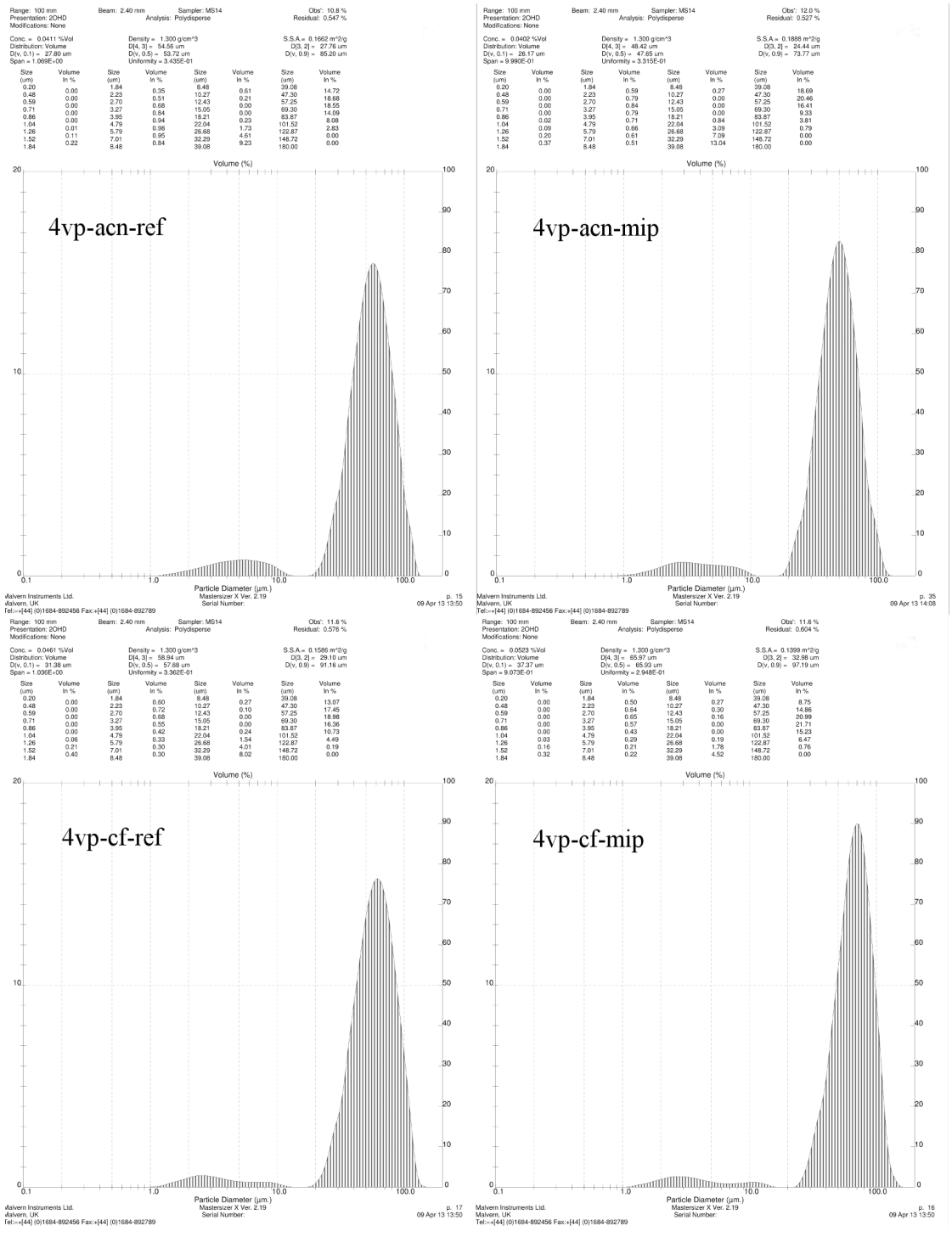

Figure S12. Upper left (4vp-acn-ref) reference (REF) polymer and upper right (4vp-acn-mip) molecularly imprinted polymer (MIP) prepared using acetonitrile (ACN) as porogen and 4-vinylpyridin (4VP) as functional monomer. Lower left (4vp-cf-ref), REF polymer and lower right (4vp-cf-mip), MIP prepared using chloroform ($CHCl_3$) as porogen and 4VP as functional monomer. For size information se table S3 page S14.

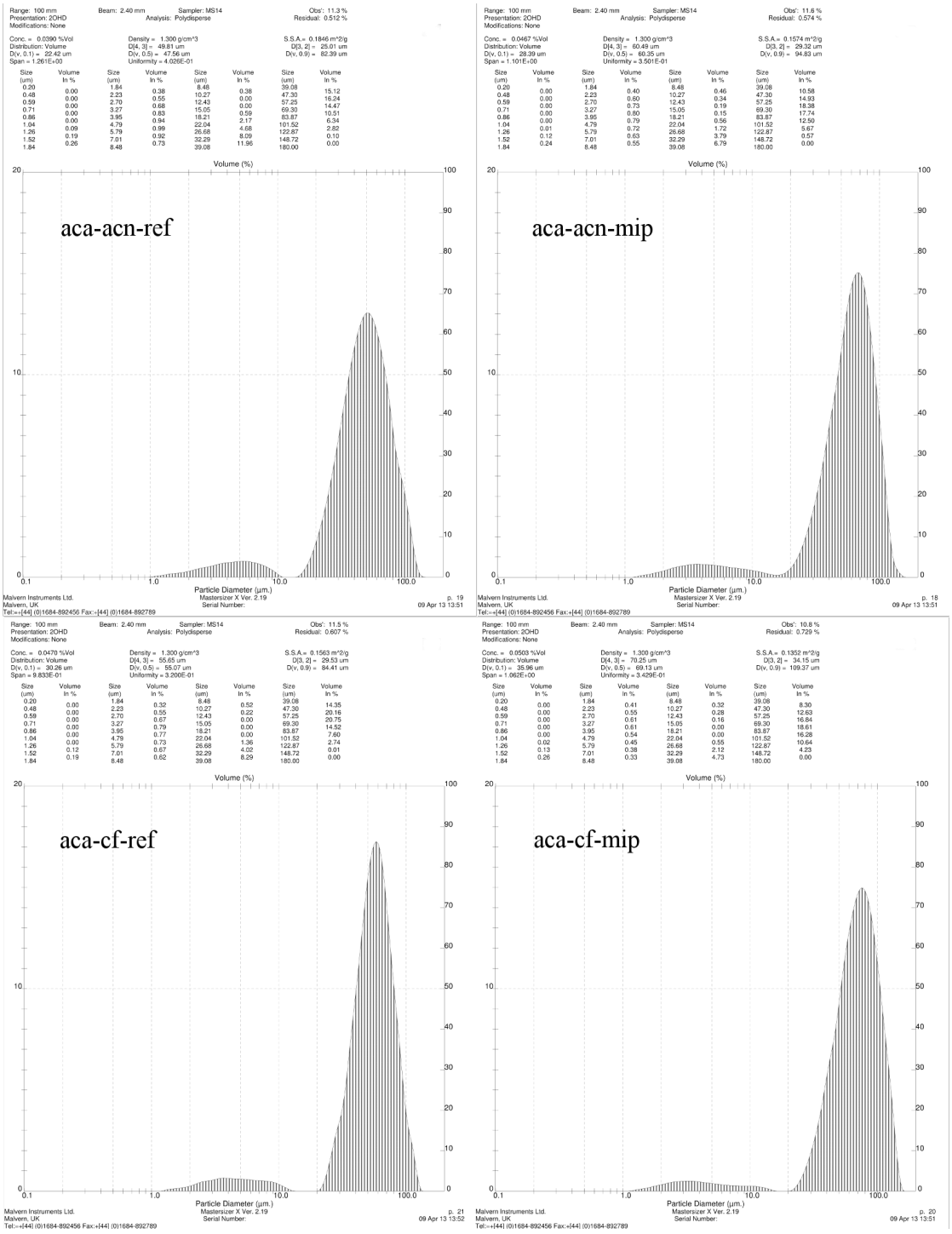

Figure S13. Upper left (aca-can-ref) reference (REF) and upper right (aca-acn-mip) molecularly imprinted polymer (MIP) prepared using acetonitrile (ACN) as porogen and acrylamide (ACA) as functional monomer. Lower left (aca-cf-ref), REF polymer and lower right (aca-cf-mip), MIP prepared using chloroform ($CHCl_3$) as porogen and ACA as functional monomer. For size information se table S3 page S14.

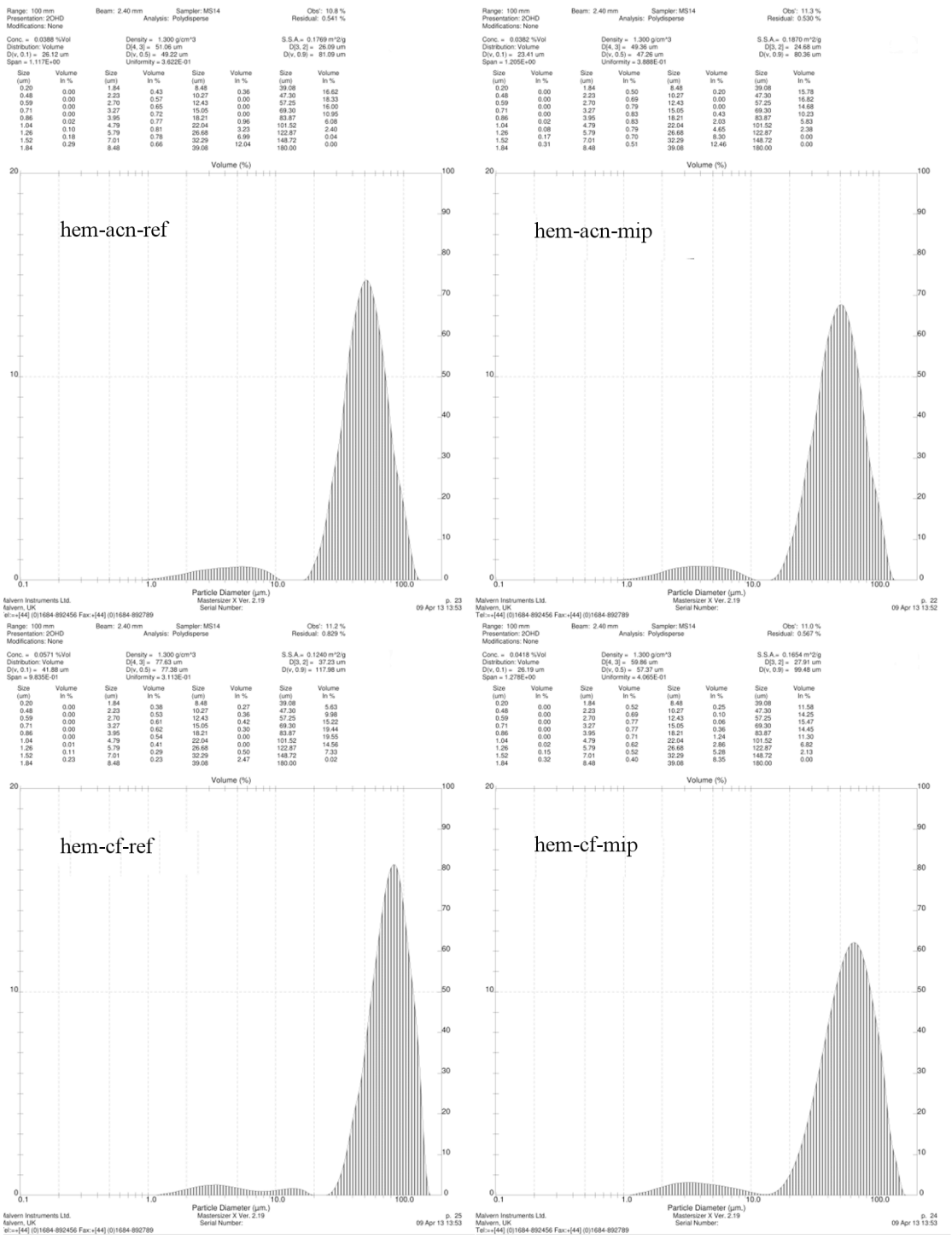

Figure S14. Upper left (hem-acn-ref) reference (REF) and upper right (hem-acn-mip) molecularly imprinted polymer (MIP) prepared using acetonitrile (ACN) as porogen and 2-hydroxyethyl methacrylate (HEMA) as functional monomer. Lower left (hem-cf-ref), REF polymer and lower right (hem-cf-mip), MIP prepared using chloroform ($CHCl_3$) as porogen and HEMA as functional monomer. For size information se table S3 page S14.

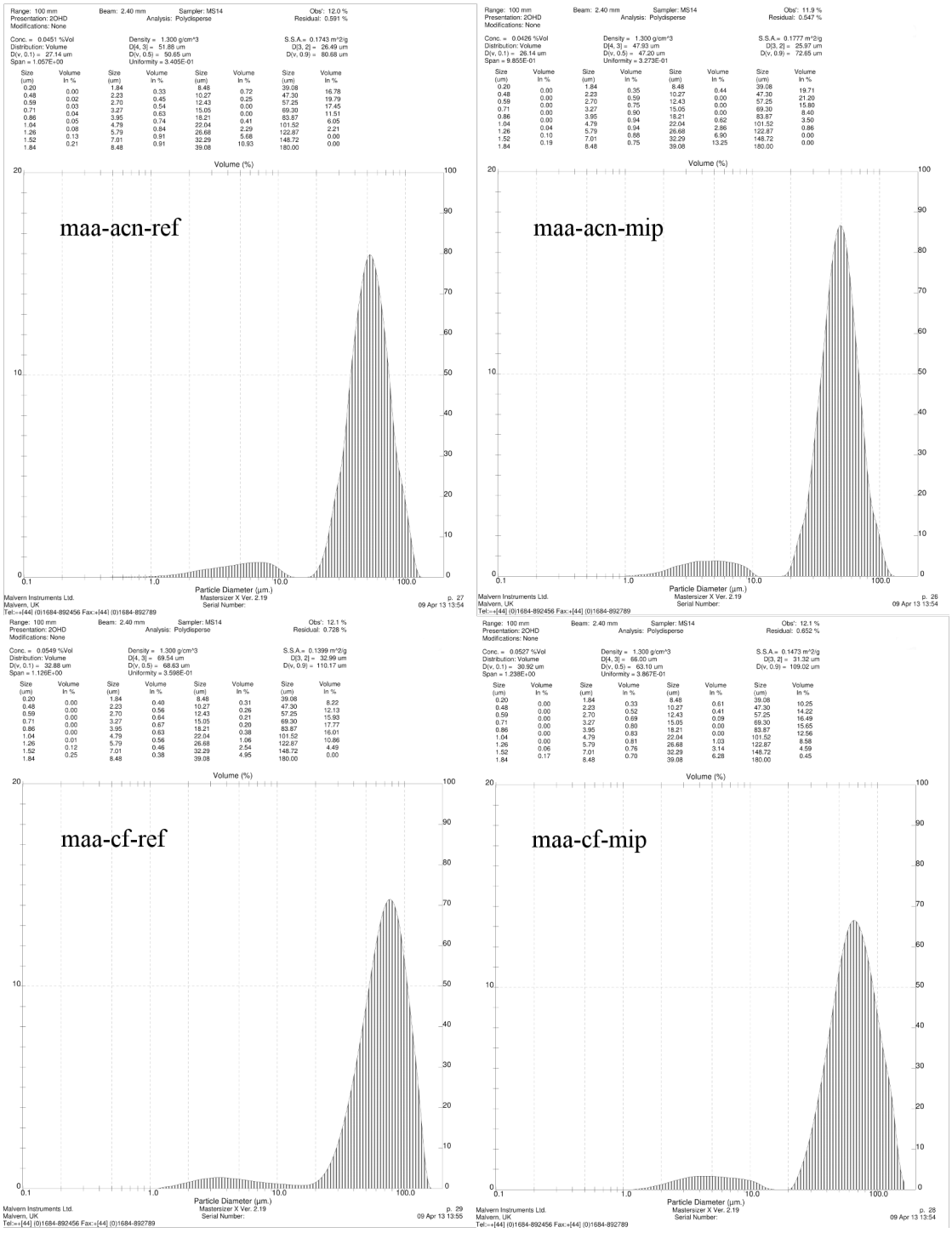

Figure S15. Upper left (maa-can-ref) reference (REF) and upper right (maa-can-mip) molecularly imprinted polymer (MIP) prepared using acetonitrile (ACN) as porogen and methacrylic acid (MAA) as functional monomer. Lower left (maa-cf-ref), REF polymer and lower right (maa-cf-mip), MIP prepared using chloroform ($CHCl_3$) as porogen and MAA as functional monomer. For size information se table S3 page S14.

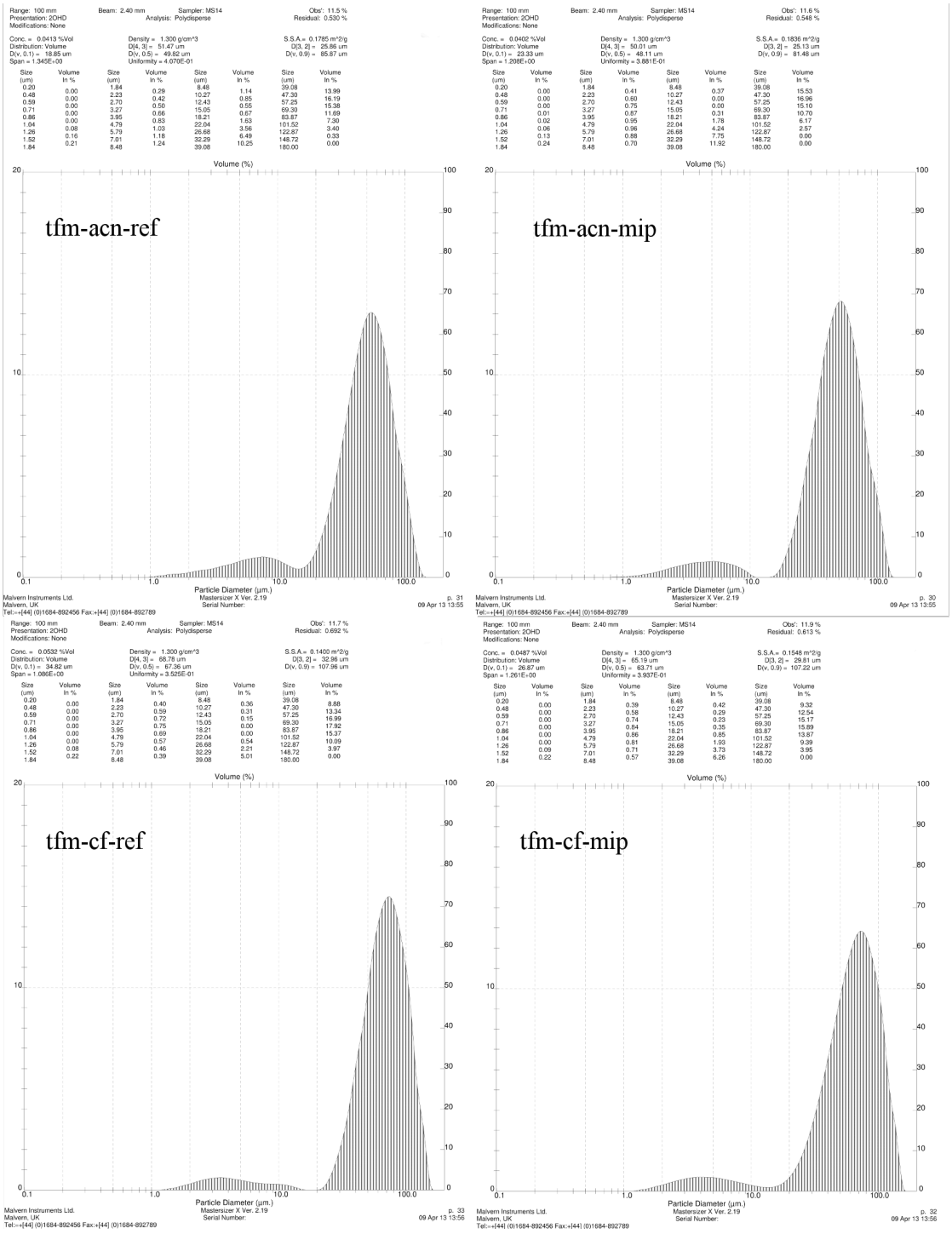

Figure S16. Upper left (tfm-acn-ref) reference (REF) and upper right (tfm-can-mip) molecularly imprinted polymer (MIP) prepared using acetonitrile (ACN) as porogen and 2-(trifluoromethyl)acrylic acid (TFMAA) as functional monomer. Lower left (tfm-cf-ref), REF polymer and lower right (tfm-cf-mip), MIP prepared using chloroform ($CHCl_3$) as porogen and TFM as functional monomer. For size information se table S3 page S14.

Table S3. Results of size determination studies using a Malvern Mastersizer MS20.

Polymer[a]	D (v, 0.1)[b]	D (v, 0.5)	D (v, 0.9)	D [4,3]	D [3,2]	Span[c]	Uniformity
MIP-4VP-ACN	26.2	47.7	73.8	48.4	24.4	1.0	0.3
REF-4VP-ACN	27.8	53.7	85.2	54.6	27.8	1.1	0.3
MIP-4VP-$CHCl_3$	37.4	65.9	97.2	66.0	33.0	0.9	0.3
REF-4VP-$CHCl_3$	31.4	57.7	91.2	58.9	29.1	1.0	0.3
MIP-ACA-ACN	28.4	60.4	94.8	60.5	29.3	1.1	0.4
REF-ACA-ACN	22.4	47.6	82.4	49.8	25.0	1.3	0.4
MIP-ACA-$CHCl_3$	36.0	69.1	109.4	70.3	34.2	1.1	0.3
REF-ACA-$CHCl_3$	30.3	55.1	84.4	55.7	29.5	1.0	0.3
MIP-HEMA-ACN	23.4	47.3	80.4	49.4	24.7	1.2	0.4
REF-HEMA-ACN	26.1	49.2	81.1	51.1	26.1	1.1	0.4
MIP-HEMA-$CHCl_3$	26.2	57.4	99.5	59.9	27.9	1.3	0.4
REF-HEMA-$CHCl_3$	41.9	77.4	118.0	77.6	37.2	1.0	0.3
MIP-MAA-ACN	26.1	47.2	72.7	47.9	26.0	1.0	0.3
REF-MAA-ACN	27.1	50.7	80.7	51.9	26.5	1.1	0.3
MIP-MAA-$CHCl_3$	30.9	63.1	109.0	66.0	31.3	1.2	0.4
REF-MAA-$CHCl_3$	32.9	68.6	110.2	69.5	33.0	1.1	0.4
MIP-TFM-ACN	23.3	48.1	81.5	50.0	25.1	1.2	0.4
REF-TFM-ACN	18.9	49.8	85.9	51.5	25.9	1.3	0.4
MIP-TFM-$CHCl_3$	26.9	63.7	107.2	65.2	29.8	1.3	0.4
REF-TFM-$CHCl_3$	34.8	67.4	108.0	68.8	33.0	1.1	0.4

[a] Polymers are either a reference (REF) polymer, prepared in absence of the template (oseltamivir) or molecularly imprinted polymer (MIP), prepared in the presence of the template, using either 4-vinyl pyridine (4VP), acrylamide (ACA), 2-hydroxyethyl methacrylate (HEMA), methacrylic acid (MAA) or 2-(trifluoromethyl)acrylic acid (TFMAA) as functional monomer and prepared using either acetonitrile (ACN) or chloroform ($CHCl_3$) as porogen. [b] D (v, 0.1), D (v, 0.5) and D (v, 0.9) are percentile readings from the measurments. D (v, 0.1) and D (v, 0.9) denote particle sizes bellow 10% and 90% respectively and D (v, 0.5) means that 50% of the particles are smaller and the other 50% are larger than the denoted size. D [4,3] denote the volume mean diameter while D [3,2] is the surface area mean (Sauter mean). [c] Span is the measurement of the width of the distribution. The smaller the value of span the narrower the distribution. [d] The uniformity is a measure of the absolute deviation from the median.

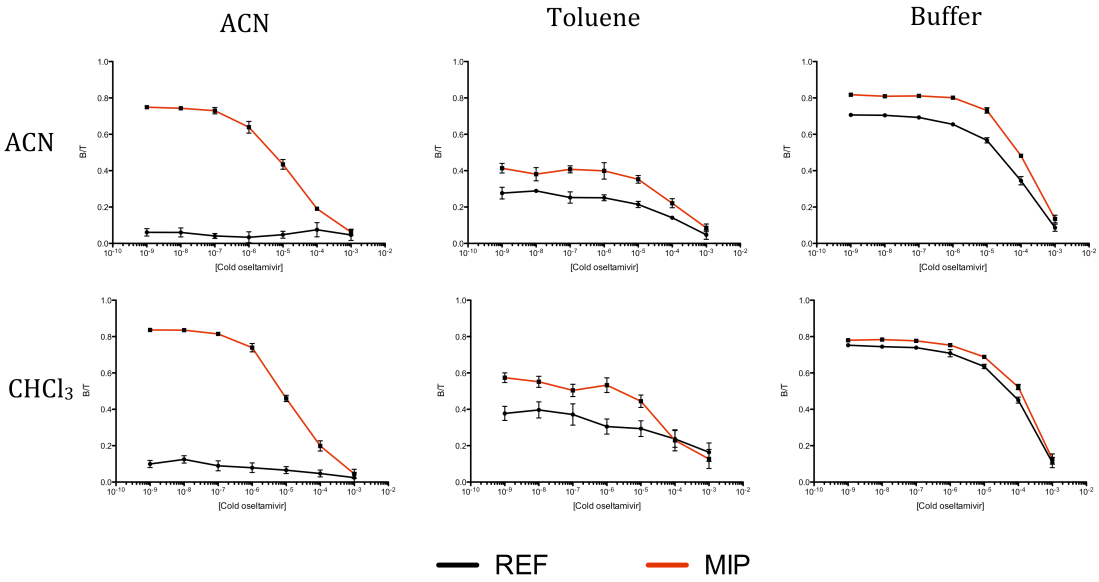

Figure S17. Competitive binding studies of the MAA based polymers (0.75 mg/mL) prepared in either ACN or $CHCl_3$ and evaluated in ACN with 0.5% (v/v) AcOH, toluene with 0.5% AcOH (v/v) or 10 mM phosphate buffer (pH 7.0).