Appendix 2
Members of the ECCACF connected with a genetic diagnostic laboratory

Austria

K Huber (Zentrallabor Donauspital, Vienna), PM Kroisel (Institut für Medizinische Biologie und Humangenetik, Universität Graz, Graz), G Utermann, HG Kraft, J Löffler (Institut für Medizinische Biologie und Humangenetik, Innsbruck), A Weinhäusel (CCRI Labor Professor Haas, Vienna).

Belgium

P Cochaux (Génétique Moléculaire, Hôpital Erasme, Brussels), P Hilbert (IPG Biologie Moléculaire, Gerpinnes), W Lissens (Center for Medical Genetics, AZ-VUB, Brussels), G Matthijs (Molecular Diagnostic Laboratory, Center for Human Genetics, Leuven), L Messiaen (Centrum Medische Genetica, UZ-Gent, Gent), K Storm (Center for Human Genetics, University of Antwerp, Antwerp), C Verellen-Dumoulin (Center for Human Genetics, UCL, Brussels).

Bulgaria

I Kremensky (Laboratory of Molecular Pathology, Sofia Medical University, Sofia).

Croatia

G Janackovic (Division of Molecular Medicine, Laboratory of Molecular Oncology, Ludjel Boskovic Institute, Zagreb), J Sertic (Laboratory for Molecular Diagnosis, Clinical Hospital Centre Zagreb, Zagreb).

Cyprus

C Deltas (Molecular Genetics, The Cyprus Institute of Neurology and Genetics, Nicosia).

Czech Republic

M Macek Jr (CF Center, Molecular Genetic Laboratory, Institute of Biology and Medical Genetics, Prague).

Denmark

M Schwartz (Department of Clinical Genetics, University of Copenhagen, Copenhagen).

France

T Bienvenu, M Delpech (Laboratoire de Biochimie et Génétique Moléculaire, Hôpital Cochin, Paris), E Bieth (Laboratoire de Génétique Médicale, Hôpital Purpan, Toulouse), P Blouin, A Cheyrou (Laboratoire Ruffie et Associés, Bordeaux), JP Bonnefont, L Thuillier (Biochimie Génétique, Hôpital Necker-Enfants Malades, Paris), D Bozon (Biochimie Pédiatrique, Lyon), J-C Chomel (Laboratoire de Génétique Cellulaire et Moléculaire, CHU de Poitiers, Poitiers), C Claval (Pol Bovin, Unité de Biologie Cellulaire, Hôpital Maison Blanche, Reims), M Claustres (Laboratoire de Génétique Moléculaire, Institut de Biologie, Montpellier), I Creveaux (Biochimie Médicale et Biologie Moléculaire, Faculté de Médicine, Clermont-Ferrand), J-M Costa (Molecular Biology Laboratory, American Hospital of Paris, Neuilly-sur-Seine), V David (Laboratoire de Génétique Moléculaire, CHU Pontchaillou, Rennes), E Denamur (Laboratoire de Biochim Génétique, Hôpital R Debré, Paris), V Dumur, G Lalau (Laboratoire de Biochimie et de Biologie Moléculaire, Hôpital Calmette, Lille), D Feldmann (Laboratoire de Biochimie, Hôpital A Trousseau, Paris), C Ferec (Molecular Genetics, Brest), M Goossens, E Girodon (Molecular Genetics, Hospital Henri Mondor, Créteil), A Iron (Laboratoire de Biochimie, Centre Hospitalier Pellagrin, Bordeaux), P Jonveaux (Laboratoire de Génétique, CHU Brabois, Vandoeuvre-les-Nancy), P Lewin (CERBA Laboratoire, Cergy Pontière), J Lunardi (Biochemie de l'AND, CHU Grenoble, Grenoble), MC Malinge (Service de Génétique, CHU Angers, Angers), P Malzac (Laboratoire de Biologie Moléculaire Appliqué, Service du Professeur Mattei, Marseille), H Mittre (Laboratoire de Biochemie B, CHU av. Georges Clemenceau, Caen), A Mantel (Hormonologie et Biologie Moléculaire, Hôpital de Bicêtre, Le Kremlin Bicêtre), J-P Moisan (Laboratoire de Génétique Moléculaire, Institut de Biologie, Centre Hospitalier Universitaire, Nantes), Y Morel, F Cabet/Bey-Omar (Biochimie Endocrinienne et Moléculaire, Hôpital Debrousse, Lyon), E Mornet (SESEP, Centre d'Etudes de Biologie, Prénatale, Université de Versailles-St-Ouentin, Versailles), JP Muh, C Gendrot (Biochemie et Biologie Moléculaire, CHU Brettoneau, Tours).

Germany

J Arnemann (Laboratory of Molecular Genetics, Frankfurt), C Aulehla-Scholz (Institut für Klinische Genetik, Frauenklinik Berg, Stuttgart), I Bauer (University of Rostock, Children's Hospital, Department of Medical Genetics, Rostock), I Böhm (Gemeinschaftspraxis, Dr Ovens-Raeder/Dr C Waldenmaier, Munich), T Eggermann (Division of Clinical Genetics, University of Tübingen, Tübingen), R Fahsold (Gemeinschaftspraxis Prager und Junge, Dresden), PC Fink (Zentralkrankenhaus St Jürgen Straße, Institut für Laboratoriumsmedizin, Bremen), W Friedl, M Jungck (Institut für Humangenetik, Universität Bonn, Bonn), U Froster (Institut für Humangenetik, Universität Leipzig, Leipzig), D Gläser (Laborpraxis Dres. Mehnert, Medizinische Genetik Neu-Ulm), A Golla, T Meitinger (Abteilung Medizinische Genetik, Munich), M Hagemann (Institut für Humangenetik und Medizinische Biologie, Martin-Luther-Universität Halle-Wittenberg, Halle/Saale), U Hammer (Molecular Diagnostics, Klinikum der Friedrich-Schiller-Universität Jena, Jena), K Held (Institut für Immunologie, Pathologie und Molekularbiologie, Hamburg), W Höppner, P Matthiesen (Gemeinschaftspraxis Leidenberger, Weise under Partner, Department Molecular Diagnostic, Hamburg), S Jakubiczka (Otto-von-Guericke-Universität, Institut für Human Genetik, Madgeburg), B Janssen (Institut für Humangenetik, Heidelberg), H-G Klein (Facharzt für Laboratoriumsmedizin, Medizinische Genetik, Planegg/Martinsried), P Kozlowski (Institut für Praenatal Medizine und Genetik, Düsseldorf), C Kraus (Institut für Humangenetik,

Erlangen), K Kutsche (Institut für Humangenetik, Universität-Krankenhaus Eppendorf, Hamburg), F Laccone (Institute of Human Genetics, Göttingen), L Lübbe (Carl-Thiem-Klinikum Institut für Pathologie, Cottbus), E Meese (Department of Human Genetics, University of Saarland, Homburg/Saar), U Müller, K Atland (Institute of Human Genetics, Justus-Liebig-University, Giessen), E Natt (DNA-Diagnostik, Institut für Humangenetik, Freiburg), C Nevinny-Stichel, (Gemeinschaftspraxis Dr W Bieger, Munich), B Pabst, S Arps (Labor Dres. med. Fenner, Hamburg), U Pantke (Humangenetische Praxis, Giessen), K Pötschick, E Spitzer, R Grosse (Praxis für Humangenetik, Berlin), J Reiss (Justus-Leibig-Universität Giessen, Institut für Humangenetik, Giessen), H Roth (Institut für Medizinische Genetik, Osnabrück), W Schmidt, U Peters (Institut für Immunologie, Pathologie und Molekularbiologie, Hamburg), E Schröder (Institute für Humangenetik, Düsseldorf), G Schülter (Humangenetik, Karlsruhe), H Skaldny (Praxis Dr Greiner, Mannheim), P Steinbach (Abteillung Medizinische Genetik, Universität Ulm, Ulm), M Stuhrmann (Institut für Humangenetik, Medizinische Hochschule Hannover, Hannover), G Wildhardt (Universität Mainz, Mainz), K Wilke (Westfälische Wilhelms-Universität, Institut für Humangenetik, Münster), R Yamamoto (Gemeinschaftspraxis für Labormedizin, Dr Eberhard und Partner, Dortmund), C Zühlke (Humangenetik, Medizinische Universität zu Lübeck), Laboratorium Dr Jung (GmbH, Cologne), Labor für Pränatale Diagnostik (Linden), Gemeinschaftspraxis für Laboratoriumsmedizin, Prof Dr med Michael Giesing und Partner (Recklinghausen).

Hungary
K Németh, A Varadi, G Fekete (Molecular Genetics 2nd Department of Pediatrics, SOTE, Budapest).

Ireland
D Barton (National Centre for Medical Genetics, Our Lady's Hospital for Sick Children, Dublin).

Israel
D Abeliovich (Department of Human Genetics, Jerusalem).

Italy
E d'Alcamo (Servizio Talassemia, Unita di Ricenca Piera Cutino, Palermo), A Amoroso (Medical Genetics, Children Hospital, Trieste), C Arduino (Centro Genetica Medica, Torino), M Bartolozzi (Sezione Genetica Medica, Grosseto), M Benettazo, PF Pignatti (Institute of Biology and Genetics, University of Verona, Verona), G Cabrini (Molecular Pathology, Cystic Fibrosis Centre, Verona), A Cantu-Rajnoldi (Anatomia ed Istologia Patologica, Sez. Genetica Molecolare, Milan), G Cossu (Centro Genetica Medica, Ozieri-Sassari), Dagna Bricarelli, P Scartezzini (Laboratoire Genetica Umana, Genoa), M Ferrari (Unit of Genetics and Molecular Diagnostics, HS Raffael, Milano), M Furbetta, A Angius, M Stasi (Genetica Moleculare, Istituto di Pediatria Clinica Sociale e Preventiva, Perugia), P Gasparino (Medical Genetics Service, IRCCS Casa Sollievo, S Glovanni Rotondo), MN Lizzio (Genetica Molecular, Clinical Pediatrics, Catania), M Lucarelli (Cystic Fibrosis Centre Laboratory, University of Rome Li Sapienza, Rome), G Novelli (Human Genetics, Tor Vergata University, Rome), L Picci, M Scarpa (Molecular Genetics Laboratory, Padua), MC Rosatelli, A Cappai, A Cao (Genetica Moleculare, Istituto di Clinica e Biologia Dell'eta' Evolutiva, Cagliari), F Salvatore (Department of Biochemistry and Medical Biotechnology, Naples), T Santostasi (Laboratoria Fibrosi Cystica, Centro Riferimeno, Bari), P Simi (UO Citogenetica e Genetica Moleculare, Instituto Clinica Pediatrica Universita via Roma, Pisa), C Toffili (Diagnosi Prenatale Molecolare Geneticamedica, Ferrara), F Torricelli (Unita Operativa Citogenetica e Genetica, Florence), G Uzielli (Centre for Human Genetics and Molecular Medicine, Florence).

Latvia
V Kroshkina (Department of Medical Biology and Genetics, Medical Academy of Latvia, Riga).

Macedonia Republic
G Efremov (Macedonian Academy of Science and Arts, Research Center for Genetic Engineering and Biotechnology, Skopje).

Norway
I Eftedal (Beate Skinningsrud, Department of Medical Genetics, University Hospital of Trondheim, Trondheim), K Eiklid (Department of Medical Genetics, Ulleval University Hospital, Oslo).

Poland
J Bal (Department of Genetics, National Research Institute of Mother and Child, Warsaw), M Witt (Institute of Human Genetics, Polish Academy of Sciences, Poznan).

Portugal
P Pacheco (Centro de Genetica Humana, Instituto Nacional de Saude Dr Ricardo Jorge, Lisbon).

Russia
N Petrova, EG Ginter (Laboratorium of Genetic Epidemiology, Research Centre for Medical Genetics, Moscow).

Slovak Republic
L Kadasi (Genexpress, Bratislava).

Slovenia
R Komel, K Vouk (Medical Centre for Molecular Biology, Institute of Biochemistry, Ljubljana), M Ravnik-Glavac (Laboratory of Molecular Pathology, Medical Faculty, Ljubljana).

Spain
G Antinolo (Unidad de Genetica Medica y Diagnostico Prenatal, Hospital Universitanio Virgen del Rocio, Sevilla), A Arnaiz-Villena (Sesvicio de Immunologia Hospital Universitario 12 de Octubre, Madrid), M Beneyto (Unidad de Genetica y Diagnostico Prenatal, Hospital Universitario La Fe, Valencia), J Benitez (Mercedes Robledo, Genetics Department, Madrid), M Carrera (Centro de Patologia Celular y Diagnostico Prenatal, Instituto Universitario Dexeus, Barcelona), X Estivill, T Casals (Centre de Genetica Medica I Molecular, Hospital Duran I Reynals, Barcelona), M Fernandez-Burriel (Unidad Genetica, Hospital Materno-Infantil, Canary Islands), G Glover (Centro de Bioquimica y Genetica Clinica, Espanardo, Murcia), J Molano (Unidad Genetica Molecular Bioquimica, Hospital La Paz, Madrid), A-M Palacio De Parada (Centro de Analisis Geneticos C.A.G.T., Zaragoza), JL San Millan (Unidad de Genetica Molecular, Hospital Ramon y Cajal, Madrid), J Telleria-Orriols, J Alonso (Department Pediatria, Facultdad de Medicina, Valladolid), D Valverde (Laboratorio Analisis Clinicos Lema Y Bandin, Vigo, Pontevedra).

Sweden
U Kristofferson (Department of Clinical Genetics, Lund).

Switzerland
M Hergersberg (Institut Für Medizinische Genetik, Universität Zurich, Zurich), S Liechti-Gallati (Leiterin Moleculare Humangenetik, Universitäts-Kinderklinik, Berne), M Morris (Molecular Diagnostic Laboratory, Division of Medical Genetics, Geneva), F Thonney, F Schordenet (Génétique Moléculaire, Division de Génétique Médicale, Lausanne).

The Netherlands
JJP Gille, LP ten Kate (Clinical Genetics, Vrije Universiteit, Amsterdam), DJJ Halley, AMW van den Ouweland (Department of Clinical Genetics, Erasmus University, Rotterdam), H Scheffer (Department of Medical Genetics, University of Groningen, Groningen).

United Kingdom
A Buckingham (Kennedy-Galton Centre, DNA Laboratory, Harrow), A Curtis (Northern Genetics Service, Human Genetics Department, Newcastle-upon-Tyne), J Dodge (Department of Child Health, University of Swansea, Swansea), R Elles, M Coleman (Regional Molecular Genetics Laboratory, St Mary's Hospital, Manchester), L Ellis (DNA Laboratory, St James's University Hospital, Leeds), A Gardner (Regional Cytogenetics Centre, Southmead Hospital, Bristol), A Gilfilland (Human Genetics Unit, Molecular Medicin Centre, Western General Hospital, Edinburgh), C Graham (Regional Molecular Genetics Laboratory, Belfast City Hospital Trust, Belfast) K Kelly (DNA Laboratory, Department of Medical Genetics, Medical School Foresterhill, Aberdeen), G Lanyon (Catherine Crew, Duncan Guthrie Institute of Medical Genetics, Royal Hospital for Sick Children, Glasgow), F MacDonald, S Bullock (DNA Laboratory, Birmingham Women's Hospital, Birmingham), R Mountford (Regional Molecular Genetics Laboratory, Liverpool, Women's Hospital, Liverpool), M Schwarz (North-West Regional Molecular Genetics Laboratory, Paediatric Genetics Unit, Royal Manchester Children's Hospital, Manchester), A Seller (Oxford Medical Genetics Laboratories, Churchill Hospital, Oxford), J Warner (Human Genetics Unit, Edinburgh), J Whittaker, R Clark (Molecular Genetics Laboratory, Cambridge).

Ukraine
L Livshits (Group of Molecular Diagnosis of Hereditary Diseases, Department of Human Genetics, Kiev).

Yugoslavia
D Radojkovic (IMGGE, Laboratory for Molecular Biology, Belgrade).

Table 1 Mutations found at a frequency higher than 1% in Europe[5–7]

Country												
Albania	dF508 (70.0)											
Austria	dF508 (63.7)	G542X (2.1)	R1162X (1.9)	G551D (1.1)								
Belarus	dF508 (63.0)	N1303K (2.7)	G542X (2.1)	W1282X (1.7)								
Belgium	dF508 (75.5)	N1303K (2.9)	G542X (2.7)	W1282X (1.5)	S1251N (1.3)	1717-1G>A (1.1)						
Bulgaria	dF508 (61.0)	N1303K (409)	G542X (3.6)	R347P (2.0)	1677delTA (2.0)	R1070Q (1.5)	W1282X (1.3)	G1244V+S912L (1.0)				
Croatia	dF508 (64.5)	N1303K (3.6)	G542X (3.3)	G551D (1.1)								
Cyprus	dF508 (46.7)	L346P (16.7)	1677delTA (6.7)									
Czechia	dF508 (71.6)	G551D (4.0)	N1303K (3.0)	G542X (2.2)	1898+1G>A (2.0)	2143delT (1.2)	CFTRdele2,3(21kb) (4.6)					
Denmark	dF508 (87.2)	394delTT (1.9)	N1303K (1.0)									
Estonia	dF508 (54.0)	394delTT (15.0)										
Finland	dF508 (46.2)	394delTT (28.8)										
France	dF508 (66.8)	G542X (3.1)	1717-1G>A (1.6)	N1303K (1.4)								
Germany	dF508 (73.2)	R553X (2.7)	R347P (1.3)	G551D (1.3)	N1303K (1.2)	G542X (1.2)	3849+10kbC>T (1.2)	CFTRdele2,3(21kb) (1.5)				
Greece	dF508 (52.2)	621+1G>T (4.5)	G542X (3.9)	N1303K (3.3)	2183AA>G (1.8)	2789+5G>A (1.8)	E822K (1.6)	R117H (1.2)	R344W (1.2)	3272-26A>G (1.0)	R1158X (1.0)	G85E (1.0)
Hungary	dF508 (54.7)	G542X (2.2)	N1303K (1.0)									
Ireland	dF508 (72.7)	G551D (6.9)	R117H (2.0)	G542X (1.0)								
Israel	dF508 (32.2)	W1282X (36.2)	G542X (5.4)	3849+10kbC>T (4.6)	405+1G>A (3.8)	N1303K (3.0)	Q359K+T360K (1.9)	S549R (1.1)				
Italy	dF508 (51.1)	G542X (4.8)	N1303K (4.8)	2183AA>G (2.7)	R1162X (2.4)	1717-1G>A (2.1)	W1282X (1.2)	R553X (1.2)				
Latvia	dF508 (54.2)	3849+10kbC>T (12.5)	N1303K (8.3)	W1282X (4.2)								
Lithuania	dF508 (30.9)	R553X (4.8)	N1303K (2.4)									
Macedonia	dF508 (56.0)	G542X (3.3)	N1303K (2.6)	621+1G>T (1.9)	3849+10kbC>T (1.9)	457TAT>G (1.3)	V1397E (1.3)					
North Africa	dF508 (32.0)	N1303K (10.2)	W1282X (8.2)	711+1G>T (7.5)	G542X (4.8)	R1162X (2.7)	L227R (1.4)	S549R (1.4)	S549N (1.4)	S549I (1.4)	G551D (1.4)	S945L (1.4)
Northern Ireland	dF508 (68.0)	G551D (5.1)	R117H (4.1)	R560T (2.9)	G542X (2.2)	621+1 G>T (2.2)	dl507 (1.7)					
Norway	dF508 (66.7)	394delTT (4.2)	R117H (3.0)	G551D (1.2)								
Poland	dF508 (52.9)	3849+10kbC>T (2.6)	G542X (2.5)	N1303K (1.7)	1717-1G>A (1.7)	R553X (1.0)	CFTdele2,3(21kb) (2.0)					
Portugal	dF508 (52.3)	R1066C (3.5)	G542X (2.3)	R334W (2.0)	A561E (2.0)	3272-26A>G (1.5)	N1303K (1.5)					
Romania	dF508 (27.0)											
Russia P	dF508 (45.0)	W1282X (2.1)	N1303K (1.6)	1677delTA (1.6)	2143delT (1.0)	CFTRdele2,3(21kb) (7.5)						
Russia M	dF508 (54.5)	N1303K (2.6)	2143delT (2.0)	2184insA (2.0)	W1282X (2.0)	G542X (1.8)	3849+10kbC>T (1.8)	CFTRdele2,3(21kb) (8.4)				
Slovakia	dF508 (59.4)	G542X (5.6)	R553X (3.4)	N1303K (3.0)	R347P (1.7)	CFTRdele2,3(21kb) (4.6)						
Spain	dF508 (54.4)	G542X (7.7)	N1303K (2.5)	1811+1.6kbA>G (1.5)	R1162X (1.3)	712-1G>T (1.1)	1609delCA (1.0)					
Sweden	dF508 (73.3)	394delTT (9.7)	3659delC (3.0)	175insT (2.4)	T338I (1.2)							
Switzerland	dF508 (43.2)	R553X (24.2)	3905insT (14.7)	G542X (3.2)	1717-1G>A (2.1)	K1200E (2.1)						
The Netherlands	dF508 (74.4)	A455E (3.3)	1717-1G>A (1.5)	G542X (1.3)	R553X (1.2)							
Turkey	dF508 (34.8)	N1303K (6.4)	1677delTA (2.8)	E92X (2.8)	R347H (2.8)	G542X (2.8)	K68N (1.4)	2043delG (1.4)	2183AA>G (1.4)		2789+5G>A (1.4)	
Ukraine	dF508 (50.0)											
United Kingdom	dF508 (75.3)	G551D (3.1	G542X (1.7)									
Yugoslavia	dF508 (66.3)	G542X (5.3)										

Sources: Deltas C., Doerk T., Graham C., Macek M. Jnr., Pacheco. P. (Personal communication, January 1999).

Table 2 Overview of total sensitivity for mutations found at a frequency higher than 1% *(January 1999)*

Country	*Total sensitivity %*	*No. mutations*	*% mutations not found*
Albania	70	1	28.1
Austria	68.8	4	35
Belarus	69.5	4	29.5
Belgium	85	6	8.4
Bulgaria	77.3	8	14.5
Croatia	72.5	4	25
Cyprus	90	8	10
Czechia	88.6	7	4.9
Denmark	90.1	3	4
Estonia	69.4	2	13.5
Finland	75	2	21.2
France	72.9	4	17.5
Germany	83.6	8	16.4
Greece	74.5	12	13.7
Hungary	57.9	3	41.1
Ireland	82.6	4	13.9
Israel	88.2	8	8.4
Italy	70.3	8	22.7
Latvia	79.2	4	20.8
Lithuania	38.1	3	66
Macedonia	68.3	7	50
North Africa	73.8	12	24.5
Northern Ireland	86.2	7	13.8
Norway	75.1	4	23.8
Poland	64.4	7	31.1
Portugal	64.8	7	27.7
Romania	27	1	57.3
Russia (sint Petersburg)	58.8	6	52.8
Russia (Moscow)	75.1	8	
Slovakia	77.7	6	21
Spain	69.5	7	17.9
Sweden	89.6	5	7.3
Switzerland	89.5	6	9.5
The Netherlands	81.7	5	13.5
Turkey	58	10	41.1
Ukraine	50	1	49.1
United Kingdom	80.1	3	13.9
Yugoslavia	71.6	2	26.4

Table 3 Intragenic polymorphisms in the *CFTR* gene

Polymorphic locus	*Reference*
IVS6a-GATT	Dörk *et al.*[45]
1001+11C→T	Cuppens *et al.*[46]
IVS8-CA	Morral *et al.*[47]
Tn (5T-7T-9T)	Cuppens *et al.*[46]
TUB9 (intron 9 1525-61 A or G)	Dörk *et al.*[45]
M470V	Dörk *et al.*[45], Cuppens *et al.*[46]
T854T	Dörk *et al.*[45], Cuppens *et al.*[46]
IVS17B-TA	Morral *et al.*[47]
IVS17B-CA	Morral *et al.*[47]
TUB18 (intron 18 3601-65 A or C)	Dörk *et al.*[45]
TUB20 (intron 20 4006-200 A or G)	Dörk *et al.*[45]
Q1463Q	Cuppens *et al.*[46]

Table 4 Cost comparative study for the most frequently used *CFTR* mutation detection methods (January 1999)

Mutation detection method	*Time scheme*			*Price of material and supplies for analysing 5 samples*	*No. mutations*
	Working time	*Waiting time*	*Total time*		
INNO-LiPA CF2	40min–2h	6h–8h	6h40min–10h	157.3–200 Euro	8 mutations
Elucigene CF12	30min–2h	5h30min–6h	6h–8h	157.3–200 Euro	12 mutations
OLA cystic fibrosis assay	1h30min–3h	4h30min–10h30min	7h–12h30min	237.5–275 Euro	31 mutations
Restriction enzyme analysis	1h15min–2h	5h–10h	7h–13h	16.2–21.3 Euro	1 mutation
Heteroduplex analysis	30min–1h	6h–8h	7h–12h15min	10–12.5 Euro	1 or 2 mutations
DGGE	1h30min–2h	6h–20h	8h–22h	20–22.5 Euro	1 exon or multiplex
SSCP	2h30min–3h	10h–22h	12h30min–25h	16.2–18.7 Euro	1 exon

These results were obtained from the comparative study of the actual cost and hands-on time for different CF mutation detection techniques. The data obtained from the workshop on DNA extraction and CF mutation detection technique held in Leuven, September 1996 were compared with the information obtained from a detailed questionnaire which was sent to laboratories which participate in the European Quality control trial 1998 (except for the OLA kit).

For each technique, the total working time and the costs were evaluated. The total time for the different techniques was divided into the working time i.e. the time needed for one person to do the practical work, and the waiting time, i.e. the time when the samples are in a machine or during a chemical reaction without any handling by a person. The costs for the *CFTR* mutation detection techniques were costs for material and supplies. Material and supplies were valued on the basis of replacement prices (Western European prices).

Table 5 Features of the most common CF mutation detection techniques (January 1999)

Mutation specific methods	
Heteroduplex Analysis	Useful for small deletions/insertions Mostly used for dF508/dI507 Other insertions/deletions eg 394delTT, 1461insAGAT Visualisation with either ethidium bromide or silver staining Cheap, easy to use
Restriction Enzyme Analysis	Ideally used for confirmation, verification or mutations detected by other methods Can be used for local specific mutation Testing of relatives for 'family' mutations Used in restriction generating PCR Specificity not absolute Relatively expensive
ARMS	Allele-specific PCR, useful for isolated (local specific) mutations Result may rely on a absence of PCR product Can be useful in determining maternal contamination May be applied to pooled samples, in a research setting only! Difficulty in designing primers Cheap once primers have been designed
RG PCR	Useful for isolated (local specific) mutations May be useful for certain applications
Reverse/Normal Dot Blots	Developed according to local population frequencies Useful for large numbers of samples Visualisation/labelling methods Difficult to establish initially May require radioactivity
INNO-LiPA	See Table 6 for mutations tested INNO-LiPA *CFTR*12 and INNO-LiPA *CFTR*17+Tn (latter includes polyT) INNO-LiPA will distinguish heterozygotes (Wild-type probes included for every mutation detected) No special equipment required, except for a shaking waterbath More robust with respect to methodology High specificity Sensitivity generally high (European-wide) but not locally variable Relatively expensive (although not per mutation) Labour costs reduced Automatable with the auto-LiPA
Elucigene	See Table 6 for mutations tested Elucigene does not generate normal alleles for mutations except dF508 More robust with respect to methodology Elucigene may be sensitive to DNA sample type High specificity Sensitivity generally high (European-wide) but not locally variable Relatively expensive (although not per mutation) Labour costs reduced
OLA	See Table 6 for mutation tested OLA will distinguish heterozygotes Requirement fo expensive equipment ABI 310 or 377 More robust with respect to methodology High specificity Sensitivity generally high (European-wide) but not locally variable Relatively expensive (although not per mutation) Labour costs reduced
Generic methods	
SSCP	Cheap, once established
DGGE	Difficult to set up (primer design) High pick-up rate, especially when multiplexed
Sequencing	For absolute confirmation of new findings Exclusion of polymorphisms
Polymorphisms	
For Prenatal Diagnosis where one or no mutations have been found	
For assessment of maternal cell contamination	
PolyT interpretation – TG_m	
For confirmation of zygosity	
Exclusion of uniparental disomy	

Table 6 Mutations detected by commercial kits (November 1999)

INNO-LiPA	
CF2:	dF508, dI507, G542X, 1717-1G>A, G551D, R553X, W128X, N1303K
*CFTR*12:	dF508, dI507, G542X, 1717-1G>A, G551D, R553X, W1282X, N1303K, S1251N, R560T, 3905insT, Q552X
*CFTR*17+Tn:	394delTT, G85E, 621+1G>T, R117H, 1078delT, R347P, R334W, E60X, 2183AA>G, 2184delA, 711+5G>A, 2789+5G to A, R1162X, 3659delC, 3849+10kbC>T, 2143delT, A455E, (5T/7T/9T)
Elucigene	
CF4:	dF508, 542X, G551D, 621+1G>T
C12	dF508, G542X, G551D, N1303K, W1282X, 1717-1G>A, R553X, 621+1G>T, R117H, R1162X, 3849+10kbC>T, R334W
CF20:	1717-1G>A, G542X, W1282X, N1303K, dF508, 3849+10kbC>T, 621+1G>T, R553X, G551D, R117H, R1160X, R334W, A455E, 2183AA>G, 3659delC, 1078delT, dI507, R345P, S1251N, E60X
CF *Poly*-T	5T/7T/9T
OLA	
CF OLA assay:	dF508, F508C, dI507, Q493X, V520F, 1717-1G>A, G542X, G551D, R553X, R560T, S549R, S549N, 3849+10kbC>T, 3849+4A>G, R1162X, 3659delC, W1282X, 3905insT, N1303K, G85E, 621+1G>T, R117H, Y122X, 711+1G>T, 1078delT, R347P, R347H, R334W, A455E, 1898+1G>A, 2183AA>G, 2789+5G>A