Protocol Title:

A Phase III, Randomized, Open-Label, Parallel-Group, Dose-Ranging Clinical Trial to Study the Safety and Efficacy of MK-0954/Losartan Potassium in Pediatric Patients With Hypertension (MK-0954 Prot. 337)

Protocol-Number: MK-0954 Prot. 337

Eudra-CT-Number: 2008-004732-20

Name of Finished Product: LORZAAR®

Name of Active Substance: Losartan-Kalium

The study listed may include approved and non-approved uses, formulations, or treatment regimens. The results reported in any single study may not reflect the overall profile of a product. Before prescribing any product mentioned in this registry, healthcare professionals should consult local prescribing information for the product approved in their country. Results presented here may include different data points from those required on http://clinicaltrials.gov/.

Title of Study:

A Phase III, Randomized, Open-Label, Parallel-Group, Dose-Ranging Clinical Trial to Study the Safety and Efficacy of MK-0954/Losartan Potassium in Pediatric Patients With Hypertension (MK-0954 Prot. 337)

Protocol Amendments:

337-**01** dated 07-August-2008; 337-**02** dated 15-February-2010; 337-**03** dated 02-March-2011;
337-**04** dated 07-June-2011 (was not implemented due to regulatory concerns); 337-**05** dated 18-November-2011;

Unique Identifier: NCT00756938

Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.

Study Center(s) / Investigator(s): Multicenter (56) in the United States, Europe, Latin America, and Asia

Publication(s): No Publication based on this study.

Studied Period:	**Clinical Phase:** III
16-Mar-2009 (date first patient entered randomized open-label period) to 14-Aug-2012 (date of last dose of last patient)	

Objective(s):

(1) To define a dose-response relationship for losartan in hypertensive children aged 6 months to 6 years, after a 21-day randomized open-label treatment period (response assessed by change from baseline in mean trough systolic blood pressure [SBP]);
(2) to investigate the safety and tolerability of losartan at doses up to 1.4 mg/kg/day in hypertensive children aged 6 months to 6 years after 12 weeks of treatment.

Study Design:

Randomized, open-label losartan, parallel-group, dose-ranging, multicenter study in approximately 100 hypertensive children, aged 6 months to 6 years. All patients were randomized to open-label losartan. The study did not include a placebo or comparator treatment group.

Number of Subjects/Patient Disposition:

Patient Characteristics (All Randomized Patients)

	MK-0954: Low Dose 0.1 mg/kg/day		MK-0954: Medium Dose 0.3 mg/kg/day		MK-0954: High Dose 0.7 mg/kg/day		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Patients in population	33		34		34		101	
Gender								
Male	20	(60.6)	18	(52.9)	20	(58.8)	58	(57.4)
Female	13	(39.4)	16	(47.1)	14	(41.2)	43	(42.6)
Age (year)								
<1	2	(6.1)	4	(11.8)	4	(11.8)	10	(9.9)
1-6	31	(93.9)	30	(88.2)	30	(88.2)	91	(90.1)
Mean (Months)	40.2		45.0		40.6		42.0	
Standard Deviation (Months)	24.4		21.5		21.2		22.3	
Median (Months)	39.0		45.0		41.5		41.0	
Range (Months)	6 to 82		7 to 81		6 to 79		6 to 82	
Age Cohorts (months)								
6-23	13	(39.4)	6	(17.6)	8	(23.5)	27	(26.7)
>23	20	(60.6)	28	(82.4)	26	(76.5)	74	(73.3)

Disposition of Patients by Study Status

	MK-0954: Low Dose 0.1 mg/kg/day		MK-0954: Medium Dose 0.3 mg/kg/day		MK-0954: High Dose 0.7 mg/kg/day		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Excluded [1]							**24**	**(19.4)**
Screen Failure Withdrew							20	(16.1)
Consent Deviation From Protocol							2	(1.6)
Lost to Follow-Up							1	(0.8)
Randomized Completed							1	(0.8)
Base Study Discontinued	**33**	**(100.0)**	**34**	**(100.0)**	**34**	**(100.0)**	**101**	**(100.0)**
[2]	**31**	**(93.9)**	**34**	**(100.0)**	**32**	**(94.1)**	**97**	**(96.0)**
Deviation From Protocol	**2**	**(6.1)**	**0**	**(0.0)**	**1**	**(2.9)**	**3**	**(3.0)**
Lost to Follow-Up	0	(0.0)	0	(0.0)	1	(2.9)	1	(1.0)
Other Protocol Specified Criteria	1	(3.0)	0	(0.0)	0	(0.0)	1	(1.0)
Continued to Extension	1	(3.0)	0	(0.0)	0	(0.0)	1	(1.0)
	28	**(84.8)**	**33**	**(97.1)**	**29**	**(85.3)**	**90**	**(89.1)**

Each patient is counted once based on the latest corresponding disposition record.

[1] One patient (3700015 - AN=000047) is counted as excluded due to deviation from protocol, but should have been counted in the Discontinued row (see details below).

[2] One patient (3700015 - AN=000047) is NOT counted in the Discontinued row (incorrect data entry); the patient has the status Excluded while it should have been Discontinued (see details below).

Patient 3700015 is counted above as being excluded at screening for deviation from protocol, but was randomized to the high dose (0.7 mg/kg /day) treatment group and completed 29 days of treatment. This patient was discontinued from the study due to the GFR=19.45 ml/min/1.73m2 as determined by the Schwartz Formula, based on serum creatinine at screening.

Diagnosis / Inclusion Criteria:

Informed parental consent was obtained and patient assent (when feasible) was obtained as required by local regulations. Criteria for entry into the open-label base study included the following: male or female patients from 6 months to 6 years of age (patient had not reached 7th birthday at time of randomization), and patient was determined to be hypertensive according to one of the following criteria:

- Patient was 6 months to < 1 year old with a mean SBP ≥ 95th percentile based on gender and age.

OR

- Patient was ≥ 1 year old with a mean systolic and/or diastolic blood pressure (DBP) ≥ 95th percentile based on gender, height and age.

OR

- Patient had co-morbidities or evidence of end organ damage with: mean SBP ≥ 90th percentile (6 months to < 1 year old) based on gender and age, or mean SBP and/or DBP ≥ 90th percentile (≥ 1 year old) based on gender, height, and age.

Dosage / Formulation Nos:

Patients were randomized to one of three different starting doses of losartan: 0.1 mg/kg/day (low dose), 0.3 mg/kg/day (medium dose), or 0.7 mg/kg/day (high dose). Study medication was titrated to the next dose level at Weeks 3, 6, and 9 for patients that were not at goal blood pressure (BP) and not yet on the maximal dose (1.4 mg/kg/day, not to exceed 100 mg/day) of losartan.

Study Drug Titration

Starting Dose	Week 3 Dose Titration (if BP[a] not at goal)	Week 6 Dose Titration (if BP not at goal)	Week 9 Dose Titration (if BP not at goal)
0.1 mg/kg/day	0.3 mg/kg/day	0.7 mg/kg/day	1.4 mg/kg/day (not to exceed 100 mg/day)
0.3 mg/kg/day	0.7 mg/kg/day	1.4 mg/kg/day (not to exceed 100 mg/day)	May add or titrate other open-label medication
0.7 mg/kg/day	1.4 mg/kg/day (not to exceed 100 mg/day)	May add or titrate other open-label medication	May add or titrate other open-label medication

[a] BP=blood pressure

Formulation numbers for the test product used to prepare suspensions were as follows:
DL00012973, DL00012975, DL00012977, DL00012990, DL00014467, DL00015400, DL00015549, DL00015748, DL00015951, DL00016202, DL00016310, DL00016452, DL00016962, DL00016959, WL00031343, WL00031341, WL00041349, WL00042584, WL00042924, WL00042926, WL00042928, WL00043772, WL00044223, WL00044225, WL00044281, WL00046182, WL00046550.

All doses were supplied as losartan dry powder in a sachet formulation for in situ reconstitution as an oral suspension. The Sponsor supplied appropriate product components in one package, including drug sachet, appropriate bottle, bottle adapter and dosing devices. The extemporaneous suspension was prepared at the study site by a pharmacist or other qualified personnel, prior to giving to the patient, by adding Ora-BlendTM SF into a bottle and emptying the sachet into the bottle. The study site personnel calculated the volume of study medication to be given to the patient each day, added the volume to be dosed each day to the bottle label, and instructed the patients' caregivers accordingly.

Duration of Treatment:

The duration of the base study was 13 weeks, comprising an approximately 1-week baseline period and a 12-week open-label treatment period. Patients who completed the base study were eligible to be invited to continue in the open-label losartan extension with follow-up visits every 3 months. The duration of follow-up varied for each patient, and at the longest, lasted until either that patient reached the Month 24 visit of the extension or until the final patient enrolled (100th) completed the 12-week base study, whichever came first.

Evaluation Criteria:

EFFICACY MEASUREMENTS:
Changes in BP from baseline were measured. The following efficacy endpoints were analyzed:
The primary efficacy endpoint was the slope of change in sitting SBP after 21 days treatment (the end of the first dose-period) as compared to baseline as a function of dose.
The secondary efficacy endpoint was the slope of change in sitting DBP after 21 days of treatment (the end of the first dose-period) as compared to baseline as a function of dose. Other secondary efficacy endpoints included the change from baseline in SBP and DBP by Day 21.
Exploratory endpoints included the change from baseline in SBP and DBP at 3-week intervals (base study) and at 3-month intervals (extension study), the percentage of patients who reach goal SBP or DBP by Day 21.

SAFETY MEASUREMENTS:
Physical examinations, vital signs measurements (sitting or supine BP, pulse, and weight), and laboratory safety evaluations (serum chemistry, hematology, and urinalysis) were conducted. Adverse experiences (AEs) were monitored. Growth was monitored using a stadiometer (or infantometer). Maturation was monitored by Tanner Staging. Echocardiograms to measure left ventricle internal dimension, interventricular septal thickness, posterior wall thickness, calculation of left ventricular mass (LVM) and left ventricular mass index (LVMI), fractional shortening, and mitral valve Doppler flow were targeted in approximately 40-50 patients at randomization (prior to Visit 4–Week 3) and at their final visit of the extension (or as close to when the patient exited the study as possible, ideally not sooner). The final visit echocardiogram was not to be performed unless the patient had been on the study medication for ≥ 6 months since the randomization visit echocardiogram.
A Data Safety Monitoring Board (DSMB) met on a regular basis to monitor the overall safety of the patients.

Statistical Planning and Analysis:
EFFICACY:
The primary analysis population for efficacy is the Full Analysis Set (FAS), including all patients who have at least one prime therapy intake, a baseline, and a post-treatment observation. The primary endpoint was assessed using an analysis of covariance (ANCOVA)-model for the change from baseline in SBP after 21 days with terms for dose (as a continuous covariate: 0.1, 0.3, or 0.7 mg/kg/day), weight and presence of co-morbidities/end organ damage (yes/no). The primary hypothesis was assessed
by testing whether the slope for dose in the above regression model was zero or not. In addition, to estimate the change from baseline in SBP in each dose regimen by Day 21, an ANCOVA-model for the change from baseline in SBP was fitted with terms for dose (as a factor), weight and presence of comorbidities/end organ damage (yes/no). Both within- and between-treatment differences are presented.
Similar analyses were performed on the secondary efficacy endpoint of change in DBP after 21 days of treatment. A longitudinal data analysis (LDA) model was used to provide supportive analyses for the change from baseline in SBP and DBP after 21 days.
Exploratory endpoints included the change from baseline in SBP and DBP at 3-week intervals (base study) and at 3-month intervals (extension study), and the percentage of patients who reached goal SBP or DBP by Day 21. The percentage of patients in each dose regimen who reached goal BP by Day 21 are presented by treatment group together with its 95% confidence interval based on the exact binomial distribution.
With 30 analyzable patients per group, the study has 92% power to detect a within-group treatment difference of 7 mmHg or 67% power to detect a 5 mmHg difference at the 0.05 level. The description of the sample size and power calculations is described the protocol [16.1.1].
Since there was only one primary hypothesis, no multiplicity adjustment was needed.

SAFETY:
The All Patients as Treated (APaT) population was used for the analysis of all safety data in this study and included all randomized patients who received at least one dose of study treatment. Safety and tolerability was assessed by clinical review of all relevant parameters including AEs, laboratory tests, growth and maturation, and echocardiogram measurements. For the base study, the broad clinical and laboratory AE categories consisting of the percentage of patients with any AE, a drug-related AE, a serious AE (SAE), an AE which is both drug-related and serious, and who discontinued due to an AE, as well as specific AEs, are summarized by counts and frequencies in 3-week intervals, and the event was counted on the treatment that was received during that 3-week period. Listings of patients with SAEs and/or patients who discontinued due to an AE are provided as well. Descriptive summaries of safety parameters are provided.
For the extension period, overall counts and frequency tables for broad clinical and laboratory AE and for specific AEs are provided. Listings of patients with SAEs and/or patients who discontinued due to an AE are provided as well. Summary tables and/or graphical displays are presented for the overall change from baseline in laboratory parameters and echocardiogram measurements, as well as listings of patients who exceeded predefined limits of change for specific laboratory parameters; these listings include the dose at which the event occurred. Z-scores for length (adjusted for gender and age) were calculated at baseline, after 12 weeks of treatment and every 6 months thereafter. The z-scores are summarized by quartiles and 10th and 90th percentiles at each of these time points.

RESULTS:
No dose-response was observed at 3 weeks between either the low vs medium or high dose regimens, as demonstrated by lack of a statistically significant result from the slope analysis of change from baseline in SBP, and as such the primary endpoint of the study was not achieved (see table below). Slope of Change from Baseline in Systolic Blood Pressure (mmHg) as Function of Dose as a Continuous Covariate by Day 21 Using an ANCOVA Model (Full Analysis Set)

MK-0954:		N	Baseline Mean (SD)	Day 21 Mean (SD)	Mean Change (SD)
Low Dose	0.1 mg/kg/day	32	111.25 (8.79)	103.94 (12.81)	-7.31 (12.53)
Medium Dose	0.3 mg/kg/day	34	113.74 (8.21)	106.09 (9.38)	-7.65 (7.49)
High Dose	0.7 mg/kg/day	33	111.15 (7.22)	104.48 (9.79)	-6.67 (7.86)
			Estimate [1] (95% CI)		p-Value [1]
Slope [1] (mmHg/mg/kg/day)			1.22 (-6.45, 8.90)		0.753

[1] From ANCOVA model for the change from baseline in SBP after 21 days with terms for dose as a continuous covariate: 0.1, 0.3 or 0.7 mg/kg/day, weight as a continuous covariate and presence of co-morbidities/end organ damage (yes/no).
N represents the number of patients included in the analysis (i.e., patients who received study treatment and had data at both time points - Baseline and Day 21).

The other objective of this trial was to demonstrate the safety and tolerability of losartan at doses up to 1.4 mg/kg/day in this group of younger aged children. As in study PN 227, with older children 6 -16 years of age, losartan was well tolerated at doses up to 1.4 mg/kg/day (maximum 100 mg/day). The AE rates were comparable across the four dose regimens (0.1 mg/kg, 0.3 mg/kg, 0.7 mg/kg and 1.4 mg/kg) that patients were exposed to during the 12 week Base Phase of the study. The overall AE rate was approximately 80% for all 99 patients exposed to losartan, with AE rates ranging from 55.6% to 66.7% for each of the four doses administered in this trial. No apparent dose response was observed even as patients moved through different dose regimens during the 3 weekly titration phases allowed in the 12 week Base Phase. See table below summarizing AEs by dose received.

Clinical Adverse Event Summary by Dose Received at Time of Event over 12 Weeks in the Base Study (All Patients as Treated)

	MK-0954: Low Dose 0.1		MK-0954: Medium Dose 0.3 mg/kg/day		MK-0954: High Dose 0.7		MK-0954: Highest Dose 1.4 mg/kg/day		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Patients in population	34		54		63		33		99	
with one or more clinical	21	(61.8)	30		36	(57.1)	22		79	(79.8)
adverse events with no	13	(38.2)	(55.6)		27	(42.9)	(66.7)		20	(20.2)
clinical adverse event	0	(0.0)	24		2	(3.2)	11		3	(3.0)
with drug-related[1] clinical	3	(8.8)	(44.4)		2	(3.2)	(33.3)		7	(7.1)
adverse events with serious	0	(0.0)	2		0	(0.0)	1		0	(0.0)
clinical adverse events			(3.7)				(3.0)			
with serious drug - related[1]	0	(0.0)	2		0	(0.0)	0		0	(0.0)
clinical adverse events	0	(0.0)	(3.7)		0	(0.0)	(0.0)		0	(0.0)
who died	0	(0.0)	0		0	(0.0)	0		0	(0.0)
discontinued[2] due to a clinical adverse			(0.0)				(0.0)			
event discontinued due to a drug -	0	(0.0)			0	(0.0)			0	(0.0)
related clinical adverse	0	(0.0)	0		0	(0.0)	0		0	(0.0)
event			(0.0)				(0.0)			
			0				0			

[1] Determined by the investigator to be related to the drug. If unknown then considered to be drug-related. [2] Study Medication Withdrawn
Percentages are calculated based on the number of subjects who received at least one dose of the specified study treatment dose and with follow-up during the Base study. Patients may be counted in more than one dose group according to each dose to which they were exposed during the 12 week randomized phase of the trial. Each subject

Dose response relationship to safety events was not evaluated during the Extension Phase but the overall AE rate was 83.3% with a rate of 5.6% for drug related events. The incidence of drug-related AEs was slightly higher than that observed in the Base Phase but still quite low. As in the Base Phase the majority of AEs were indicative of common intercurrent illnesses seen in this young age group. In the Extension Phase only one patient discontinued therapy due to an adverse event of allergic dermatitis, not felt to be study drug related.

Conclusions:

In young children 6 months through 6 years of age with hypertension (with or without co-morbidities, end-organ disease or concomitant antihypertensive therapy):

- No observable dose response effect was achieved during the first 3 weeks of losartan dosing at 0.1 mg/kg, 0.3 mg/kg or 0.7 mg/kg
- Although no direct comparison was made with placebo, a consistent blood pressure lowering effect was observed for all doses through both the 12 week Base Phase and the 2 year Extension Phase
- Losartan, at doses as high as 1.4 mg/kg, was generally well tolerated and extends the already established safety profile of this angiotensin II receptor blocker (ARB) to this young age cohort.

Date of the Report: 05-March-2013

List of Investigator's and Independent Ethics Committees

Address	Protocol - Study No.	C/REB/IRB	Committee Chairperson	Number of Subjects Randomized
Argentina				
Centro Infantil del Rinon, Monteagudo 726, San Miguel de Tucuman, 4000 ARG	MK 0954 337-0015	Comite Independiente de Etica para Ensayos en Farmacologia Clinica / Fundacion de Estudios Farmacológicos y de Medicamentos <Prof. Luis M. Zieher>	Luis M. Zieher	4
Hospital Italiano de Bueno Aires, Sascon 450, Buenos Aires 1181 ARG	MK 0954 337-0060	Comité de Ética de Protocolos de Investigación - Hospital Italiano de Buenos Aires Departamento de Docencia y Investigación	Dra. Karin Kopitowski	0
Brazil				
Hospital Pequwno Principe, Desembargador Motta 934, Curitiba 80.250-060 Brazil	MK 0954 337-0016	Comitê de Ética em Pesquisa de Seres Humanos HPP	Prof. Dr. Luiz Antonio Munhoz da Cunha	14
Hospital de Base da Faculdade de Medicina de Sao Jose do Rio Preto, Av. Brigadeiro Faria Lima 5416, 15090-000 Brazil	MK 0954 337-0017	Comitê de Ética em Pesquisa - Faculdade De Medicina De Sao Jose Do Rio Preto	Prof. Dr. Humberto Liedtke Junior	1
Instituto da Crianca, Av Doutor Eneas de Carvalho Aguir 647, Sao Paulo 05403-000 Brazil	MK 0954 337-0018	CAPPesq Prof.	Dr. Euclides Ayres de Castilho	3

Instituto Materno Infantil Professor Fernando Figueira, Rua dos Coelhos 300 6 andar, Recife 50070-550 Brazil	MK 0954 337-0019		Comitê de Ética em Pesquisa - Instituto de Medicina Integral	Jose Eulalio Cabral Filho, M.D.	5
Hospital Infantil Joana de Gusmao, Av Princesa Isabel 395, Florianopolism 88025-301 Brazil	MK 0954 337-0053		Comitê de Ética em Pesquisa Envolvendo Seres Humanos do HIJG	Mauricio Laerte Silva	1
Instituto de Cardiologia do Rio Grande do Sul, Av Princesa Isabel 395, Porto Alegre 90620-001, Brazil	MK 0954 337-0054		Comitê de Ética em Pesquisa - Instituto Cardiologia Do Rio Grande Do Sul Fundacao Universitaria De Cardiologia	Dr. Ari Taden Lirio dos Santos	0
Universidade Federal de Goias, Primeira Avenida SN Setor Leste Universitario, goiania 74605-020 Brazil	MK 0954 337-0061		CEPMHA/HC/UFG	José Mário Coelho Moraes	0
Instituto de Pesquisa Clinica para Estudos Multicentricos, Rua Francisco Getulio Vargas, 1130 Bloco S. Caxias do Sul 95070-560 Brazil	MK 0954 337-0063		Comitê de Ética em Pesquisa da Universidade De Caxias Do Sul	Prof. Izidoro Zorzi	0
/ Hospital Sao Paulo, rua Leandro dupret, 240 Vila Mariana, Sao Paulo, 04025-010 Brazil	MK 0954 337-0065		Comitê de Ética em Pesquisa Hospital São Paulo	Prof. Dr. Jose Osmar Medina Pestana	0

Chile					
Hospital de Ninos Roberto del Rio, Zanartu, 1084 Independencia, Santiago 8380418, Chile	MK 0954 337-0020		Comité de Ética de la Investigación S.S.M.N.	Dr. Carlos Navarro Cox	3
/ Hospital Luis Calvo Mackennaa, Antonio Varas 360 Providencia, Santiago Chile	MK 0954 337-0021		Comité de Ética Pediátrico Hospital Luis Calvo Mackenna	Marianella Caneo	0
Colombia					
Hosputal Pablo Tobon Uribe, Calle 78B #69-240, Medellin Antioquia, Colombia	MK 0954 337-0022		Comité y Ética en Investigaciones del Hospital Pablo Tobon Uribe	Antonio Jose Lopera Upegui	2
Fubdacion Cardio Infantil, Calle163 A No28-40, Bogota Cundin, 1, Colombia	MK 0954 337-0023		Comité de Ética en Investigación Clínica Fundacción Cardio Infantil, Instituto de Cardiologia"	J, Sinay Arévalo Leal	0
Clinica las Americas, Diag 75B#2A-80/140, Medellin Antiguia 0 Colombia	MK 0954 337-0024		Comité de Ética Hospitalaria e Investigación Clinica Las Americas	Juan Pedro Velásquez Berruecos	0
Guatemala					
Randall Lou Meda Private Clinic and Foundation for Children with Kidney Diseases, 6 avenida3-22 zona 10 809, Guatemala 01010	MK 0954 337-0025		Comite Etica Independiente Guatemala, C.A.	Dr. Herman Sanchez	15

Private Clinic, 4a. Calle 7-53 zona 9 Edificio Torre Azul, Oficina 809, Guatemala 01009	MK 0954 337-0026		Comite Etica Independiente Guatemala, C.A.	Dr. Herman Sanchez	7
Hungary					
Semmelweis Univ. 1st Dept of Peds, Bokay u 53, Budapest 1083 Hungary	MK 0954 337-0041		Semmel Weis University Regional and Instituitional Committee of Science and Research Ethics	Prof. Dr. Peter Sotonyi	1
Borsod County Teching Hospital Szentpeteri Kapu 72-76. Miskolc 3526 Hungary	MK 0954 337-0043		Regionális Tudományos Kutatásetikai Bizottság Borsod-Abaúj-Zemplén és Heves Megye	Dr. Valikovics Attila	0
India					
/ Appollo Hospital Educational and research Foundation, Lake View Road, K. K. Nagar Madurai 625020 India	MK 0954 337-0038		Ethics Committee Apollo Speciality Hospitals Madural	Dr. M.T. Malaiyarasan	0
Medisys Clinsearch India PVT Ltd. Bangalore Diabetes Centre 4c 426 4th Cross 2nd Block Kalyannagar, Bangalore 560043 India	MK 0954 337-0040		Medisys Clinisearch Ethical Review Board	Dr. Latha Reddy	0
Rainbow Hospitals 22 Road #10 Banjara Hills, Hyderabad 500034 India	337-0042		Institutionals Ethic Committee, Global Hospitals	Justice Eshwar Prasad	0
Maulana Azad Medical College, Bahadur Shah Zafar Marg, New Delhi 110002 India	MK 0954 337-0056		Intitutional Ethic Committee Maulana Azad Medical College	Dr. A. S. Bais	8

Lithuania					
Vilniaus universiteto ligonines Santariskiu kliniku filialas, Santariskiu 4, Vilnius LT-08406 Lith	MK 0954 337-0037		Only Central IRB IEC Lietuvos Bioetiko Komitetas – Bioethics Committee of Lithuania	Eugenijus Gefenas	14
/ Klaipedos vaiku ligonine, Donelaicio 7, LT-92140 Lith	MK 0954 337-0046		Only Central IRB IEC Lietuvos Bioetiko Komitetas – Bioethics Committee of Lithuania	Eugenijus Gefenas	1
Norway					
Haukeland Universitetssykehus HF, Jonas Liesvei 65, Bergen N-5021 Norway	MK 0954 337-0036		Regional Komite for Medisinsk OG Helsefaglig Forskningsetikk Nord-Norge Rek Nord	Ellisiv B. Mathiesen	1
Philippines					
National Kidney + Transplant Inst. East Ave, Diliman, Quezon City, 1100 Philippines	MK 0954 337-0035		Clinical Trial and Research unit - National Kidney and Transplant Institute	Romina A. Danguilan, M.D.	2
The Medical City Hospital, Suite 408 Medical Arts Tower Ortigas Ave, Pasig City Metro Manila 1605 Philippines	MK 0954 337-0044		The Medical City Intitutional Review Board	Milagros T. Jocson, MD	4
Philippine General Hospital, 240 A OPD Bldg Taft Ave, Ermita, Manila 1000 Philippines	MK 0954 337-0052		UPMREB – UP Manila Research Ethics Board	Jacinto Blas V. Mantaring III, MD	4

Spain					
Hospital Universitario La Fe. Servicio de Nefrologia Infantil. Avenida Campanar, n 21, 46009 Valencia Spain	MK 0954 337-0055		Central IEC IRB only Comité Ético de Investigación Clínica Hospital Univeritario La Paz	Antonio Gil Aguado	1
Hospital Universitario La Paz, Servicio de Nefrologia Infantil, Paseo de la Castellana 261 Planta Baja, Madrid 28046 Spain	MK 0954 337-0057		Central IEC IRB only Comité Ético de Investigación Clínica Hospital Univeritario La Paz	Antonio Gil Aguado	0
Romania					
Institutul pentru Ocrotirea Mamei si Copilului "Alfred Resuscu" Bd. Lacul Tei nr. 120, Bucharest 020395 Romania	MK 0954 337-0047	n	Only Central IRB IEC National Ethics Committee for the Clinical Study of Medicine	Dr. Adriana Nicolau	1
Spitalul Clinic de Urgenta pentru Copii" Lois Turcanu"Timisoara, Str. Dr. Losif Nemoianu nr.2, Timisoara 300011 Romania	MK 0954 337-0048		Only Central IRB IEC National Ethics Committee for the Clinical Study of Medicine	Dr. Adriana Nicolau	1
UK					
Royal Manchester Children's Hospital, Manchester Inst. Of Nephrology + transplantation, Manchester M139WL UK	MK 0954 337-0029		NRES – National Research Ethics Service Committeee North West	Kath Osborne	1
Southampton General Hospital, Tremona Rd. Southampton S0166YD UK	MK 0954 337-0033		Trust Research & Development – Southamptom University Hospital NHS	Angela Jackson	0

Great Ormond St. Hospital for Children NHS Trust, Great Ormond St. London WC1N3JH UK	MK 0954 337-0045		Great Ormond Street Hospital for Children NHS Trust – Joint Research & Development	Dr. Vanshree Patel	1
United States					
1835 Maple LLC, Williamsville NY 14221	MK 0954 337-0001		WIRB	Theodore D Shultz, JD	0
Harbor Univ of California at LA Medical Sciences Campus, 1000W Carson St Box 491 Torrence CA 90509	MK 0954 337-0002		LA BioMedical Research IRB	Liz Burrola, CIP; John F. Wolf, MD	0
Univ of Kentucy 1760 Nicholasville Road, Suite 602 Lexington KY 40503	MK 0954 337-0003		University of Kentucky	Thomas Foster	2
Childrens Hospital and Regional Medical Center 4800 Sand Point Way NE A-7931 Nephrology Seattle WA 98105	MK 0954 337-0004		Seattle Children's IRB	Douglas S. Diekema, M.D. MPH	1
DUKE Univ Medical Center, Box 3959 DUMC, Durham NC 27710	MK 0954 337-0005		DUKE Medicine IRB	Sandra J. Grimes	0
Childrens Hospital Medical Center of Akron, One Perkins Square, Akron OH 44308	MK 0954 337-0006		Akron Children's Hospital	Robert W. Novak	0
/ Miami Childrens Hospital 3200 S.W. 60 Court, Suite 304, Miami FL 33155	MK 0954 337-0007		WIRB	Theodore D Shultz, JD	0

Childrens Heart Center at Saint Vincent 8333 Naab Rd, Suite 320 Indianapolis IN 42660	MK 0954 337-0008		WIRB	Theodore D Shultz, JD	0
/ Cedars Sinai Medical Center, 8635 W. Third Street Suite 1165 W. LA CA 90048	MK 0954 337-0009		Cedars-Sinai Medical Center IRB	Scott Cunneen, M.D., Michael Lewis, M.D., Ilana Cass, M.D.	0
/ The Children's Hospital of Alabama 1600 7th Ave, ACC516, Birmingham AL 35233	MK 0954 337-0010		WIRB	Theodore D Shultz, JD	0
/ Levine Children's Hospital 1628 E Morehead Street, Suite 200 Charlotte NC 28207	MK 0954 337-0011		Copernicus Group IRB	Tracy Way	0
/ Univ of CA San Fran, 533 Parnassus Ave, Rm U585 Box 0748, San Fran CA 94143	MK 0954 337-0012		Clinical and Translational Science Institute (CTSI) UCSF Committee on Human Research	Jessica Welsh	0
/ CHOC Cardiology P.S.F. Inc., Children's Hosp of Orange County, 455 S. Main Street Suite 430, Orange CA 92868	MK 0954 337-0013		CHOC IRB	Tara Brewer, esq.	0
/ Arkansas Children's Hospital 800 Marshall Street, Slot 512/14 Little Rock AR 72202	MK 0954 337-0014		University of Arkansas for Medical Science IRB	William Evans	0
/ Emory Univ. 2015 Uppergate Drive NE, Atlanta GA 30322	MK 0954 337-0027		Emory University IRB	Tiesha Murray, BS	1

Marshfield Clinic Research Foundation, 1000 North Oak Ave, Marshfield WI 54449	MK 0954 337-0028		MarshField Clinic Research Foundation IRB	Deb Tauschek	2
/ Oregon Health and Science 707 SW Gaines Rd, CDRCP Portland OR 97239	MK 0954 337-0049		Oregon Health & Science	Susan B. Bankowski, M.S., J.D.	0
/ Univ. of Utah Pediatrics, Division of Nephrology + Hypertension, 30 North 1900 East Medical Drive, Salt Lake City UT 84132	MK 0954 337-0051		University of Utah IRB	Josi Wood	1