

# The c4c project: national hub presentation

Pokorná P. and Slanař O.

# Institutions

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This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 777389. The Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

# Background

- The project is implemented under the Innovative Medicines Initiative (IMI2).
- The project is co-funded by the European Union and the European pharmaceutical industry.
- The project involves 34 academic centers and 10 commercial partners.

# Aim

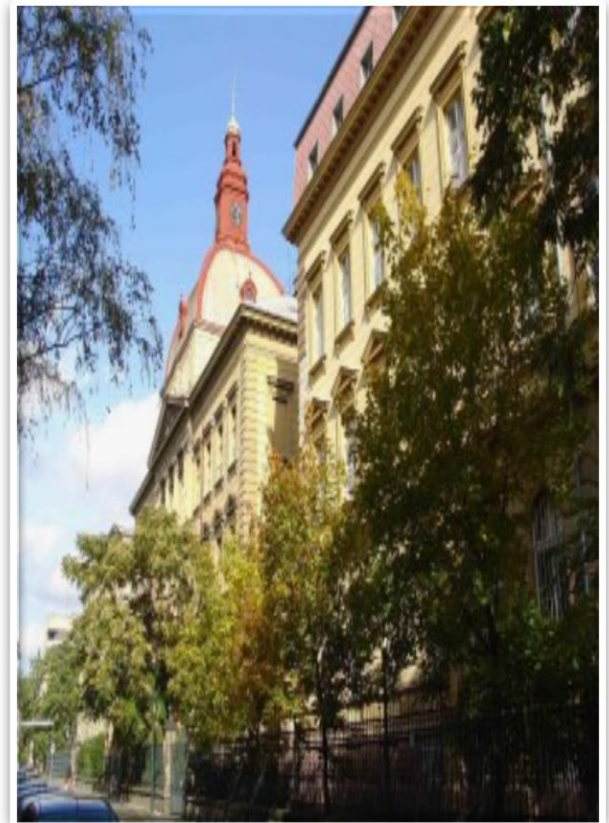
- The aim of the project is to create a pan-European network of clinical centers for pharmacology education and neonatal/pediatric clinical trials in **the Czech republic and Slovakia**



# CHARLES UNIVERSITY (1348) FIRST FACULTY OF MEDICINE (1798) IN PRAGUE



# DEPARTMENT OF PHARMACOLOGY AND DEPARTMENT OF PEDIATRICS



## Private: National Hubs

Home / Network / Private: National Hubs

<https://www.cuni.cz/UK-9448.html> by Petra Koopl 6.12.2018

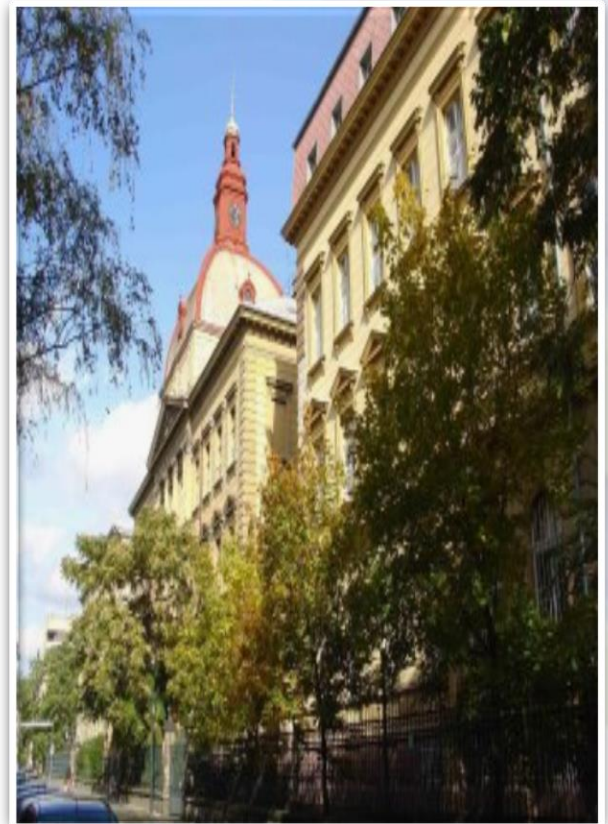




# DEPARTMENT OF PEDIATRICS AND ADOLESCENCE MEDICINE, GENERAL UNIVERSITY HOSPITAL IN PRAGUE

## PEDIATRIC RESEARCH CENTER

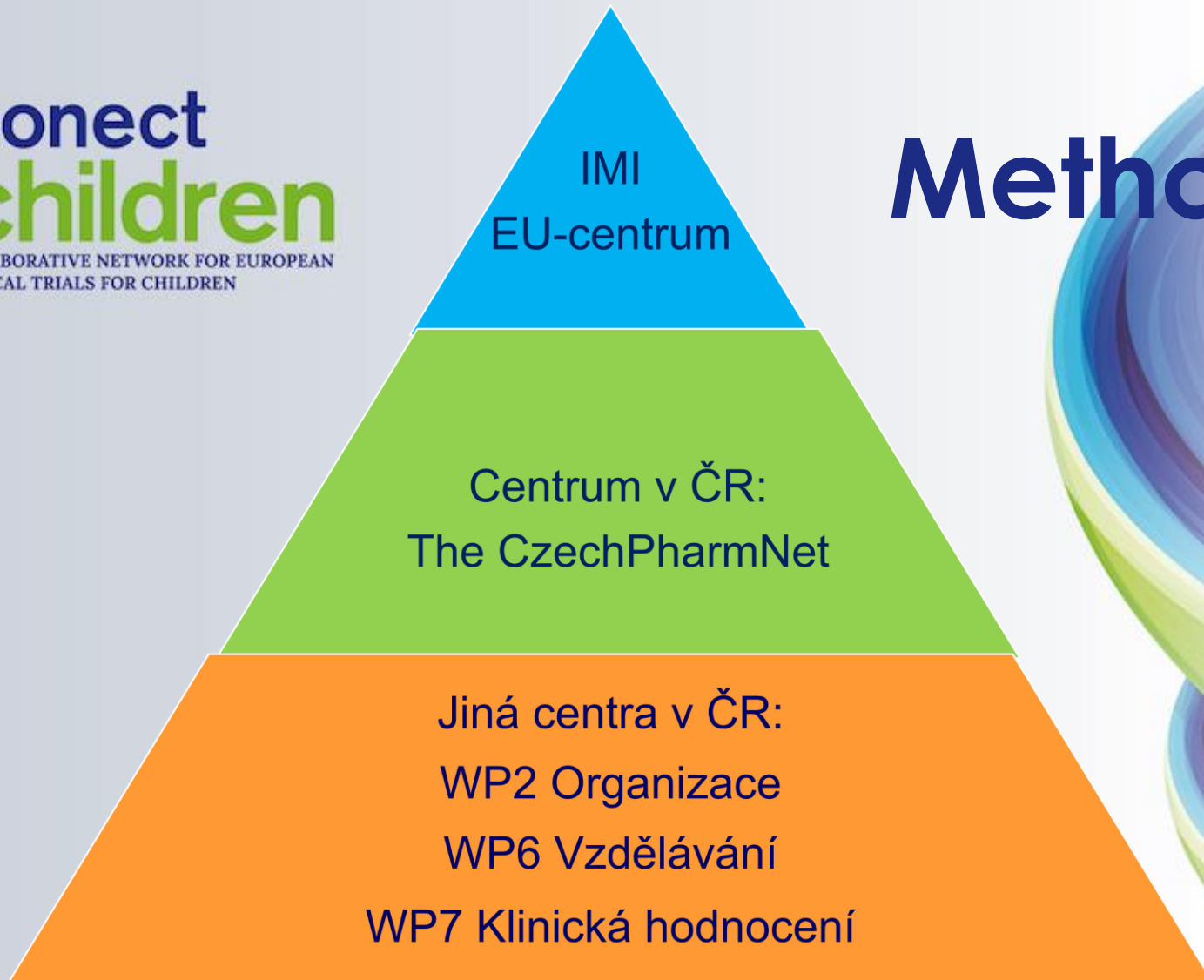
ECMO	2011
HYPOTHERMIA	2007
METABOLIC DISEASES CENTER	1970
PHARMACOLOGY	2005
RHEUMATOLOGY CENTER	
NATIONAL CENTER FOR MEDICAL GENOMICS	





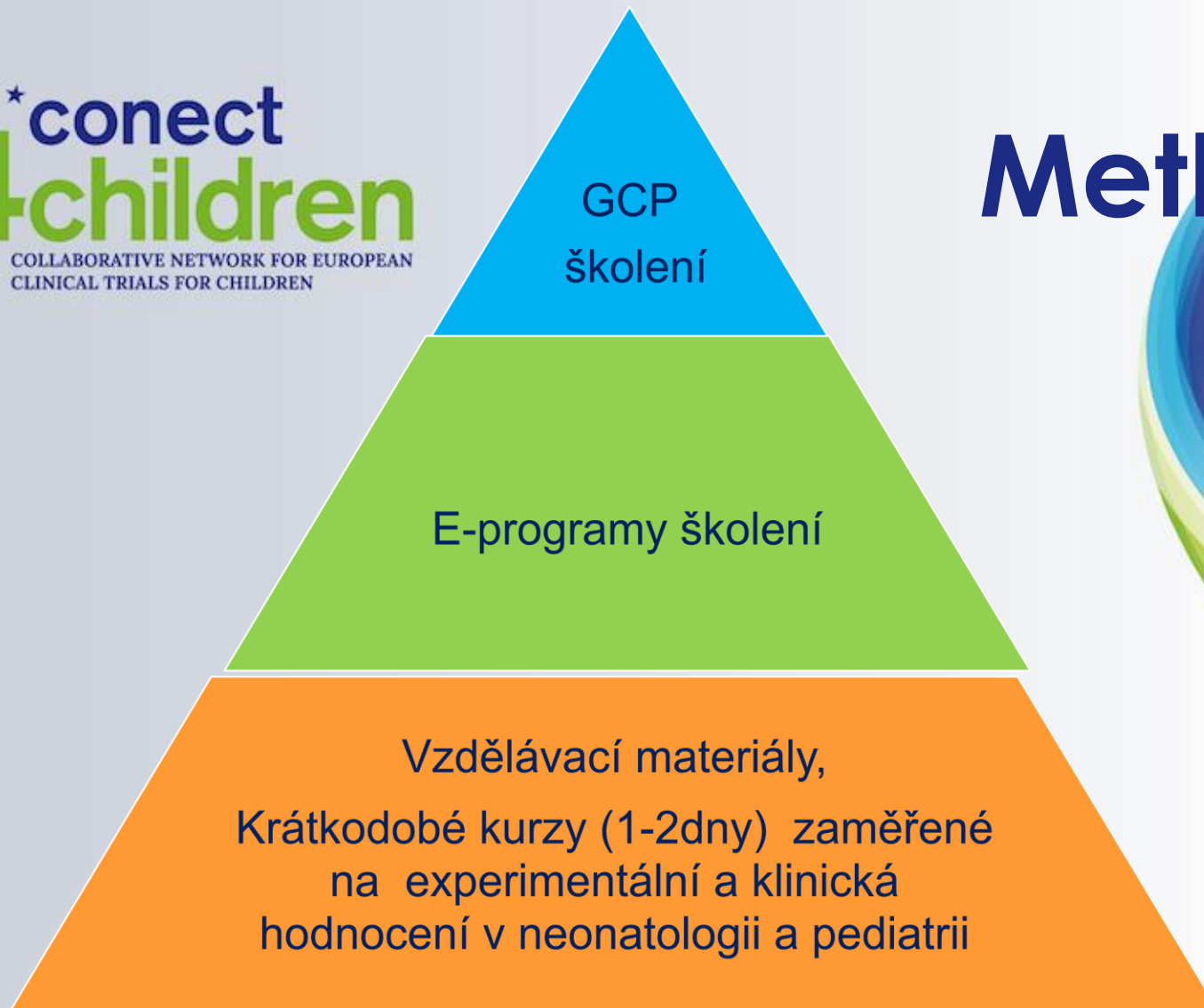
# Methods

- The Innovative Medicines Initiative – **international collaboration**



# Methods

- The Innovative Medicines Initiative – **national collaboration**





# Methods

- Applicant responsible for communication with the c4c:  
CUNI - C4C application based on the CzechPharmNet – Network
- Title: A multidrug PK/PD analysis for anticonvulsive pharmacotherapy in neonates and children up to three years of age

30.11 2018 (the 1st submission) **25.1 2019 (the 2nd submission)**

# Results

PharmDr. Jan Hartinger, PhD

PharmDr, Martin Šíma, PhD

Ing. Jiří Douša

Prof, Ondřej Slanař, PhD

PkEdu -2nd stage development

*CzechPharmNet linked to c4c*

# Projekt Connect4Children (c4c): spolupráce v oblasti klinické farmakologie v neonatologii

P. Pokorná<sup>1,2,3</sup>, O. Slanař<sup>1</sup>

- 1) Ústav farmakologie I. LF UK a VFN v Praze, Česká republika
- 2) Klinika dětského a dorostového lékařství I. LF UK a VFN v Praze, Česká republika
- 3) Intensive Care and Department of Pediatric Surgery, Erasmus MC - Sophia Childrens Hospital, Rotterdam, Nizozemsko



## Úvod

Projekt Connect4Children je plánován pro období 2018-2024 (<http://www.imi.europa.eu/>). Karlova univerzita se zapojila do projektu dne 23.12.201. Farmakologický ústav I. LF a VFN spolu s Klinikou dětského a dorostového lékařství I. LF UK a VFN se staly koordinačním centrem pro Českou a Slovenskou republiku. Projekt je realizován v rámci iniciativy pro inovativní léčiva (IMI2). Jedná se o projekt spolufinancovaný Evropskou unií a evropským farmaceutickým průmyslem. Do projektu je zapojeno 34 akademických center a 10 komerčních partnerů (obrázek 1).

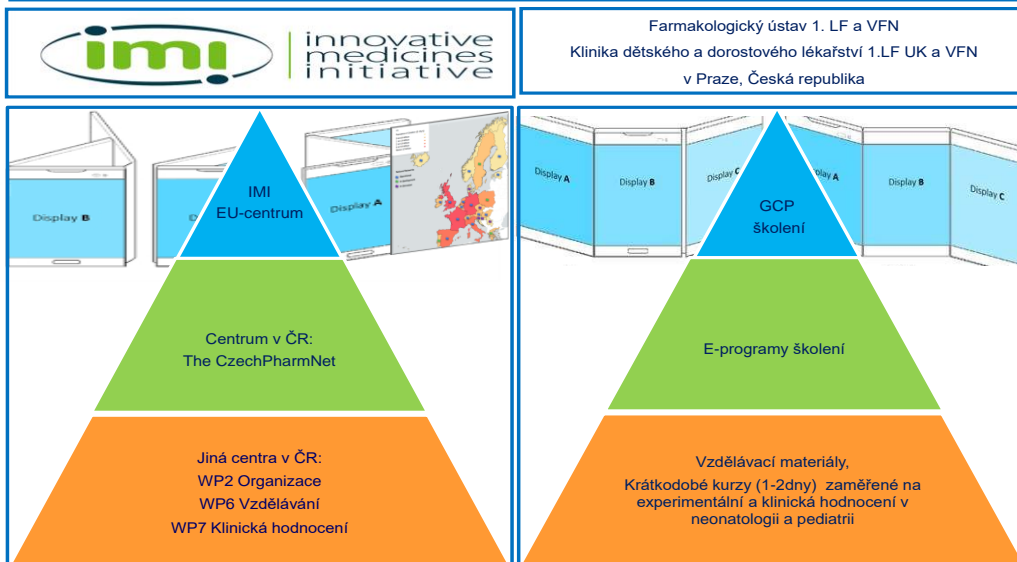
## Cíl a metody

Cílem projektu je vytvořit celoevropskou síť klinických center pro provádění neonatologických a pediatrických klinických hodnocení. Karlova univerzita se bude podílet na projektu zapojením do sítě klinických center (WP7), farmakologického výzkumu (WP2) v neonatologii a pediatrii, včetně podpory scientific advice c4c a propojení s CzechPharmNet a vzdělávacího modulu (WP6), jehož cílem je vytvořit integrovaný vzdělávací systém pro všechny zúčastněné v neonatologickém a pediatrickém klinickém hodnocení (obrázek 2).

## Výsledky

Obrázek 1: The Innovative Medicines Initiative: mezinárodní spolupráce

Obrázek 2: The CzechPharmNet: celostátní spolupráce (WP6)



Pozn. Display A, B: EU – centrum a spolupráce s koordinačním centrem v ČR

Display A, B, C: koordinační centrum v ČR (WP) a spolupráce na celostátní úrovni

## Závěr

Projekt je **první výzvou** všem pracovištím v České a Slovenské republice ke spolupráci v oblasti neonatologické a pediatrické klinické farmakologie.

**Kontakt** MUDr. Pokorná Pavla PhD: [pavla.pokorna@vfn.cz](mailto:pavla.pokorna@vfn.cz); Prof. MUDr. Slanař Ondřej PhD: [oslan@lf1.cuni.cz](mailto:oslan@lf1.cuni.cz)

**Poděkování:** Prof. Mark Turner, leader projektu, Prof. MUDr. Jiří Zeman PhD, Doc MUDr. Tomáš Honzík, PhD a Prof. Dick Tibboel **Podpora naší práce:** Projekt RV- VFN(64-165/2012) Praha, Project of Erasmus Sophia Childrens Hospital Rotterdam a c4C EU-projekt

## Step 1 Project introduction 2018:

## Step 2 Network development 2019

## Step 3 Third sites: Czech Neonatal Society

## Bořetice – CzNscommittee 24.1.2019

## Presentations on network c4C project:

2018 Ipocrates Educational Seminars

2018 the Czech Pharmacology Society

2018 the Czech Pediatric Society

2018 the Czech Neonatal Society

2020 European Pharmacology Society

2023 ESDPPP in Prague



- Perinatologické centrum intenzivní péče
- Perinatologické centrum intermediární péče





## WP 2 /WP 6– National Infrastructure

**CHARLES UNIVERSITY**



**Czech Neonatology Society**

**Czech Medical Society of JEP** Assoc. Prof. Jiří Dort M.D., Ph.D. – chairman



**Perinatal centers, intermediate care**



**Seminars, GCPs, MEETINGS**



[www.neonatology.cz/en](http://www.neonatology.cz/en)



## WP 2 /WP 6– National Infrastructure

**CHARLES UNIVERSITY**



**Czech Pediatric Society**

**Czech Medical Society of JEP** Prof. MUDr. J. Zeman DrSc – chairman



**Society for Primary Pediatric Care Czech Pediatric Society**

Head Secretary Czech Medical Association of J.E. Purkyne MUDr.  
Hana Cabrnová



**Seminars, GCPs, MEETINGS**



**OSPDL ČLS JEP**

WP 7– A multidrug PK/PD analysis for anticonvulsive pharmacotherapy  
in neonates and children up to three years of age



**CHARLES UNIVERSITY**



**Czech Pediatric Society and Neurology Society**  
**Czech Medical Society of JEP and Czech Neonatology Society**  
**Czech Medical Society of JEP and Society for Primary Pediatric Care Czech Pediatric Society**



**CLINICAL TRIALS multidisciplinary - doc MUDR Čabala, Radomír**  
**Department of Analytical Chemistry, Faculty of Natural Sciences, Charles University in Prague,**  
**Prague, Czech Republic. Institute of Forensic Medicine and Toxicology, General University Hospital**  
**in Prague, Prague, Czech Republic**

# A multidrug PK/PD analysis for anticonvulsive pharmacotherapy in neonates and children up to three years of age

## Objectives

**To** create a *PK model for individualized dosage of selected anticonvulsants* (on a group of about 20 patients per drug model and the treatment phase (acute and chronic phase)

- to study PK parameters ( $V_d$ , CL,  $T_{1/2}$ ) and PD (clinical, subclinical seizures - aEEG, EEG, video-EEG) during the acute phase of treatment (24 h-7 days), or with AEDs during the chronic phase of treatment (>1month)



# A multidrug PK/PD analysis for anticonvulsive pharmacotherapy in neonates and children up to three years of age

## Aims

1.

TO BUILT AN INFRASTRUCTURE ON CLINICAL PHARMACOLOGY FOR CARE GIVERS (PHARMACOTHERAPY WITH AEDs)

2.

TO DEVELOP THE DOSAGE RECOMMENDATIONS ON TREATMENT FOR SEIZURES FOR A DRUG MODEL IN NEONATES AND CHILDREN UP TO THREE YEARS OF AGE

A multidrug PK/PD analysis for anticonvulsive pharmacotherapy  
in neonates and children up to three years of age

## ***Study design***

**PHASE I:** A RETROSPECTIVE DATA COLLECTION AND DATA ANALYSIS

**PHASE II:** A PROSPECTIVE PK/PD OBSERVATIONAL STUDY  
PROTOCOL PK/PD STUDY  
PHARMACOLOGY INFRASTRUCTURE BUILT VIA NaTHuBS

**ACUTE PHASE** OF TREATMENT (24h-7days)  
**CHRONIC PHASE** OF TREATMENT (>1mo)

**PHASE III** – LONG TERM OUTCOME PARAMETERS VIA NaTHuBS

# A multidrug PK/PD analysis for anticonvulsive pharmacotherapy in neonates and children up to three years of age

## **Methods**

**A multi-center, multinational and interdisciplinary observational PK/PD** study for acute and chronic phase of treatment for seizures with anticonvulsive drugs (AEDs)

**PHASE I** A retrospective analysis (1/2 year) to collect data

**PHASE II** A prospective timepoint schedule of PK/PD multidrug analysis during acute phase of anticonvulsive treatment, 2 to 5 blood samples per patient will be collected. While during chronic treatment 2 samples

**PHASE III** follow up programme

# A multidrug PK/PD analysis for anticonvulsive pharmacotherapy in neonates and children up to three years of age

## ***Patients***

### ***Main Inclusion criteria***

Gestational age ( $\geq 37$  weeks of gestation to 3 years)

term  $\geq 37$  weeks gestational age -28 days of PNA

young infants 29 days – 1 year

children up to three years

Anticipated need for anticonvulsive treatment for at least 24 hours – 7 days (acute phase) or at least  $>1$  month (chronic treatment)

# Conclusion

1. TDM simulation – training programme, GCPs in preparation

2. Questionnaire I – WP 2/6 and Questionnaire II – WP 7

1. 3. 2019

[Home page - Czech Neonatology Society, Pediatric Society](#)



Dear colleague,

I would like to ask you for your help with mapping the current situation in the use of anticonvulsive drugs in the Czech Republic in children **under the age of three**.

The information obtained in this survey research will later be used as one of the initial materials for planned studies.

Thank you in advance for your answers.

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Your name .....

Address of your general pediatric practice .....

.....

E-mail .....

Phone number .....



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How many patients are registered at your practice? .....

How many of your patients **under the age of three** suffer with convulsion? .....

Which are the primary diagnosis of these patients?

.....

.....

.....

.....

How many of these patients are chronically treated with anticonvulsive drugs? .....

Who initially prescribed these drugs to them? Do you cooperate with any of the specialists when deciding on their treatment?



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How do you set therapeutic goals and develop treatment plans? (benefits X adverse effects...)

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.....

How do you succeed in meeting these goals? Have you noticed any subgroup of patients whose disease is particularly difficult to manage?

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How many of these patients use any of **barbiturates**, e.g. phenobarbital? .....

What are the indications for their use? .....

.....

.....



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How many of these patients use the **valproic acid**? .....

What are the indications for its use? .....

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What algorithm do you use to decide on the drug dose? .....

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# Parents initiatives

 nedoklubko



## EFCNI\_PM\_Elternmeeting-Rom181108



# Contacts

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- Prof. MUDr. Slanař Ondřej PhD: [oslan@lf1.cuni.cz](mailto:oslan@lf1.cuni.cz)

FOUNDATION of Prof. **MUDr. Helena Rašková, DrSc., dr. h. c.** 1993-2010

