Clinical gelenics: examples of applications in the national context and in developing countries

CLINICAL GELENICS: EXAMPLES OF APPLICATIONS IN THE NATIONAL CONTEXT AND IN DEVELOPING COUNTRIES

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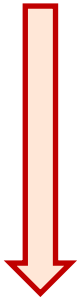
THE GALENICS:
AN ANSWER TO THE HOSPITAL PECULIAR NEEDS

- Modulation of the amount of API in the preparation
- Formulation of associations of API which, if present in the same preparation, may show greater efficacy
- Therapeutic treatments for patients with different ages with special needs and/or different problems (children and elderly)
- Treatments of patients with cancers or degenerative pathologies that cause a severe pain with characteristics that greatly vary from patient to patient

NATIONAL CONTEXT



DEVELOPING COUNTRIES

- Customize the dosages and pharmaceutical forms according to the local needs of patients
- Employ local staff, teaching them a new "job", so that it will be possible to open suitable school
- Minimize the financial commitment necessary to prepare these medicines, respecting the quality of medicinal products

DIFFERENT COUNTRIES, SAME NEED OF QUALITY

THE GALENICS:
AN ANSWER TO THE HOSPITAL PECULIAR NEEDS

NATIONAL CONTEXT → **DEVELOPING COUNTRIES**

DIFFERENT COUNTRIES: SAME NEED OF QUALITY

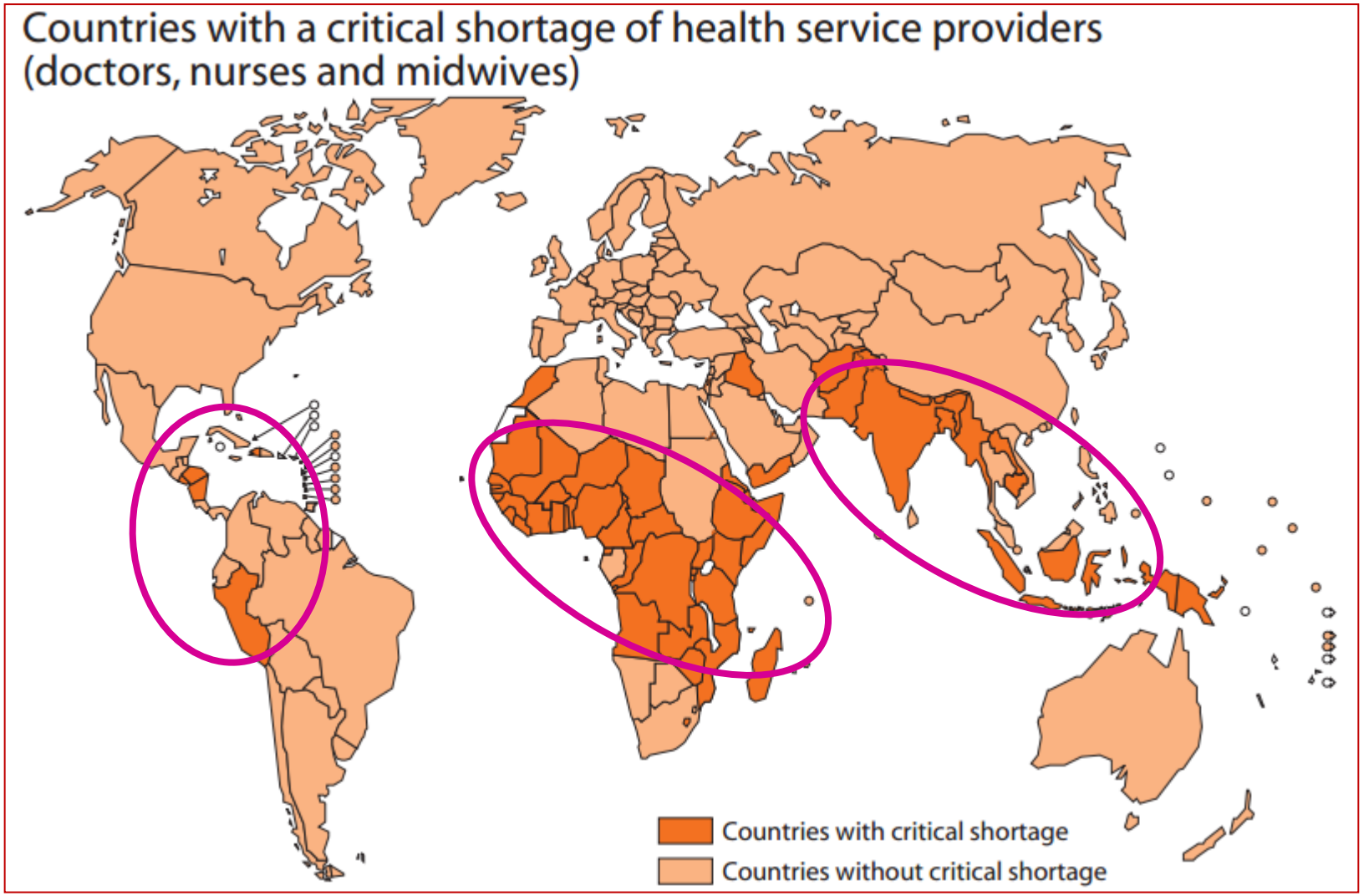
ITALY

PROJECT "POLO ONCOLOGICO DI TORINO"	1. Extension of the stability of anticancer drugs 2. Development of a method for monitoring the microbiological stability of the cytotoxic preparations
CLINICAL STUDY PROTPROS	Evaluation of chemopreventive activity of galenics, comparable to dietary supplement, containing lycopene, selenium and green tea polyphenols
CLINICAL STUDY MONAPOL	Evaluation of cholesterol-lowering activity of a galenic, comparable to a dietary supplement, containing monacolin k and policosanol in subjects with mild to moderate hypercholesterolemia uncomplicated unfamiliar: randomized controlled double-blind study

DEVELOPING COUNTRIES (DC)

***A.P.P.A.*® GALENIC LAB IN HAITI**	1. Study of oral liquid pediatric formulations 2. Stability study of the prepared liquid pharmaceutical forms 3. Development of a method for the preparation of sterile solutions (antibiotics and cytostatic drugs) 4. Project for the introduction of new oral and sterile formulations for pediatric use

ACCESS TO HEALTH SERVICES: INEQUALITIES BETWEEN NORTH AND SOUTH OF THE WORLD



The World Health Report 2006 - working together for health
Chapter 1: Health workers: a global profile

PROBLEMS RELATED TO THE LIFE STILE

«…water-borne diseases are not caused by lack of antibiotics but by **dirty water**, and by the political, social, and economic forces that fail to make clean water available to all; heart disease is caused not by a lack of coronary care units but by the **lives people lead**, which are shaped by the environments in which they live; obesity is not caused by moral failure on the part of individuals but by the excess availability of high-fat and high-sugar foods …»

"Closing the gap in a generation: Health equity through action on the social determinants of health" – WHO Commission on Social Determinants of Health - 2008

Borana Singing wells, Kenya

World Health Organization

ESSENTIAL MEDICINES

Essential medicines are those that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness.

Essential medicines are intended to be available within the context of functioning health systems at all times in **adequate amounts**, in the **appropriate dosage forms**, with assured **quality** and adequate **information**, and at a **price** the individual and the community can afford.

BUT…

World Health Organization
REGIONAL OFFICE FOR Africa

- More than **fifty percent of the population** in the Region **have no regular access to essential medicines.**
- **Medicine supply** and **regulatory systems** are weak
- **Financial** as well as **human resources** are inadequate to ensure delivery of pharmaceutical services and ensure access to essential medicines.
- Circulation of **poor quality medicines**, high medicine **prices**, unethical promotion and **irrational use** of medicines poses additional challenges.

COUNTERFEIT MEDICINES

*A counterfeit medicine is one which is **deliberately and fraudulently mislabeled with respect to identity and/or source**. Counterfeiting can apply to both branded and generic products and counterfeit products may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredients or with fake packaging.*

WHO - General information on counterfeit medicines

"IMPERFECT" COUNTERFEITS

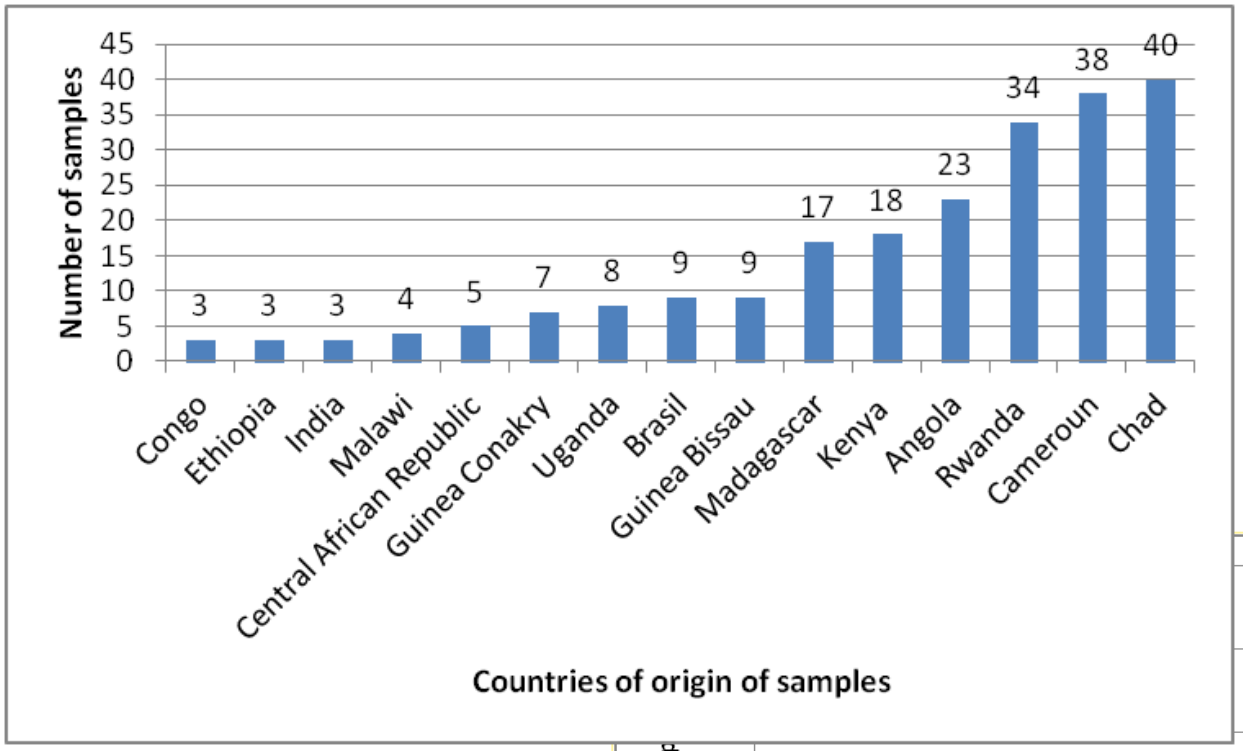
«these products contain the right components, with an incorrect concentration and/or formulation resulting in defective quality specifications. In the vast majority of cases, they are devoid of any therapeutic efficacy»

"CRIMINAL" COUNTERFEITS

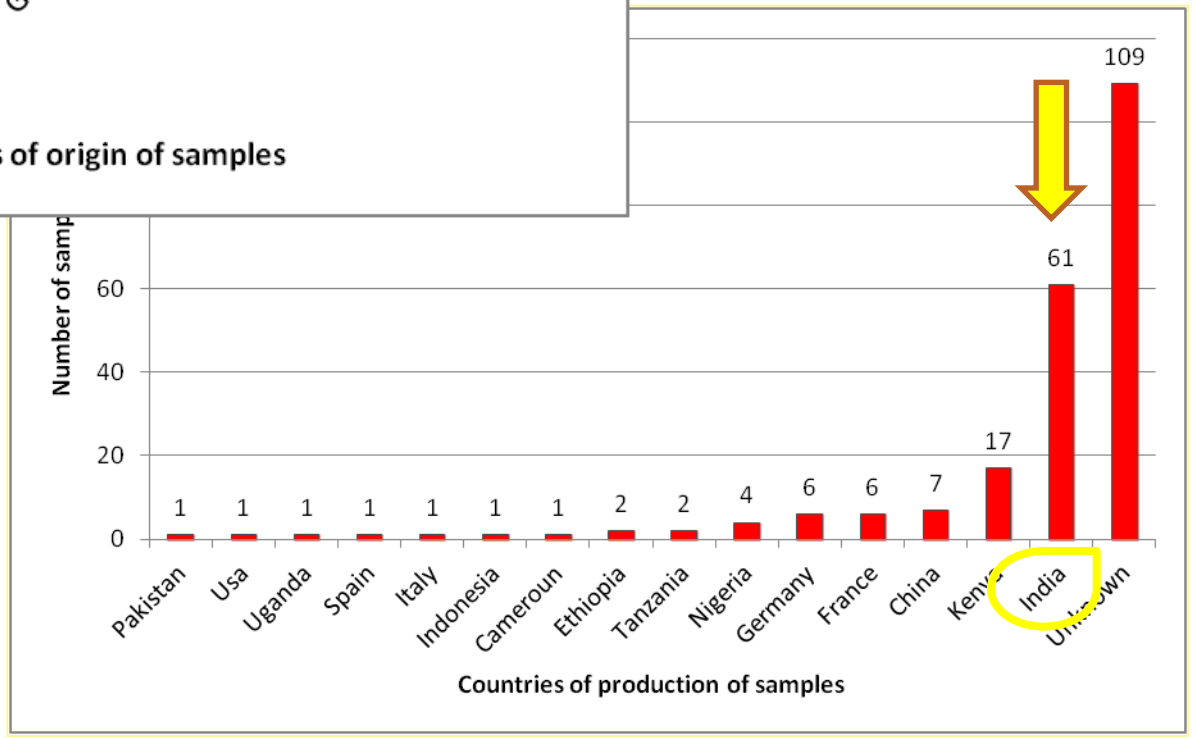
«they are apparently similar to the original medicinal product, but do not contain any active ingredient and can even include harmful or toxic substances. They are usually sold at high prices and for the treatment of serious pathologies. Consequences for users of criminal counterfeits can be fatal»

Di Giorgio D. Counterfeit drugs. The phenomenon and enforcement activities. Milano: Tecniche nuove; 2010.

COUNTERFIET MEDICINES IN DC: ANALYSIS OF THE PHENOMENON



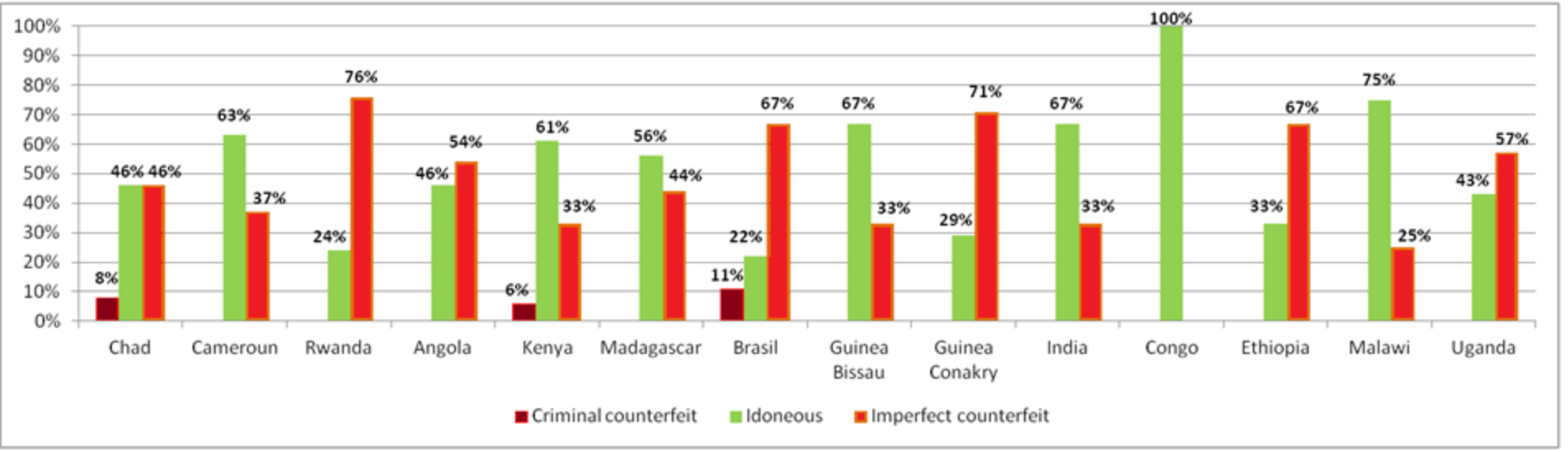
Analysis of 196 samples of medicinal products

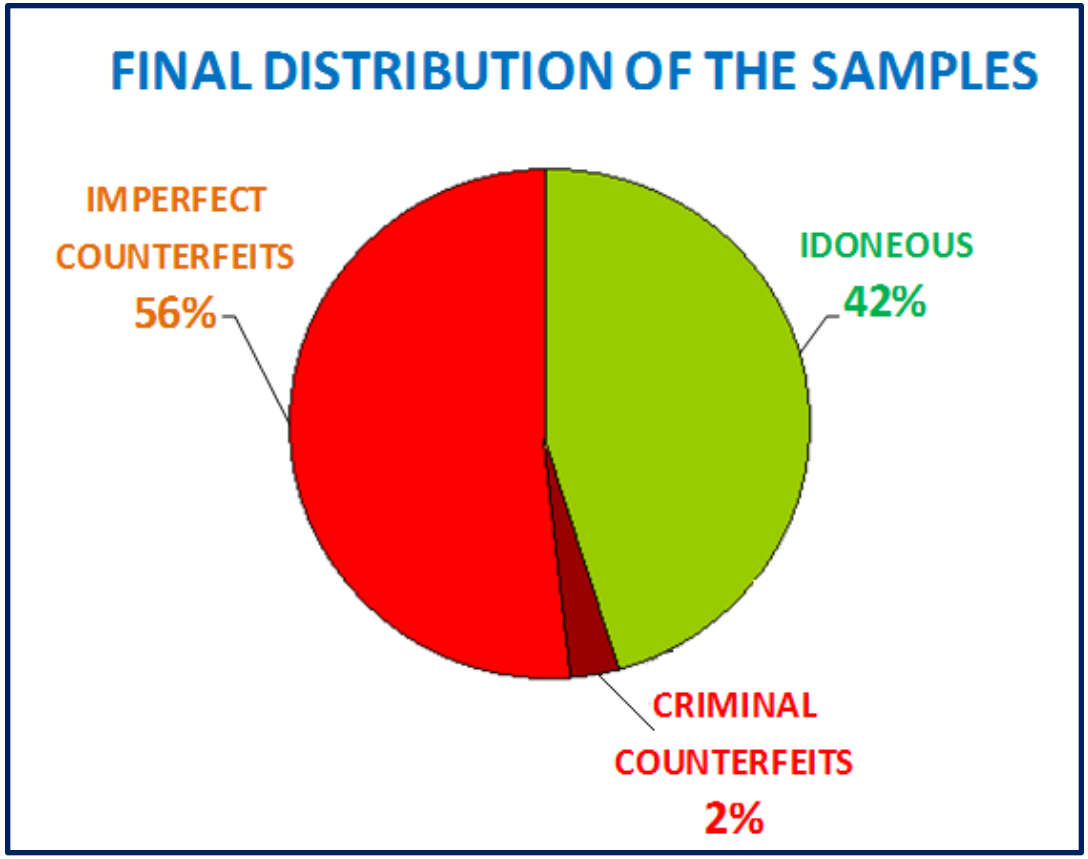


F.Baratta, A. Germano, P. Brusa

Diffusion of counterfeit drugs in developing Countries and stability of galenics stored for months under different conditions of temperature and relative humidity

Croat Med J. 2012; 53: 173-184





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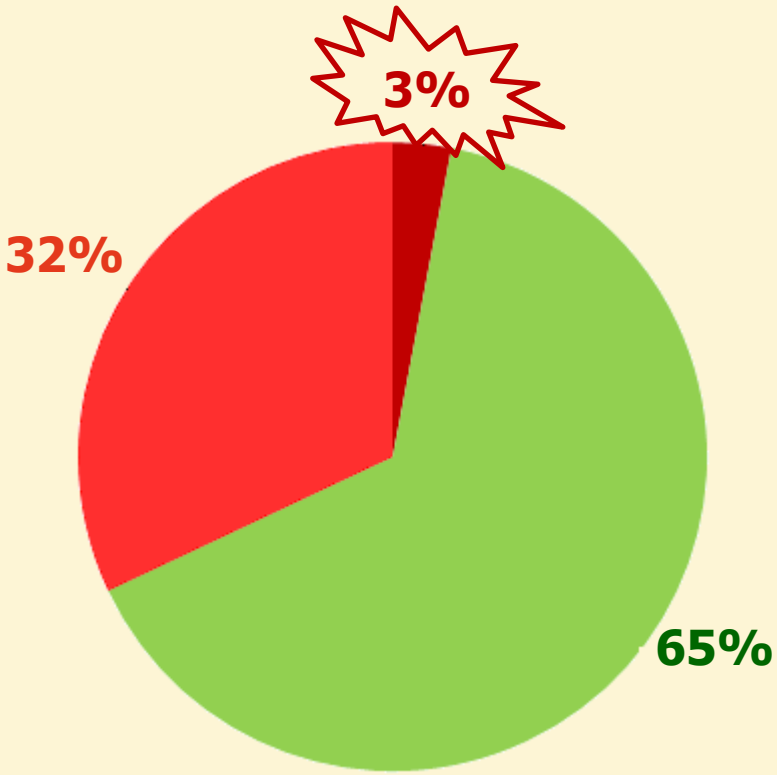
CAMEROUN 2012



Criminal counterfeit

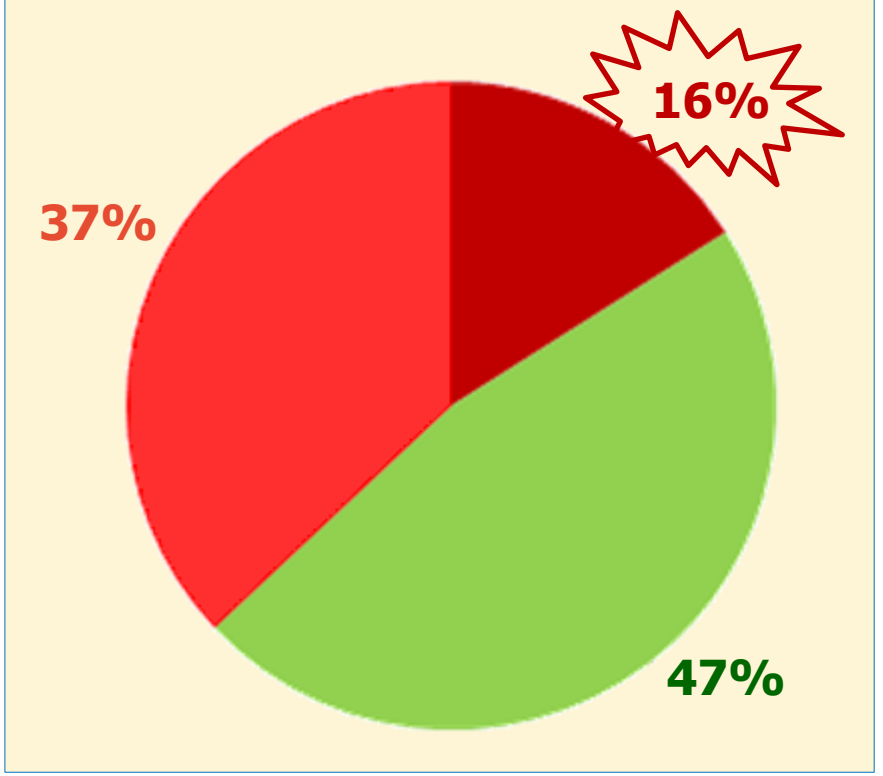
Idoneous

Imperfect counterfeit

PHARMACEUTICAL FORMS TESTS (Ph Eur)

- Uniformity of content (2.9.6)
- Uniformity of mass (2.9.5)
- Disintegration (2.9.1)
- Friability (2.9.7)
- Hardness (2.9.8)
- Sterility (2.6.1)

CAMEROUN 2013



A.P.P.A.® PROJECT

PLANNING, CARRYING OUT, STARTING LABS IN ORDER TO PREPARE GALENIC MEDICINAL PRODUCTS AND RELATIVE QUALITY CONTROL IN DEVELOPING COUNTRIES

With the patronage of:

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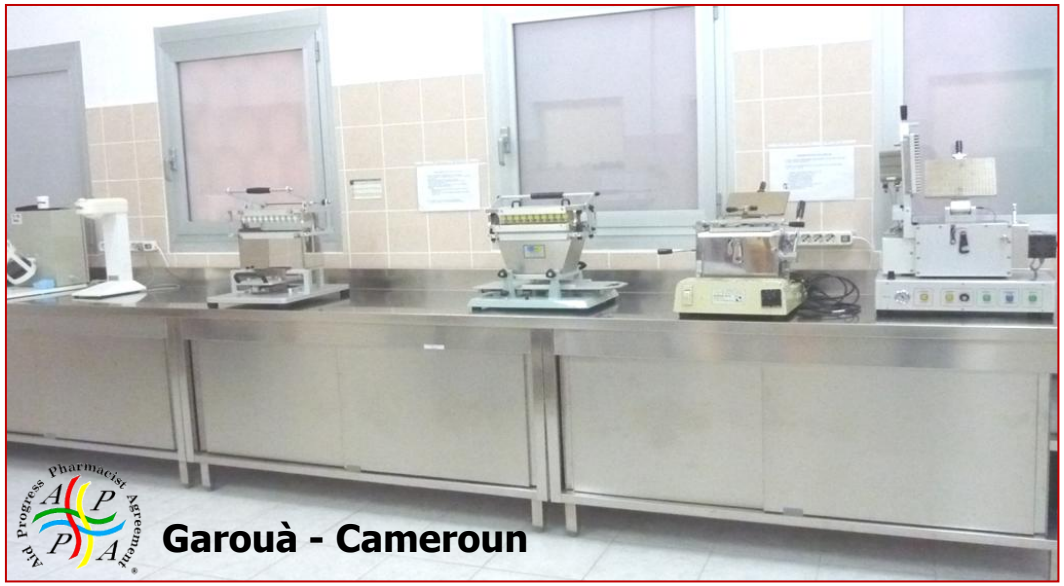


BASIC CONDITIONS FOR OPENING

A LAB FOR THE PREPARATION OF GALENIC MEDICINAL PRODUCTS

- **HIGH PERCENTAGE OF COUNTERFEIT MEDICINES IN THE AREA**
- **LOCAL POOR AVAILABILITY OF QUALITY MEDICINES**
- **HIGH COST OF INDUSTRIAL MEDICINES**
- **APPROVAL OF LOCAL AUTHORITIES**

SAINT DAMIEN PAEDIATRIC HOSPITAL
PORT-AU-PRINCE - HAITI

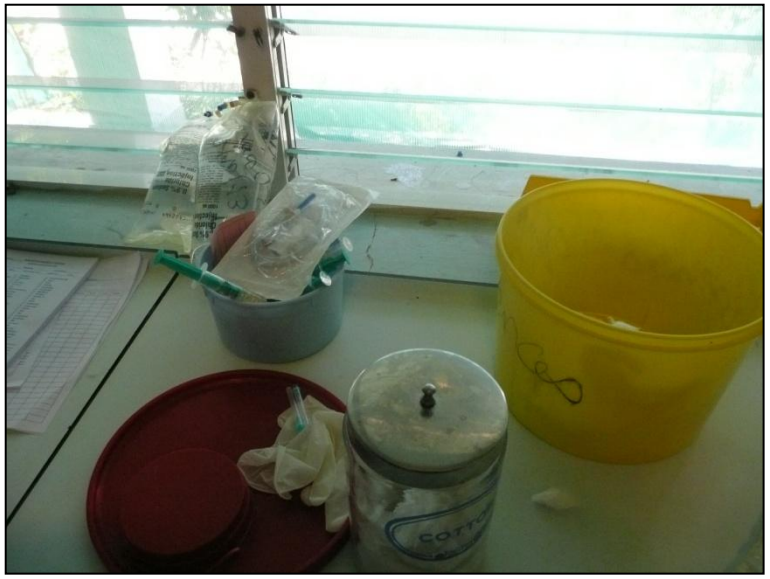
A. STUDY OF **ORAL LIQUID PEDIATRIC FORMULATIONS**

B. STABILITY TESTS OF THE ACTIVE MOLECULES AND OF THE PREPARATION IN ACCORDANCE WITH THE EMA GUIDELINES

C. DEVELOPMENT OF A METHOD FOR THE PREPARATION OF **STERILE SOLUTIONS** (ANTIBIOTICS AND CYTOSTATIC DRUGS)

HAITI: WHY?

MEDICINAL PRODUCTS			
LOT	**API**	**PROVENANCE**	**RESULTS**
6C090	Acetazolamide 250 mg	Haiti	**Unsatisfied:** Uniformity of content (2.9.6), Friability (2.9.7)
0302609	Ampicillin 1g	India	**Unsatisfied**: Bacterial endotixins (2.6.14.)
071202	Chloramphenicol 1g	USA	**Suitable**
09K4840 A	Phenobarbital 30 mg	Haiti	**Unsatisfied**: Friability (2.9.7), Hardness (2.9.8)
08E2978-A	Phenobarbital syrup 18mg/5ml	Haiti	**Suitable**
08111487	Propanolol 40mg	Brasil	**Unsatisfied**: Uniformity of content (2.9.6)
L08111487	Spironolactone 25mg	Domenican Republic	**Suitable**



PAEDIATRICS: WHY?

PREPARATION OF CAPSULES FOR CHILDREN FROM INDUSTRIAL HIGH-DOSE TABLETS

PROBLEMS:

- ✓ Method of preparation
- ✓ Quality of industrial tablets
- ✓ Stability of the preparations
- ✓ Administration of capsules for the neonatal and paediatric treatment

CAPSULES PRODUCED IN 2010			
LOT	**API**	**PROVENANCE**	**RESULTS**
200910-A	Acetazolamide 25 mg	St Damien Hospital	**Unsatisfied**: Uniformity of content (2.9.6)
A-200S10-A	Acetazolamide 25 mg	St Damien Hospital	**Suitable**
121110-B Exp	Captopril 1,25 mg	St Damien Hospital	**Unsatisfied**: Uniformity of mass (2.9.5)
230610-C	Phenytoin 10 mg	St Damien Hospital	**Suitable**
230610-G	Phenytoin 10 mg	St Damien Hospital	**Suitable**

A. STUDY AND FORMULATION OF ORAL LIQUID PAEDIATRIC FORMULATIONS:

METHODOLOGICAL APPROACH

✓In agreement whit local medical doctors the **drugs** for the paediatric therapy are **chosen** and then **formulated**: **liquid oral** formulations are preferred and appropriate excipients are selected.

✓For each formulation a **specific card** (written in **local language**) has been prepared. The card shows the procedure of preparation and the characteristics of each component present in the formulation.

✓Each preparation have been tested to check its **quality** and its **stability** under different environmental conditions in accordance with the EMA guidelines.

PREPARATIONS PEDIATRIQUES	
SIROPS	*ACIDE ASCORBIQUE 10 mg/ml*
	CANREONATE DE POTASSIUM 1 mg/ml
	FER SULFATE 5 mg/ml
	IBUPROFENE 20 mg/ml
	PROPANOLOL 0,5 mg/ml
	RANITIDINE 15 mg/ml
	SALBUTAMOL 0,4 mg/ml
	VITAMINE B_6 1 mg/ ml
SOLUTIONS	*CAPTOPRIL 1 mg/ml*
	FUROSEMIDE 1 mg/ml
GOUTTES	*NIFEDIPINE 1 mg/gtt*
	RANITIDINE 4 mg/gtt
	SALBUTAMOL 0,2 mg/gtt
	VITAMINE B6 0,5 mg/gtt
SUSPENSIONS	*VITAMINE B COMPLEX 5,8 mg/ml*
	MAGNESIUM ET ALUMINIUM HYDROXYDE 200 mg/ml

PROPANOLOL CHLORHYDRATE SIROP 0,5 mg/ml

Formulation pour 100 ml:

Propanolol chlorhydrate	0,05 g
Carboxyméthylcellulose sodique	1,00 g
Sodium citrate	0,21 g
Acide citrique monohydraté	0,28 g
Eau dépurée	72,28 g
Nipagine sodique	0,07 g
Saccharose sirop	32,23 g

Caractéristiques chimiques-physiques:

Poudre cristalline blanche ou blanchâtre, il est inodeur et avec un goût amer.
Soluble dans l'eau (1:20) et dans l'alcool (1:20).
p.f. = 163-166 °C.

Propriétés pharmacologiques:

Le propranolol a activité β-bloquant, il est un antagoniste compétitif des deux récepteurs β_1 et β_2, non cardiosélectif.
Il est utilisé dans l'hypertension.

Posologie pédiatrique:

2,5-5mg correspondant à 5-10 ml.

Preparation:

1. Solubliser la nipagine sodique dans l'eau dépurée.
2. Ajouter le sodium citrate et l'acide citrique monohydraté dans la solution.
3. Ajouter le propranolol chlorhydrate.
4. Ajouter la carboximéthylcellulose sodique peu à la fois, mélanger très lentament.
5. Ajouter le saccharose sirop.
6. Contrôler le pH. (il ne doit pas être superieur à 4,5).

Instructions et contre-indication:

Contre-indiqué pour les patients avec des maladies obstructives chroniques des voies aériennes.

Stabilité et conservation de propranolol:

Conserver dans des récipients bien fermés, à l'abri de la lumière et de l'air.

B. STABILITY STUDY OF THE PREPARED LIQUID PHARMACEUTICAL FORMS

Method:

STORAGE CONDITION	T (°C)	RH	PERIOD COVERED BY DATA	ANALYTICAL METHOD
Standard	25±2	60±5%	12 months, analysis at time zero (T0) and every 30 days (from TS-1 to TS-12)	UV-VIS spectrophotometric assay
Refrigerator	5±3	-	12 months, analysis at time zero (T0) and every 30 days (from TR-1 to TR-12)	
Accelerated	40±2	60±5%	3 months, analysis at time zero (T0) and every 30 days (from TA-1 through TA-3)	

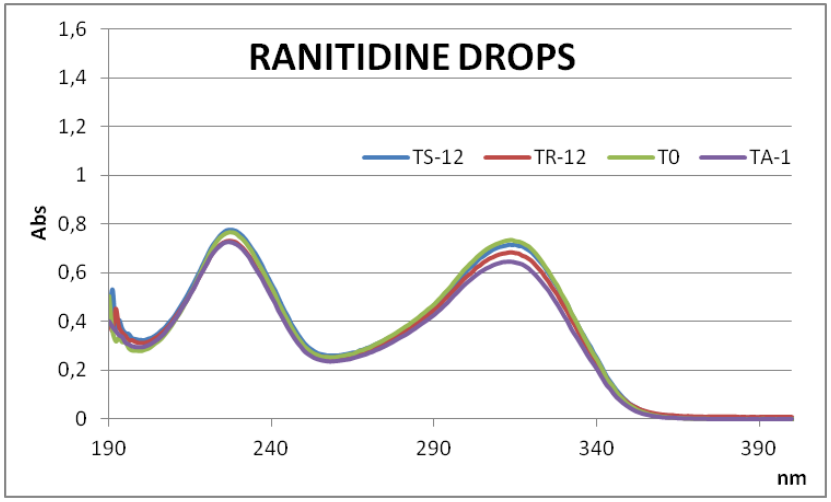
EMA Guideline on stability testing: stability testing of existing active substances and related finished products, 2003, CPMP/QWP/122/02, rev 1 corr

EVALUATION OF THE EXPIRATION DATE

STABILITY STUDY: RESULTS

PREPARATIONS PEDIATRIQUES	
SIROPS	*ACIDE ASCORBIQUE 10 mg/ml*
	CANREONATE DE POTASSIUM 1 mg/ml
	FER SULFATE 5 mg/ml
	IBUPROFENE 20 mg/ml
	PROPANOLOL 0,5 mg/ml
	RANITIDINE 15 mg/ml
	SALBUTAMOL 0,4 mg/ml
	VITAMINE B_6 1 mg/ ml
SOLUTIONS	*CAPTOPRIL 1 mg/ml*
	FUROSEMIDE 1 mg/ml
GOUTTES	*NIFEDIPINE 1 mg/gtt*
	RANITIDINE 4 mg/gtt
	SALBUTAMOL 0,2 mg/gtt
	VITAMINE B6 0,5 mg/gtt
SUSPENSIONS	*VITAMINE B COMPLEX 5,8 mg/ml*
	MAGNESIUM ET ALUMINIUM HYDROXYDE 200 mg/ml

The stability has been demonstrated for **12 MONTHS** for **all formulations**



BUT **housing** and **environmental** conditions are **not suitable** for a proper storage of the preparations

VALIDITY PERIOD: **3 MONTHS**

QUALITY CONTROL AND QUALITY ASSURANCE

Galenics, in accord with the European Law (Ph Eur), must guarantee "the quality as a fundamental support to the security and the efficacy"

D.C.

PHARMACEUTICAL FORMS TESTS

Ointments for skin application; Suppositories:
- Verify of accuracy of followed procedures
- Control of aspect
- Control of the amount to sell
- Control of the solidity of packing

Stiff capsules:
- Verify the accuracy of followed procedures
- Control of aspect and solidity of capsules
- Control of the number of capsules prepared
- Mass uniformity of capsules

Liquid medicinal products:
- Verify the accuracy of followed procedures
- Control of the amount of product to sell
- Control of the solidity of packing

RAW MATERIALS: Organoleptic control
Melting point

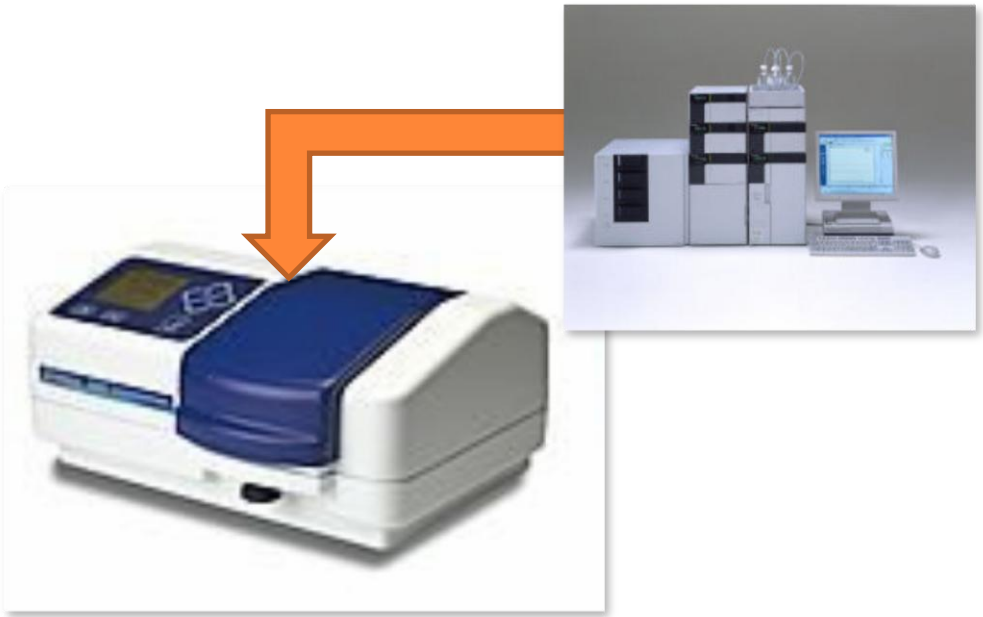
ITALY

STABILITY TESTS (EMA)

PHARMACEUTICAL FORMS TESTS (Ph Eur)
Uniformity of content (2.9.6)
Uniformity of mass (2.9.5)
Disintegration (2.9.1)
Friability (2.9.7)
Hardness (2.9.8)
Sterility (2.6.1)

QUALITY CONTROL AND QUALITY ASSURANCE

ANALYSIS	METHOD REF.	ACCEPTANCE CRITERIA
General aspect	Visual	Posological unit integrity
Uniformity of content	Ph. Eur. 7 ed. Assay 2.9.6	Each individual content is between 85% and 115% of the average content (10 dosage units)



SPECTOPHOTOMETRY UV/VIS

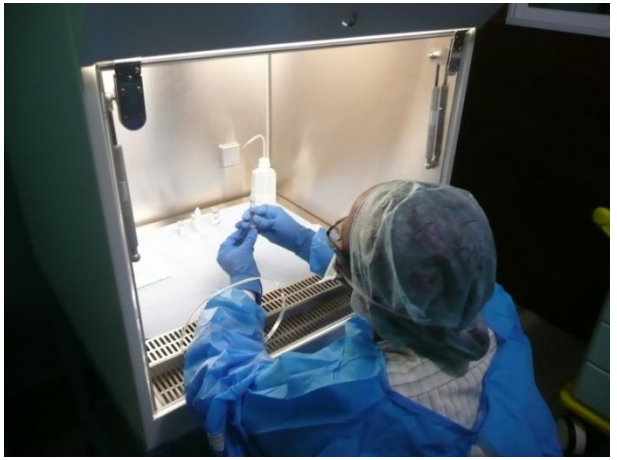
STANDARDIZATION OF RESULTS
LOW COSTS
SIMPLE EXECUTION

"…reuse, repair equipment and goods instead of throwing them in a landfill, ***exceeding the consumerist obsession of the obsolescence of objects*** *and the tension to the new…"*
A. Salza "Niente. Come si vive quando manca tutto. Antropologia della povertà estrema", Sperling & Kupfer 2009

C. DEVELOPMENT OF A METHOD FOR THE PREPARATION OF STERILE SOLUTIONS (ANTIBIOTICS AND CYTOSTATIC DRUGS)

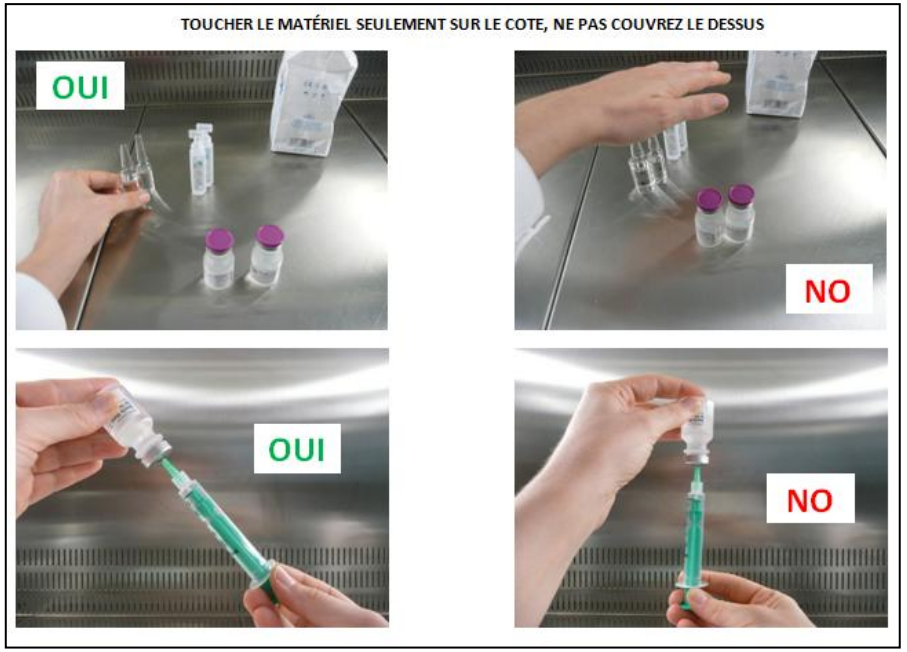
Application of specific procedures for the preparation of:

- Lyophilized medicinal products
- Infusion bags
- Solutions



POS PREPARATION SAC D'INFUSION

Opérations préliminaires	Propreté hotte	La hotte stérile doit être nettoyé et stérilisée avec une fréquence à définir en base à la quantité de matériel à préparer et aux capacités de l'opérateur. Tandis que est matériel injectable est nécessaire une fréquence variable d'hebdomadaire ou mensuel. Effectuer la propreté avec des désinfectants énergiques, alcool.
	Lavage mains	Avant de commencer des opérations en hotte stérile, l'opérateur doit se laver les mains, si possible avec un détergent avec action désinfectante.
	Préparation matérielle	En base à la place disponible, avant de commencer tout le matériel nécessaire à l'opération doit être mis sous hotte ou dans les environs de la même pour consentir à l'opérateur de limiter les déplacements.
Matériel	Flacon/s de medicament/s, sac/s d'infusion, seringues de volume proportionné, instrument apte pour l'ouverture des embouts en aluminium, gaze stérile, désinfectant (alcool 70°), sparadrap ou ruban.	
Procédure opérationnelle	1) Après avoir ouvert la hotte stérile, transférer le matériel, en manière compatible avec la place disponible, sous hotte ou dans les environs de la même. 2) Préparer le premier stock[2] de sacs à "compléter": Enlever le couvercle d'aluminium pour exposer le bouchon en gomme (opération à effectuer aussi pour les flacons du médicament à additionner) Il est nécessaire désinfecter la partie de bouchon à percer avec une gaze stérile imprégnée de désinfectant (alcool 70°)[3]. 3) Enlever la seringue du propre emballage (rigoureusement sous hotte); enlever le capuchon qui couvre l'aiguille, faire attention a ne pas se piquer; insérer l'aiguille dans le flacon du médicament; aspirer le contenu lentement; extraire l'aiguille; enfiler l'aiguille dans le sac d'infusion; livrer le contenu lentement; extraire l'aiguille. 4) Répéter la procédure pour tous les autres sacs du stock présent sous hotte. 5) Reconstitué tous les sacs à préparer; réinsérer le capuchon qui couvre l'aiguille, faire attention de ne pas toucher l'aiguille stérile et de ne pas piquer; poser la seringue sur l'étage du hotte, prête pour la préparation du stock suivant; agiter les sacs soigneusement jusqu'à le complet mélange des composants. 6) Couvrir le bouchon en gomme du sac avec une gaze stérile imprégnée de désinfectant et arrêter la gaze sous hotte avec le sparadrap ou ruban. 7) Répéter les opérations du point 2 au point 6 pour les stocks suivants. Pour la même stock utiliser la même aiguille. Remplacer la seringue si l'aiguille vient contaminée. Évaluer si démarche à la substitution de la seringue à chaque nouveau stock. Remplacer TOUJOURS la seringue quand se change le médicament ou sa concentration.	



THE GALENICS:
AN ANSWER TO THE HOSPITAL PECULIAR NEEDS

NATIONAL CONTEXT → **DEVELOPING COUNTRIES**

DIFFERENT COUNTRIES: SAME NEED OF QUALITY

ITALY

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CLINICAL STUDY PROTPROS	Evaluation of chemopreventive activity of galenics, comparable to dietary supplement, containing lycopene, selenium and green tea polyphenols
CLINICAL STUDY MONAPOL	Evaluation of cholesterol-lowering activity of a galenic, comparable to a dietary supplement, containing monacolin k and policosanol in subjects with mild to moderate hypercholesterolemia uncomplicated unfamiliar: randomized controlled double-blind study

DEVELOPING COUNTRIES (DC)

***A.P.P.A.*® GALENIC LAB IN HAITI**	1. Study of oral liquid pediatric formulations 2. Stability study of the prepared liquid pharmaceutical forms 3. Development of a method for the preparation of sterile solutions (antibiotics and cytostatic drugs) 4. Project for the introduction of new oral and sterile formulations for pediatric use

CLINICAL STUDY MONAPOL

Cooperation between Dept. of Scienza e Tecnologia del Farmaco of Turin, Order of Pharmacists of the Province of Turin

Monascus purpureus → fermentation on rice →
- monacolins (monacolin k): high affinity for the HMG-CoA reductase enzyme
- action given by a set of factors not strictly related to monacolin k

Policosanols →
- ↓LDL, ↓ triglycerides
- ↑HDL

OBJECTIVE

To verify the profiles of effectiveness and tolerability of a galenic comparable to a dietary supplement containing a dry extract of fermented red rice by *Monascus purpureus* associated with another one titrated in policosanols

MONAPOL STUDY: FLOW CHART

- **210 subjects,** presenting mild to moderate, uncomplicated, unfamiliar hypercholesterolemia, currently outside indication comparing to the start of treatment with inhibitors of HMG-CoA reductase
- **3 groups** of treatment: pure *vs* control *vs* placebo;
- 2 phases
- 2 cps/day for three months;
- **Evaluation of plasmatic concentration**: basal and after 3 months of treatment;
- **Blood analysis**: basal and after 3 months of treatment;
- **Self diagnostic evaluation**: baseline, after 45 days (only in phase I) and after 3 months of treatment;
- Chance of participate in a subsequent open-label treatment for a period of three months.

Department of Scienza e Tecnologia del Farmaco (TO)

A. EVALUATION OF THE CORRECT DOSAGE AND SET UP OF GALENIC FORMULATION
B. STABILITY TESTS OF THE ACTIVE MOLECULES AND OF THE PREPARATION IN ACCORDANCE WITH THE EMA GUIDELINES
C. EVALUATION OF PLASMATIC CONCENTRATION BY HPLC ANALYSIS

A. EVALUATION OF THE CORRECT DOSAGE AND SET UP OF GALENIC FORMULATION

Literature evaluation
Evaluation of the legislation in force
Application of specific procedures for the preparation of stiff cps
Quality and assurance control based on FU XII - Ph Eur assays

GALENIC FORMULATION: STIFF CAPSULES

Administration: 2 cps / day

Group 1 (galenic preparation similar to a food supplement):

Dose administered per day: monacolin k 3 mg/day, policosanol 20 mg/day

Components:

- Red yeast rice extract: title in monacolin k equal to 3.1%;
- Biocosanol®: title in policosanol equal to 91.2% of which hexacosanol 14.7%, octacosanol 56.1%, triacontanol 20.4%;
- Maize starch pregelatinised: q.b.

Group 2 (active pharmaceutical ingredient):

Dose administered per day: lovastatin 3 mg/die

Components:

- Lovastatin: 1,5 mg/cps;
- Maize starch pregelatinised: q.b.

Group 3 (placebo):

Components: Maize starch pregelatinised : q.b.

B. GALENIC FORMULATION: STABILITY STUDY

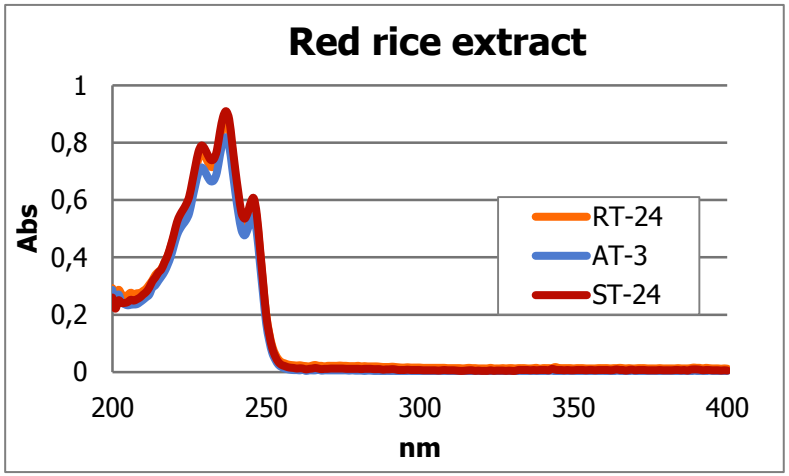
Method:

STORAGE CONDITION	T (°C)	RH	PERIOD COVERED BY DATA	ANALYTICAL METHOD
Standard	25±2	60±5%	12 months, analysis at time zero (T0) and every 30 days (from TS-1 to TS-12)	UV-VIS spectrophotometric assay
Refrigerator	5±3	-	12 months, analysis at time zero (T0) and every 30 days (from TR-1 to TR-12)	
Accelerated	40±2	60±5%	3 months, analysis at time zero (T0) and every 30 days (from TA-1 through TA-3)	

EMA Guideline on stability testing: stability testing of existing active substances and related finished products, 2003, CPMP/QWP/122/02, rev 1 corr

Results:

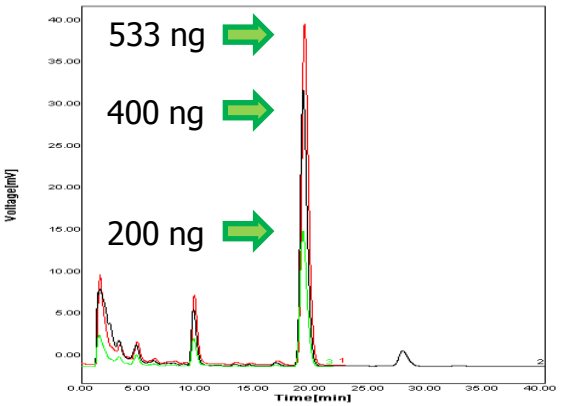
All formulations have proved to be stable in "Refrigerated" conditions (RT-24) and "Standard" conditions (ST-24) for **24 months**, in "Accelerated" conditions (AT-3) for **3 months**



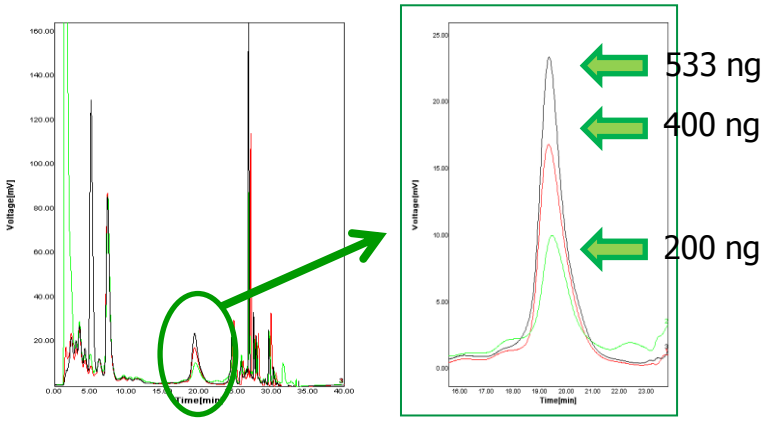
C. EVALUATION OF PLASMATIC CONCENTRATION BY HPLC ANALYSIS

Developing of an HPLC method (UV detector) to evaluate the **monacolin k** concentration in the plasma of enrolled subjects

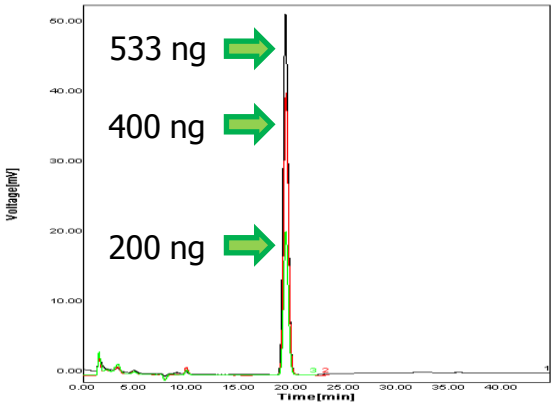
Mobile phase: 0.1% phosphoric acid - acetonitrile, flow rate: 0.5 ml / min, λ = 238 nm
HiQ sil column C18HS, 3um, 4.6 mm L IDx100mm
HPLC composed by: Biotech model 2003 degasser; CBM-10A Shimadzu communications bus module; SPD-10° VP Shimdzu UV-Vis detector; LC-10AD VP Shimadzu liquid cromatograph



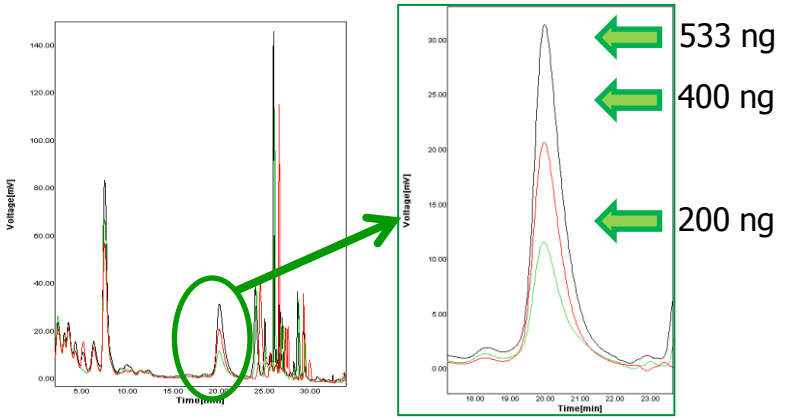
Stoch solution (SSm) of monacolin K



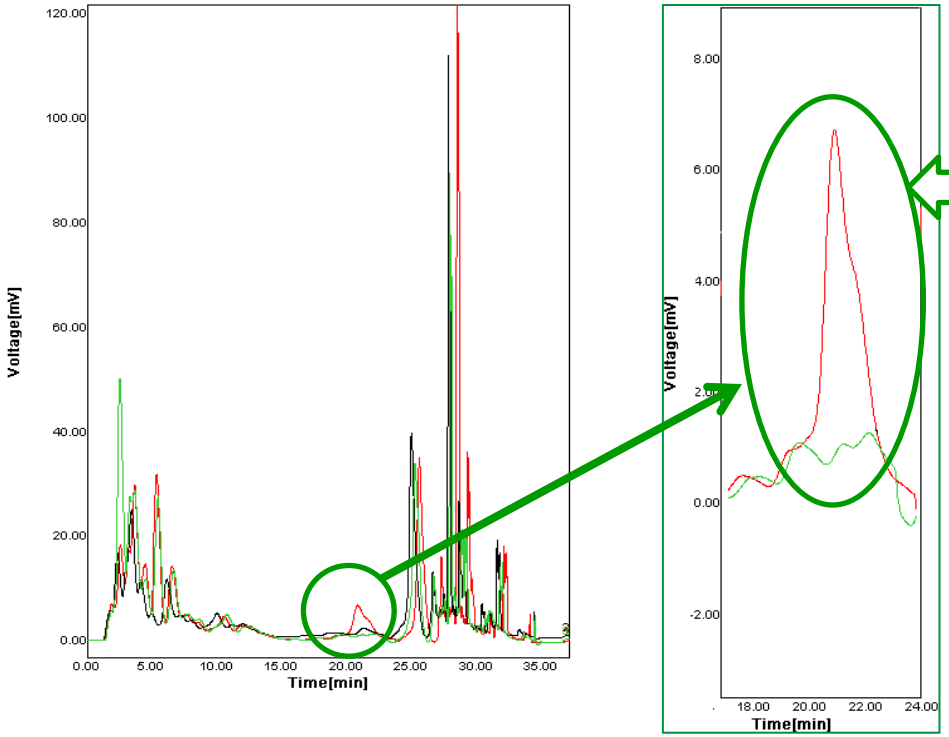
Plasma enriched with SSm



Stoch solution (SSl) of lovastatin



Plasma enriched with SSl



probable peak of monacolin k

Overlapping of a baseline analysis (green) and quarterly (red) in the plasma of a subject

CONCLUSIONS

- The application of a standard procedure for the preparation the galenics administered during the study can guarantee their **stability for 24 months**.
- The developed HPLC procedure allows to highlight the concentration of monacolin k in the **plasma of enrolled subjects**
- Actually **31 subjects** have been enrolled.
- The phase I of the study is finished and the phase II of the study is in progress.

MINISTERO DELLA SALUTE: LINEE GUIDA SUGLI INTEGRATORI ALIMENTARI

SOSTANZE CON APPORTO MASSIMO GIORNALIERO DEFINITO

Riso rosso fermentato (Monascus purpureus)
monacolina mg 10
Avvertenza supplementare:
Per l'uso del prodotto si consiglia di sentire il parere del medico.
Non usare in gravidanza, durante l'allattamento e in caso di terapia con farmaci ipolipidemizzanti

Rextat®
Lovinacor®
Tavacor®

LOVASTATINA 10 mg
Indicazioni terapeutiche riportate in RCP
Ipercolesterolemia primaria inclusa l'ipercolesterolemia familiare o l'iperlipemia mista (tipo IIa e IIb) quando la sola risposta alla dieta e ad altre misure non farmacologiche (aumento dell'attività fisica e se indicato riduzione del peso corporeo) sia risultata inadeguata.
Ipercolesterolemia non corretta dalla sola dieta in soggetti ad alto rischio di un evento cardiovascolare maggiore (soggetti con rischio superiore del 20%, colesterolo totale maggiore di 190 mg/dl e colesterolo LDL maggiore di 115 mg/dl). Ipercolesterolemia non corretta dalla sola dieta in pazienti con cardiopatia ischemica, per la riduzione del rischio di infarto del miocardio.