Commercialising African Herbal Products for the EU market – prospects and problems

Denzil Phillips International Ltd
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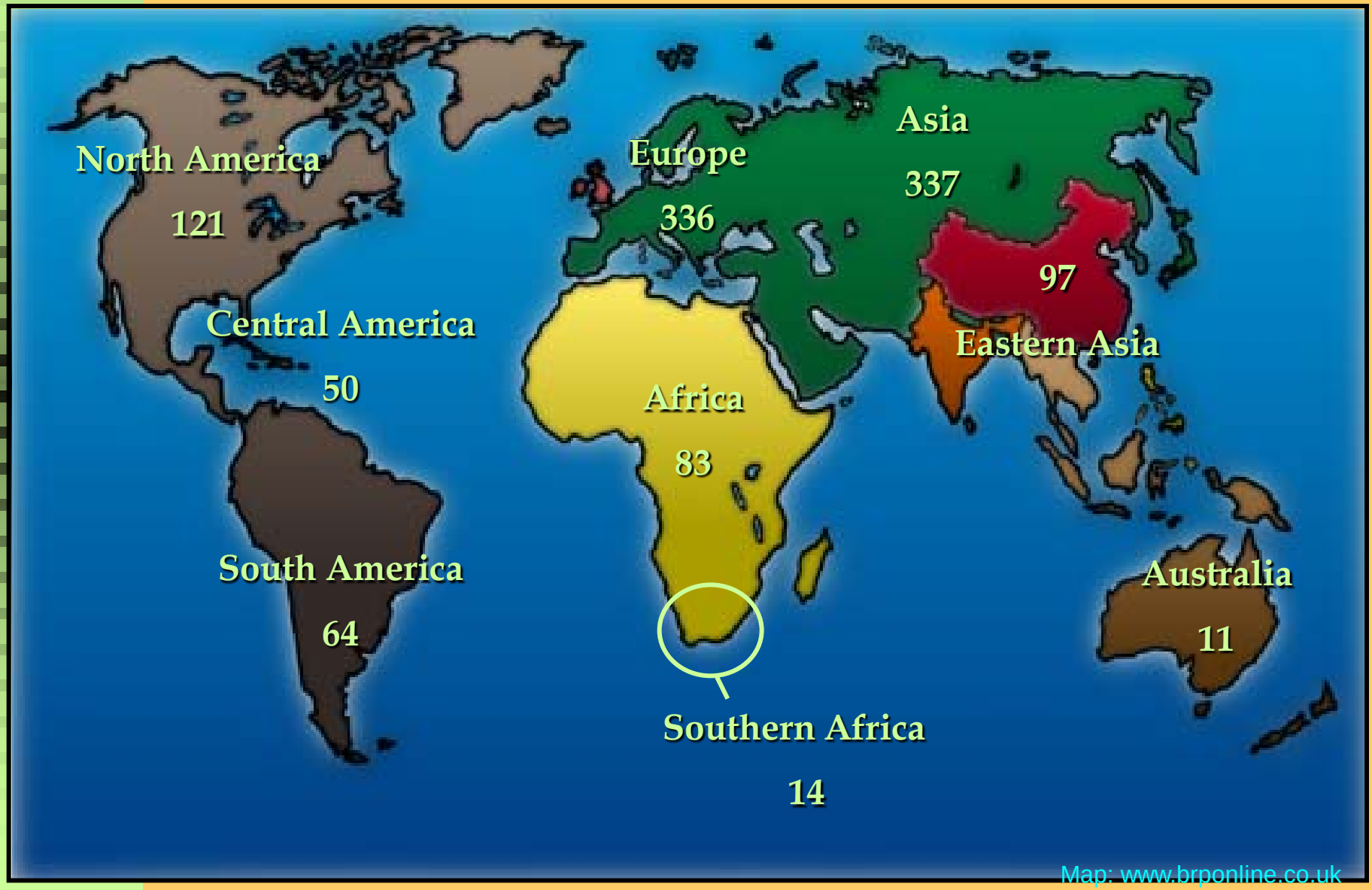
www.denzil.com
www.thmpd.eu

CONTINENTAL DIVERSITY OF COMMERCIALISED MEDICINAL PLANTS



Examples of African medicinal plants of current interest in product development

1. **Round leaf buchu -** ***Agathosma betulina***
2. **Bitter aloe -** ***Aloe ferox***
3. **Moringa –** ***Moringa oleifera***
4. **Rooibos tea -** ***Aspalathus linearis***
5. **Bulbine -** ***Bulbine frutescens***
6. **Honeybush tea** ***- Cyclopia*** **genistoides**
7. **Devil's claw -** ***Harpagophytum procumbens***
8. **Ghaap -** ***Hoodia gordonii***

9. “African potato” - *Hypoxis hemerocallidea*

10. Sceletium – *Sceletium tortuosum*

11. *“Umckaloabo” - Pelargonium sidoides*

12. African ginger - *Siphonochilus aethiopicus*

13. Cancer bush - *Sutherlandia frutescens*

14. Pepperbark tree - *Warburgia salutaris*

15. Cola Nut – *Cola Nitida*

AAMPS

Association for
African Medicinal Plants Standards

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PROĐINVEST is a programme of the Group of ACP States and the European Commission for the promotion of investment and technology transfers in ACP countries. Its management has been entrusted to the Centre for the Development of Enterprise (CDE) under the supervision of EuropeAid Cooperation Office of the European Commission (EuropeAid).

AAMPS - African Medicinal Plants Monographs**

Acacia senegal (L.) Willd.	Acacia
Adansonia digitata L.	Baobab
Aframomum melegueta K. Schum.	Grains of Paradise
Agathosma betulina (Bergius) Pillans	Buchu
Aloe ferox Mill.	Bitter Aloes
Antidesma madagascariensis Lam.	Bois Bigaignon
Aphloia theiformis (Vahl.) Benn.	Fandamane
Artemisia afra Jacq.	African Artemisia
Aspalathus linearis (Burm. f.) Dahlg.	Rooibos
Balanites aegyptica (L.) Del.	Desert Date
Boswellia spp	Frankincense
Bulbine frutescens (L.) Willd.	Bulbine
Cajanus cajan (L.) Huth	Pidgeon Pea
Carissa edulis Vahl.	Natal Plum
Catharanthus roseus (L.) G. Don.	Madagascan Periwinkle
Centella asiatica (L.) Urb.	Gotu Kula
Cola spp	Kola Nut
Combretum spp	Combretum
Commiphora myrrha (Nees) Engl.	Myrrh
Crossopteryx febrifuga Benth.	African Bark
Cyclopia genistoides (L.) R. Br.	Honeybush
Danais fragrans (Lam.) Pers.	Liane
Euphorbia hirta L.	Garden Spurge
Garcinia kola Heckel	Bitter Kola
Griffonia simplicifolia (Vahl ex DC) Baill.	Griffonia
Harungana madagascariensis Lam. ex Poir.	Haronga

Hibiscus sabdariffa L.	Roselle
Hoodia gordonii (Masson) Sweet ex Decne.	Hoodia
Harpagophytum procumbens (Burch.) DC.	Devils Claw
Hypoxis hemerocallidea Fisch. & C.A. Mey.	African Potato
Ipomoea pes-caprae ssp. brasiliensis (L.) R. Br.	Railroad Vine
Kigelia africana (Lam.) Benth.	African Sausage Tree
Mondia whitei (Hook. f.) Skeels.	White Ginger
Moringa oleifera Lam.	Moringa
Nauclea spp	Nauclea
Pelargonium sidoides DC.	Umckaloabo
Prunus africana (Hook. f.) Kalkman	African Cherry
Rauvolfia vomitoria Afzel.	Devil Pepper
Ravenala madagascariensis J.F. Gmel.	Ravenala
Sceletium tortuosum (L.) N.E. Br.	Sceletium
Siphonochilus aethiopicus (Schweinf.) B.L. Burtt.	African Ginger
Strophanthus gratus (Wallich & Hook. ex Benth.) Baillon	Strophanthus
Sutherlandia frutescens (L.) R. Br.	Cancer Bush
Terminalia sericea Burch.	Silver Terminalia
Toddalia asiatica (L.) Lam.	Toddalia
Trichilia emetica Vahl.	Natal Mahogony
Vernonia spp	Vernonia
Voacanga africana Stapf.ex Eliot	Voacanga
Warburgia salutaris (Bertol. f.) Chiov.	Warburgia
Xylopia aethiopica (Dunal) A. Rich.	Senegal Pepper
Xysmalobium undulatum R. Br.	Milk Bush

The European Union (EU)

27 states and 27 regulatory systems

Regulatory Harmonisation – Dream or Reality?

- Diversity/Complexity is the Reality
- 25 EU member States = 25 Regulatory Models

Pan-EU Approach is very difficult to achieve

- Health and safety still considered ultimately a national not a EU issue

EU Market Sizes

- Functional Foods US $3.5 billion
- Food Supplements US $ 2.5 billion
- Herbal Medicines US $4 billion
- Essential Oils US $ 250 million

= Opportunity

EU Key Regulations

Novel Foods

Food Supplements

Functional Foods

Health Claims/Labelling

Medicines

EU-Key Issues

Quality

Safety

Labelling

GMP, GAP, GLP

Efficacy

Virtual Market Place (www)

Regulatory Options for Herbals in the EU

Food Supplement Directive since July 2002

- Vitamins and Minerals
- Positive Lists of Ingredients
- Maximum Levels
- GMP
- Claims
- New Product Development

Other Substances?

- Amino Acids
- Essential Fatty Acids
- Fibre
- Carotenoids, etc
- Botanicals

Food Supplement Directive – the benefits

- Harmonisation
- Pan European Marketing
- Manufacturing
- Market Growth
- Standards

Novel Foods

A ‘novel’ food is a food or food ingredient which has not hitherto been used* for human consumption to a *significant* degree within the EU and include foods containing, consisting of or produced from GMO’s.

*prior to 15th May 1997

Case History – Tahitian Noni® Juice (Morinda citrifolia)

- Application to Belgium by Morinda Inc (2000)
- Was Assessed by MS
  - Toxicological Tests (High Dose)
  - Intended Market/ Consumption forecast
  - Allergy Studies Required
- Current Status – Approved since June 2003 for marketing in EU without claims
- Cost of application estimated at US $1 million

Functional Foods

- No legislation planned per se
- Will be covered under new regulation ‘Addition of Vitamins, Minerals and certain other substances to foods’
- Fortified Food – specifically what food can be fortified ?
- labelling laws will be tightened

Health Claims in the EU

- Proposal for Regulation of Claims
  - **Nutrition** (e.g. low fat, low sugar)
  - **Health** (e.g. Calcium aids in the development of strong bones and teeth)
  - **Health** (e.g. Sufficient calcium may reduce the risk of osteoporosis in later life)
- Prohibited Claims – Non-specific, Alcoholic products, psychological/behavioural functions

Health Claims

Opportunity:

- Enhanced Function
- Reduction of Disease Risk Factor

BUT

- Claim Substantiation
- Pre-Marketing Approval
- Scientific Evaluation by EFSA

Health Claims

Implications for Food Supplements and Nutraceuticals

- All Health Claims will have to be scientifically substantiated
- Many Claims prohibited/restricted
- Consumer access to information at risk

Other Issues - Foods

- GM/Traceability
- Contaminants
  - Dioxins
  - Irradiation
  - Heavy metals
  - Alfatoxins
  - ‘Undesirable substances’

THMPD

- The Traditional Herbal Medicinal Products Directive 2004/24/EC
- April/May 2004 – agreed, implementation started.
- October 2005 – Member States must have legal framework in place for registration
- April/May 2011 – transitional period ends

THMPD – key points

- Simplified Registration of Herbal Medicines
- Scope - Inclusion of Herbs/nutrients (non-biological/ancillary)
- Quality based on Pharmaceutical GMP
- 30 years traditional use - 15/30 Flexibility
- Labelling/Advertising – product's safety and efficacy rely exclusively on information obtained from its long term use and experience

THMPD – key points

- Under the Directive 2004/24/EC on traditional herbal medicinal products (THMP) applicants are required to produce bibliographic or expert evidence of traditional use. At least 15 of the 30 years of use must relate to the European Union.
- The requirement to prove medicinal use for a period of 30 years can also be satisfied if number or quantity of ingredients have been reduced over that period of time.
- Whenever the product complies with a Community Monograph as established by the HMPC, the requirement to demonstrate traditional use is lifted.

THMPD Advantages

- Regulatory Clarity
- Product Information/Claims/Advertising possible
- Quality assured
- Consumer Confidence
- Market Credibility
- Market Development

THMPD – proof of tradition, sources

- Any published information referring to specific product, e.g. advertizing material, published product characteristics, product listings in (historic) drug compendia as well as specific product related archive materials, e.g. brochures, sales lists, invoices etc.
- Any published information on the use of licensed herbal medicines in EU Member States, e.g. Martindale, Rote Liste etc.
- Any other bibliographic evidence, e.g. text books, pharmacopoeia (for proof of use in ethnic populations resident in the EU, non-EU pharmacopoeia such as Ayurvedic may also be used) etc.
- Lists of herbs traditionally used in EU Member States, e.g. Commission E, ESCOP, WHO, GSL, MHRA list etc.
- evidence from medical doctors, herbal practitioners or experts in the field

THMPD – EU member states

- **In EU :Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, UK**
- **Outermost regions: Azores and Madeira, Canary Islands, French Guyana, Guadeloupe, Martinique and Réunion**

THMPD – community monographs

Aloe (F)
Anisi fructus (F1, PF2)
Anisi aetheroleum (F)
Betulae folium (PF)
Calendulae flos (PF)
Echinaceae purpureae (PF)
Eleutherococci radix (PF)
Foeniculi amari fructus (F)
Foeniculi amari fructus aetheroleum (F)
Foeniculi dulcis fructus (F)
Frangulae cortex (F)
Lini semen (F)
Lupuli flos (PF)
Melissae folium (F)
Menthae piperitae aetheroleum (F)
Menthae piperitae folium (PF)
Passiflorae herba (F)
Plantaginis ovatae semen (F)
Plantaginis ovatae seminis tF)
Primulae radix (F)
Primulae flos (F)
Psyllii semen (F)
Rhamni purshianae cortex (F)
Rhei radix (F)
Sennae folium (F)
Sennae fructus (F)
Thymi herba (F)
Valerianae radix (F)

PF: Assessment close to finalisation (pre-final),
F: Final opinion adopted (2007)

Herbal substances[1)]	TUR[2)]
Total (85)	**260**
Pelargonii radix	29
Hyperici herba	18
Harpagophyti radix	18
Valerianae radix	13
Passiflorae herba	9
Visci albi herba	9
Echinaceae purpureae radix	8
Salviae folium	8
Rhodiolae roseae rhizoma	7
Cimicifugae rhizoma	6
Echinaceae purpureae herba	6
Hippocastani semen	5
Melissae folium	5
Thymi herba	5
Arnicae flos	4
Crataegi folium cum flore	4
Equiseti herba	4
Sabalis serrulatae fructus	4
Tanaceti parthenii herba	4

THMPD - Outstanding Issues for Industry

- Fees
- Costs
- Strategy for Product Ranges
- Current Licences
- Effect on SMEs
- Foreign traditions (TCM etc)

A Practical Guide to

Licensing Herbal Medicinal Products

handbook & workshop

Do you manufacture herbal products?
Have you applied for registration of your products yet?

Licensing of herbal products in the UK and European Union is changing. The Traditional Herbal Medicinal Product Directive (THMPD) was implemented in the UK in 2005 and allows herbal products to be registered under medicines law. By 2011, every pharmaceutical company manufacturing herbal medicines that are sold in the UK and European Union must have obtained a market authorisation.

As a manufacturer of such products, you need to ask the following:

- What type of herbal products are you manufacturing?
- Are you required to license your herbal products and what type of license do you need?
- Would your product comply with regulations?
- What evidence and manufacturing data do you need to provide?
- What are the packaging and leaflet requirements for your product?

And most importantly:

- How do you apply for a license?

A Practical Guide to Licensing Herbal Medicinal Products is a handbook soon to be published by Pharmaceutical Press that answers all these questions and also provides full guidance on license application, including how forms should be filled in, who they should be submitted to and what costs are involved. As part of the publication process, the text was subjected to rigorous review by eminent experts in the field, including the Medicines and Healthcare products Regulatory Agency (MHRA).

All the official legal guidelines and forms are included within the book, which also includes step-by-step guidance on filling out the application forms.

Published in ring-binder format – this book will be easy and practical to use in guiding you and your company from the initial decision making process through to receiving a license.

Available:
May 2009
Price: £250.00

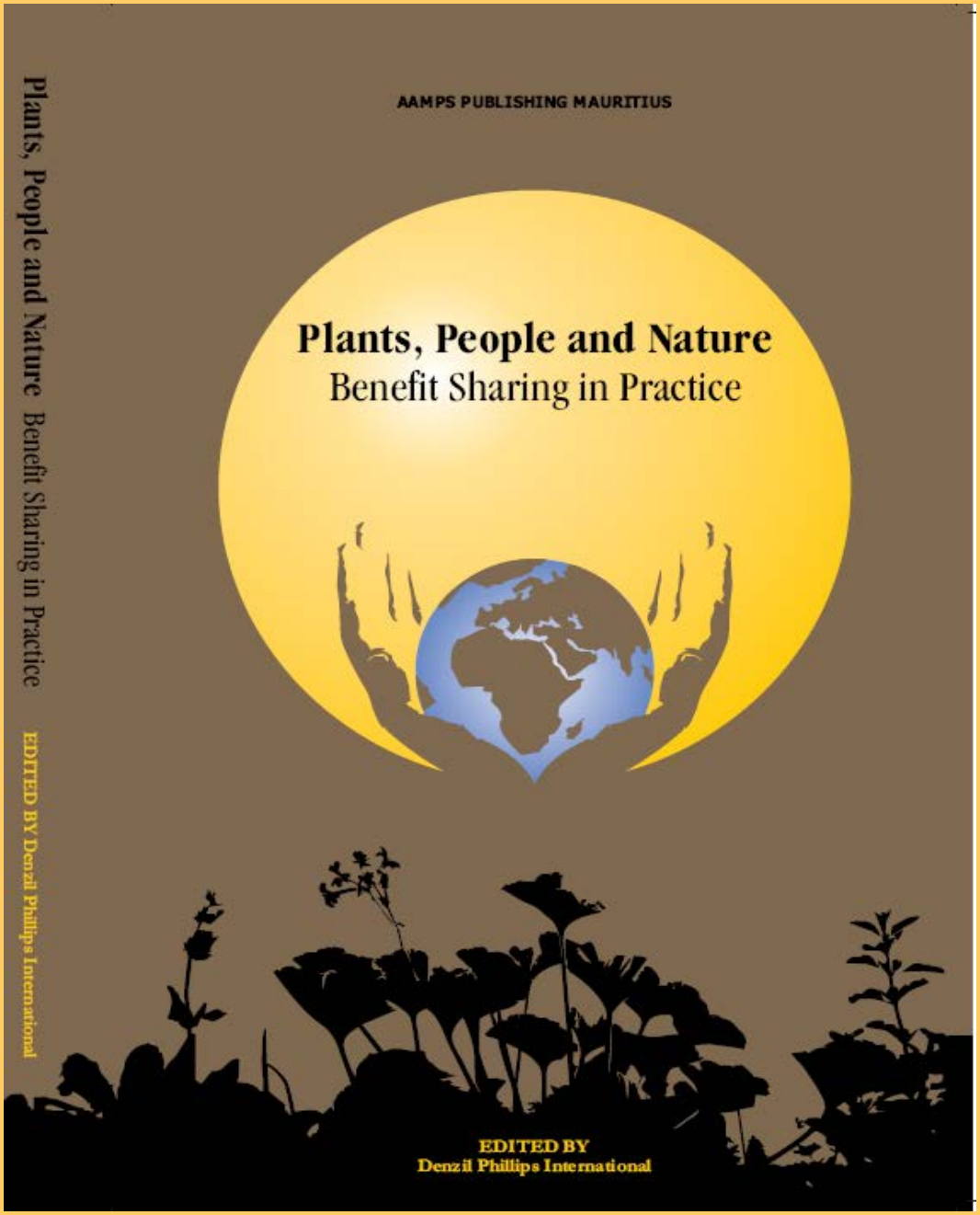
ISBN: 978 0 85369 765 7

Written by experts in the field, authors include:

Thomas Brendler, Director of Plantaphile, is a consultant and ethnobotanist with a number of phytomedicine books and publications to his credit. As well as developing and managing projects for industry on the use of plants in medicine, food and cosmetics, he is involved in medicinal plant research around the world, focusing on Africa and the Pacific Islands.

L Denzil Phillips is Founder Director of Denzil Phillips International, a company specialising in commercial research and development in the field of medicinal and aromatic plants and related botanical substances. Denzil has worked on developing herbal products with international corporations, private exporters, banks, governments and international development agencies in more than 30 countries.

Stefan Spiess is Managing Director of Gruenwalder Gesundheitsprodukte GmbH. Stefan is a qualified pharmacist and food chemist. As head of regulatory control for the Hexal group, he supervised over 300 product license applications. He is a QP and a specialist on clinical and pharmacological expert reports, stability testing and registration strategies.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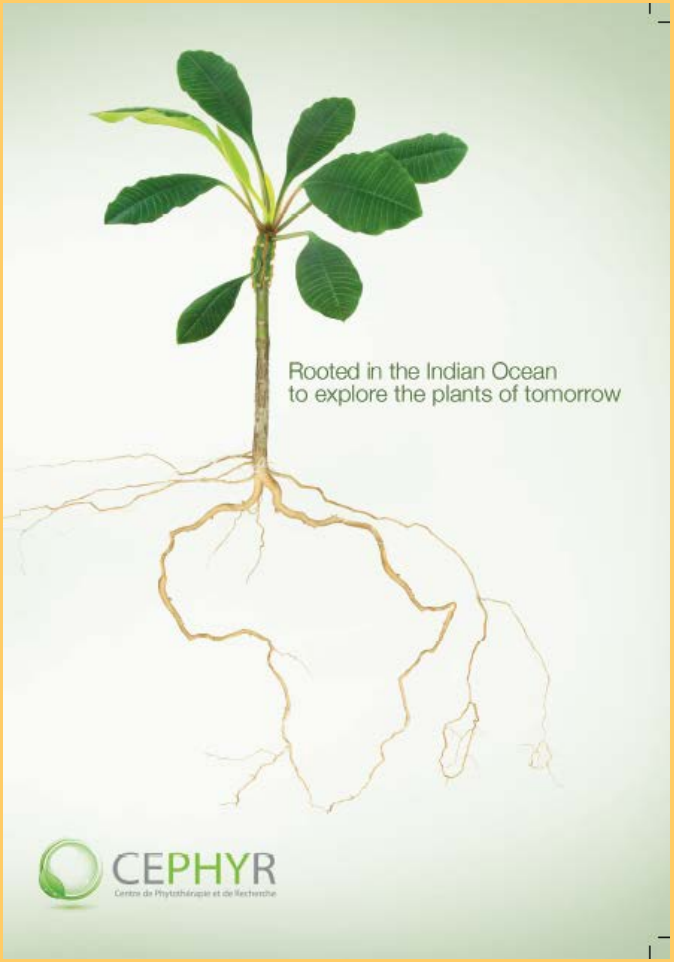

OUR TEAM

CIDP has a multidisciplinary team of 100 persons consisting of:

- Specialists doctors
- Pharmacists
- Clinical Trial Managers
- Clinical Trial Coordinators
- Biologists
- Biostatisticians
- Data managers

We also work in collaboration with a network of over 30 medical investigators under contract, who are also experienced specialists, recognized in their respective fields and trained in clinical trials.

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