

**USP** U.S. PHARMACOPEIA  
The Standard of Quality™

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## Regional Approaches to Monitoring Drug Quality

International Federation of Pharmacy  
Beijing, China  
September 3, 2007

Nancy L. Blum, M.P.H., M.A.  
Vice President, International Technical Alliance Programs

**USP** **Pharmaceutical Standards-Setting**

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- ◆ Founded in 1820
- ◆ The *United States Pharmacopeia* and the *National Formulary (USP-NF)*
- ◆ Reference Standards
- ◆ Products exported to the U.S. which meet USP standards will meet requirements of U.S. federal law



**USP** **Mission Statement**

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**USP promotes the public health by developing and disseminating quality standards and information for medicines, healthcare delivery, and related products and practices.**

**USP** **Not-for-profit, Voluntary organization**

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- Board of Trustees & Board Committees
- Convention Membership
- Council of Experts & Expert Committees
- Subcommittees (Committee Chair)
- Advisory Panels (CoE Chair)
- Stakeholder Forums & Project Teams
- Advisory Bodies
- Council of the Convention (President & EVP-CEO, with advice and consent of BOT)

**USP** **The USP Convention Membership**

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Colleges and Schools of Medicine and Pharmacy, State Medical and Pharmaceutical Societies and Associations (311)

Manufacturers, Distributors, Trade and Affiliated Associations (up to 25)

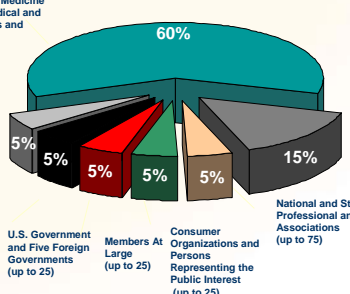
Non-U.S. International Organizations and Pharmacopeias (up to 25)

U.S. Government and Five Foreign Governments (up to 25)

Members At Large (up to 25)

Consumer Organizations and Persons Representing the Public Interest (up to 25)

National and State Professional and Scientific Associations (up to 75)

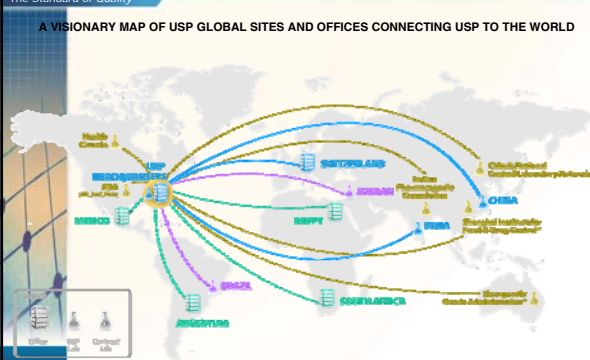


(Note: Does not include Board of Trustees, Honorary or ex-officio members, or Convention Committee Members)

**USP** **Current and Proposed Future Sites & Account Management Offices**

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A VISIONARY MAP OF USP GLOBAL SITES AND OFFICES CONNECTING USP TO THE WORLD



Global Sites and Offices: Mexico, India, Singapore, China, South Korea, Japan, Brazil, Argentina, Europe, USA, Canada.

### USP involvement in anti-counterfeiting

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- International Medical Product Anti-Counterfeiting Taskforce (IMPACT), WHO
- U.S. Dept. of Commerce, Office of Health and Consumer Goods, International Trade Administration, Taskforce on Anti-counterfeiting
- USP Drug Quality and Information Program





### A USP DQI Case Study on Antimalarials in Mekong Sub-Region

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**Goal**  
To strengthen national capacity to monitor the quality of antimalarial medicines at the local level of the medicines regulatory authority and within the national malaria programs in Cambodia, Laos, Vietnam, Thailand and Yunnan of China.

**Objectives**


- To assess the quality of selected antimalarial medicines in high prevalence areas.
- To use the findings to advocate change, raise awareness and encourage drug regulatory authorities to take appropriate measures to address the problem



### USP DQI Drug Quality Surveillance in Mekong region



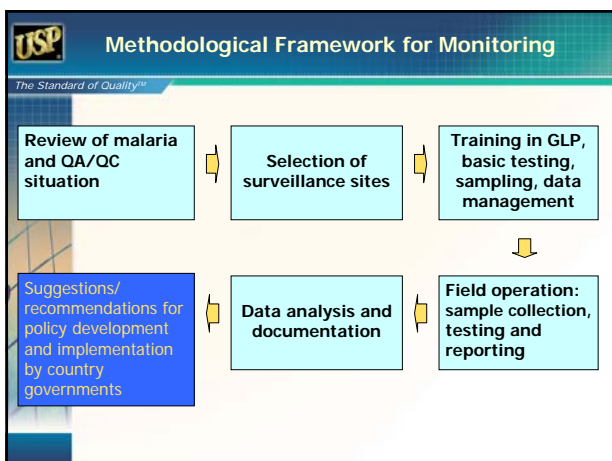
**Thailand**  
**Cambodia**  
**Vietnam**  
**Lao PDR**  
**Yunnan, China**



### Number of Sites and Samples Collected and Tested

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Country (No. of sites)	Sentinel sites	Sample
Cambodia 7	Battambang, Pursat, Paillin, Preah Vihar, Koh Kong, Bantheay Mean Cheay, Svay Rieng	195
Laos 6	Champasack, Savannakhet, Attapeu, Sayaboury, Xiengkhouang, Luangnamtha	188
Thailand 4	Kanchanaburi, Trat and Chanthaburi, Mae Hong Son, Ranong	173
Vietnam 4	Binh Phuoc, Daklak, Lai Chau, Quang Tri [as of Feb 2006, there are 9 sites in Vietnam]	105
Yunnan 2	Mengla, Ruili	83
<b>TOTAL</b>		<b>744</b>



### Minilab & Basic Tests: Testing at Central & Peripheral Levels

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Activity and requirements	Level of testing	Quantity/number of samples
<b>Sample collection</b> Basic tests	Sentinel site	Test: 100% of samples collected. Send: - all doubtful samples to NDQC Lab for verification - 5-10% of failed samples - 5-10% of passed samples
<b>Verification</b> Basic tests	NDQC or designated Lab	Test: 100% samples received from sentinel sites. Send: - all doubtful samples to NDQC/Ref Lab - 5-10% failed samples - 5-10% passed samples
<b>Confirmation</b> Pharmacoepial specification	NDQC or Reference Lab	Test: all samples received from NDQC Lab/designated Lab

**USP Results of Testing by Country**

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	ART	DIH	CHQ	MEF	QUI	S/P	TET
Cambodia	8/22 36%	0/12 0%	1/54 2%	1/21 5%	11/25 44%	na	3/61 5%
Laos	3/8 38%	na	2/55 4%	0/3 0%	1/38 3%	0/25 0%	0/59 0%
Thailand	1/16 6%	na	0/50 0%	0/25 0%	2/29 7%	0/5 0%	0/48 0%
Vietnam	1/20 5%	na	0/26 0%	0/1 0%	2/32 6%	0/26 0%	na
Yunnan	3/18 17%	na	2/31 7%	na	1/23 4%	0/11 0%	na
	16/84 19%	0/12 0%	5/216 %	1/50 %	17/147 12%	0/67 0%	3/168 2%

Substandard (low API content) Failed dissolution Substandard (low API content) Low assay Low bioequivalence

**USP Countries take action**

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- ◆ **Vietnam:** Recall ordered of a specific lot number of fake artesunate tablets from all 64 provinces
- ◆ **Laos:** Recall issued to all 17 provinces, products confiscated and legal action underway.
- ◆ **Cambodia:** IEC on fake drugs in general. FDD organized workshop with police, customs, manufacturers, distributors and providers.
- ◆ **China:** Substandard quinine injections, chloroquine tablets and fake artesunate were confiscated and drug outlets and clinics were fined and had licenses revoked.
- ◆ **Thailand:** Regulatory authority is working with local manufacturers and distributors to improve GMPs.



**USP GPHF-Minilab®**

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- Simple and inexpensive test methods to verify 42 active ingredients
- Portable
- Easy to Interpret
- Reproducible



**USP GPHF-Minilab®**

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- ◆ Basic Lab Equipment
- ◆ Reference Standards
- ◆ Analytical Reagents





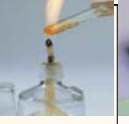
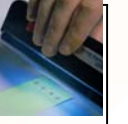
Kit for TLC assays



Kit for colour reactions

**USP GPHF-Minilab®: Test Methods**

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Visual Inspection	Disintegration Test	Colour Reactions	Thin Layer Chromatography
			

**USP GPHF-Minilab®: Current Applications**

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<b>Antibacterial Medicines</b> Amoxicillin, Ampicillin, Cefalexin, Chloramphenicol, Ciprofloxacin, Cloxacillin, Cotrimoxazole, Erythromycin, Penicillin V, Tetracycline	<b>Further Anti-infective Medicines (Antifungals, Anthelmintics, Antiprotozoals)</b> Griseofulvin, Mebendazole, Metronidazole
<b>Antiasthmatic &amp; Antiallergy Medicines</b> Aminophylline, Prednisolone, Salbutamol	<b>Antimalarial Medicines</b> odiaquine, Artesunate, Artemether, Chloroquin, Lumefantrine, Mefloquin, Primaquine, Quinine, Sulfadoxine/Pyrimethamine, Tetracycline
<b>Analgesic Medicines</b> Acetylsalicylic acid, Metamizole, Paracetamol	<b>Antituberculosis Medicines</b> Ethambutol, Isoniazid, Pyrazinamide, Rifampicin, Ciprofloxacin
<b>Other Medicines</b> Furosemid, Gilbenclamid	<b>Anti(retro)viral Medicines</b> Didanosine, Indinavir, Lamivudine, Nevirapine, Stavudine, Zidovudine - Oseltamivir

**USP** GPHF-Minilab®: **Future**  
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**More Applications**

- ◆ Antimalarials (arteether, atovaquone, piperazine, pyronaridine etc.)
- ◆ Antibiotics (ceftriaxone, ceftazidime, doxycycline, vancomycin)
- ◆ Anthelmintics (albendazole, praziquantel)
- ◆ Antiretrovirals (lopinavir, retronavir)
- ◆ Antifungals ( fluconazole, ketoconazole, itraconazole, nystatin)
- ◆ Antihypertensives (atenolol, enalapril, captopril, nifedipine)
- ◆ Anti-ulcer medicines (cimetidine, ranitidine, omeprazole, lansoprazole)
- ◆ Lipid lowering agents (atorvastatine, lovastatine, pravastine, simvastatine)
- ◆ „Lifestyle medicines“ (sildenafil, tadalafil, vardenafil)
- ◆ Vitamins (ascorbic acid, nicotinamide, pyridoxine, thiamine, retinol)

**USP** GPHF-Minilab®: **Cost Estimate**  
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**1 Minilab** with full starter set of ref stds and reagents for 1000 assays **3320 €**

**Transport to country** (for example Asian region) **~ 1050 €**

**Transport in country** to end user **~ 100 €**

**Customs Clearance** **~ 500 €**

**Total cost estimate** **~ 4970 €**

**Optional:**  
**Training, pocket balance, authentic reference standards for anti(retro)virals**  
**Tailor-made Minilabs for antimicrobial, antiviral, antimalarial & TB medicines testing**

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**Genuine or Fake?**

**VISUAL INSPECTION**

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**Fake**



**Fake**



**Fake**



**Genuine**



**Counterfeit Holograms on Fake Antimalarial Medicines in Mekong Countries**

**USP** **Tool for Visual Inspection of Medicines**  
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- ◆ FIP
- ◆ International Council of Nurses
- ◆ USP
- ◆ Packaging
  - Container and closure
  - Labeling
- ◆ Physical characteristics
- ◆ Report to WHO

**USP** **Physical Inspection of Solid Dosage Forms**  
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- ✓ Uniformity of Shape
- ✓ Uniformity of Size
- ✓ Uniformity of Colour
- ✓ Coating
- ✓ Markings
- ✓ Presence of empty capsules
- ✓ Presence of open or broken capsules
- ✓ Presence of weak point in body of capsule
- ✓ Is the capsules' cap and body separated?
- ✓ Capping or cavitations of tablets or capsules
- ✓ Polishing (free of powders)
- ✓ Evidence of embedded or adherent foreign matters
- ✓ Breaks
- ✓ Cracks
- ✓ Splitting
- ✓ Pinholes
- ✓ Stickiness

**USP** **What information should be on the label – and why??**  
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Trade name: Oblong Novalgin®  
The drug's scientific name: Active ingredient: Metamizol Sodium  
10 Tablets of 0.5 g  
Company Logo:

Batch number, Manufacturing date, Expiry date

The number of units per container: 10

Dosage form indicating the route of administration: 10 Tablets of 0.5 g

The drug's strength: 0.5 g

The manufacturer's full address: Produced by Hoechst GmbH, S.A.E. Case P.C.C. 104316, Under license of Hoechst AG, Frankfurt (Main), Germany

**USP** **What's the problem??**  
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Location of storage temperature: Store at 2° to 8°C

AMGEN: Degree sign present

COUNTERFEIT: Degree sign not present

Source: [www.amgen.com](http://www.amgen.com)

**USP** **What's the problem??**  
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**Fake Quinine Sulfate**

ឈ្មោះអាណិស្ត្រាមុខ	: កីឡា
ឈ្មោះអីប៊ី	: កីឡាស៊ីនត្រាត ៣០០ អ.ត្រ
កម្រិតទម្ងន់	: ៥០០០ (្រម)
លេខស្នង	: 220530
លេខបញ្ជី	: 2A 2410/28 1A 1505/30
ថ្ងៃផុតពីសីត	: ១០-៣-០៣
ថ្ងៃផុតពីសីត	: ១០-៣-០៥
ប្រភពអាណិស្ត្រាមុខ	: Brany Pharmaceutical, Part
ប្រភពអីប៊ី	: មិនស្គាល់

Brand name	: QUININE SULPHATE
I.N.N	: Quinine Sulphate 500mg
Packaging	: 1000 Tabs/Btl
Lot N°	: 20530
Reg. N°	: 2A 2410/28 1A 1505/30
Mfg. date	: 10-03-07
Exp. date	: 10-03-06
Claimed Source	: Brany Pharmaceutical, Part
Real Source	: Unknown

**USP** **Applications: Material Authentication → TruScan™**  
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- Handheld Raman for material verification
- Battery powered (>5 hours)
- Rugged & Lightweight
- Integrated Barcode scanner
- Web-based administration
- Network synchronization

**USP** **Applications: Anticounterfeiting → TruScan™**  
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**Counterfeit Identification**

- High degree of accuracy
- Takes less than one minute to analyze an unknown
- Can scan through plastic, glass, blister packs, clear gel-caps
- Can analyze powders, tablets, and liquids
- Currently being evaluated by FDA and used by top 10 global pharmaceutical companies
- No on-going cost for consumables or service

**USP** **Counterfeit drug detection**  
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**Method Development**

- Authentic sample used to create method
- User places tablet in tablet holder
- User selects method (Brand + dosage)
- User presses Scan button
- Scan time is usually seconds
- Instrument gives Pass or Fail result

**User runs analysis**

**Results**

<p>Method Result: <b>Pass</b> Add Note</p> <p>Sample ID: 00000004 Method: quinine sulfate</p>	<p>Method Result: <b>Fail</b> Add Note Discard</p> <p>Sample ID: 00000005 Method: quinine sulfate</p>
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## MCH clinic in Mozambique

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*Thank you*