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International Meeting of World Pharmacopoeias

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29 February–2 March 2012

REVIEW OF WORLD PHARMACOPOEIAS

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1. Introduction

Pharmacopoeia: the word derives from the ancient Greek *φαρμακοποιΐα* (*pharmakopoiia*), from *φαρμακο-* (*pharmako-*) ″drug″, followed by the verb-stem *ποι-* (*poi-*) ″make″ and finally the abstract noun ending *-ια* (*-ia*). These three elements together can be rendered as ″drug-mak-ing″ or ″to make a drug″.

A pharmacopoeia, pharmacopeia, or pharmacopoea, in its modern sense, is a legally binding collection, prepared by a national or regional authority, of standards and quality specifications for medicines used in that country or region. A quality specification is composed of a set of appropriate tests that will confirm the identity and purity of the product, ascertain the strength (or amount) of the active substance and, when needed, its performance characteristics. Reference substances, i.e. highly-characterized, physical specimens, are used in testing to help ensure the quality, such as identity, strength and purity, of medicines. The texts cover pharmaceutical starting materials, excipients, intermediates and finished pharmaceutical products (FPPs). General requirements may also be given in the pharmacopoeia on important subjects related to medicines quality, such as analytical methods, microbiological purity, dissolution testing, stability, etc. (*1*).

The role of a modern pharmacopoeia is to furnish quality specifications for active pharmaceutical ingredients (APIs), FPPs and general requirements, e.g. for dosage forms. The existence of such specifications and requirements is necessary for the proper functioning or regulatory control of medicines. Pharmacopoeial requirements form a base for establishing quality requirements for individual pharmaceutical preparations in their final form. According to the information available to the World Health Organization (WHO), 140 independent countries are at present employing some 30 national as well as the African, European and International Pharmacopoeias (*2*). Compared to national and regional pharmacopoeias, *The International Pharmacopoeia* (Ph. Int.) is issued by WHO as a recommendation with the aim to provide international standards – including less technically demanding alternatives where needed - for adoption by Member States and to help achieve a potentially global uniformity of quality specifications for selected pharmaceutical products, excipients and dosage forms.

After discussion with many representatives of world pharmacopoeias and in response to feedback, WHO has initiated steps based on WHO's first attempts during various meetings of the International Conference of Drug Regulatory Authorities (ICDRA), especially the 10th ICDRA meeting held in Hong Kong in 2002 and a further discussion among regulators during the 11th ICDRA meeting held in Madrid in 2004, to organize an official meeting entitled *International meeting of world pharmacopoeias* for participation of all WHO Member States' pharmacopoeias worldwide, be they national, regional or international. The aim was to discuss topics of common interest and challenges. The meeting dates were 29 February–2 March 2012. In order to prepare for the meeting in a timely manner, WHO sent a preliminary agenda and *Questions to pharmacopoeias* in advance to receive feedback and enable comprehensive input to the agenda. The questions, participants‘ presentations and the meeting report are shown on the meeting web site (*3*).

This document presents a summary of the answers to the *Questions to pharmacopoeias* provided by representatives of world pharmacopoeias participating in the international meeting, and of other related information received from those that were unable to actively participate in this meeting.

2. History and background

Overwhelming empirical knowledge of mankind gained during centuries and constant effort to establish better health care possibilities have led to the creation of a list of origin, preparation and healing properties of medicines.

The term *Pharmacopoeia* first appears as a distinct title in a work published in Basel, Switzerland in 1561 by Dr A. Foes, but does not appear to have come into general use until the beginning of the 17th century. Today's pharmacopoeias focus mainly on assurance of quality of products by various tools of analytical sciences.

The aim to achieve a wide global harmonization of quality specifications for selected pharmaceutical products, excipients and dosage forms came with increased globalization and reciprocal collaboration. History of these approaches goes back to 1902–1925 when agreements established a ″Unified″ Pharmacopoeia. In 1929 the "Brussels Agreement" stipulated the League of Nations to carry out related administrative functions. Eight years later, in 1937, the first meeting of the ″Technical Commission of Pharmaceutical Experts″ was held. An important date in the history of quality assurance of medicines is 1948, when the First World Health Assembly (WHA) approved the Expert Committee on Unification of Pharmacopoeias to continue this work. One year later, the WHA renamed it the Expert Committee on International Pharmacopoeia (*1*).

Attendees at the ICDRA side meetings and ICDRA sessions thereafter championed the need for a worldwide approach in terms of pharmacopoeial specifications, especially stated by the participants from Brazil, China, Czech Republic, India, Russian Federation, Thailand, Zimbabwe and by telephone with the Council of Europe and the United States Pharmacopeia (USP). Recommendations emerged from these side meetings, including holding an international meeting for those involved in the development of pharmacopoeial specifications, putting the topic of pharmacopoeias on the agenda of the forthcoming ICDRA, encouraging international harmonization efforts by WHO to develop common specifications and international reference standards with special focus on those for which no pharmacopoeial monographs exist as yet, making all efforts to help combat counterfeit drugs, reinforcing the close links between regulatory authorities and pharmacopoeias, and discussing the importance of impurity profiles and limits at an international level, especially for internationally-traded starting materials.

3. Questions to pharmacopoeias

This summary is based on the answers to the *Questions to pharmacopoeias* (below) provided by representatives of world pharmacopoeias participating in the 2012 international meeting at WHO headquarters.

Box 1. Questions to pharmacopoeias

1.	Name of pharmacopoeia
2.	Pharmacopoeia referred to in national/regional legislations - if yes, which?
3.	National/regional legislation includes reference to other - national, regional, international pharmacopoeias(s) - if yes, which?
4.	Publication of latest edition
5.	Update frequency - Annually, biannually, other (please specify)
6.	For which products does the pharmacopoeia provide specifications? APIs, dosage forms, herbal products, biologicals, traditional medicines, etc. (please specify)

7.	Number of texts included in the pharmacopoeia Monographs for APIs, finished dosage forms, biologicals, general monographs
8.	Collaboration with and/or being part of a (different) national/regional pharmacopoeia - if yes, which?
9.	Publication of harmonized pharmacopoeial texts within the pharmacopoeia if yes, which pharmacopoeia, which type, how many?
10.	Interaction with stakeholders, including regulators?
11.	Strategy for the future?

Name of the pharmacopoeia, latest publication and update frequency

The pharmacopoeia, as a public tool, maintains quality of medicines by collecting the recommended procedures for analysis and specifications for the determination of *e.g.* pharmaceutical substances, excipients and dosage forms, and in most cases consists of a general part (tests, methods and general requirements) and a specific part in the form of monographs, i.e. monographs for pharmaceutical substances. Pharmaceutical analysis as an exact science represents a platform through which state-of-the-art research can affect quality safety and efficacy of medicines directly by applying those scientific results into everyday practice by pharmacopoeias. Transparency and scientific progress are the driving engines behind the need to constantly update all pharmacopoeias. Despite differences in language and medicines regulation among countries all around the world, internationalization and unifying principles in terms of maintaining quality of medicines should be discussed to establish proper medicines for all.

To keep countries' pharmacopoeias up-to-date for the reasons mentioned above, pharmacopoeial commissions constantly update their pharmacopoeias. The updates themselves are performed by publishing supplements and addenda or by partial revision.

More than half the pharmacopoeias represented by the participating delegations, pharmacopoeias are being updated annually. See the table below with comprehensive information about the name of the world pharmacopoeias, their update frequency and latest editions.

Table 1. Names, update frequencies and latest editions of pharmacopoeias

Scope **Organization, region or country**	**Name of pharmacopoeia**	**Update frequency**	**Latest edition**	**Year**
International:				
World Health Organization (Ph. Eur. Obs.)	The *International Pharmacopoeia*	Annually	4th Edition, Vols 1, 2 2nd Supplement	2006 2011
Regional:	Europe			
European Union	European Pharmacopoeia (Ph. Eur.)	New Edition every three years. Supplements three times a year (Mar, Jun, Nov)	7th Edition (7.0) 7th Edition (7.4)	2010 2012
National :	Europe	(Ph. Eur. Members)		
Croatia	Hrvatska Farmakopeja	(Translation does not follow the frequency of publication of Ph. Eur.)	Croatian Pharmacopoeia with comments	2007
Czech Republic	Český lékopis	Annually as Supplements	Edition (MMIX) Supplement	2012

Scope Organization, region or country	Name of pharmacopoeia	Update frequency	Latest edition	Year
Finland	Ph. Eur.	(see Ph. Eur.)	(see Ph. Eur.)	(see Ph. Eur.)
France	Pharmacopée française	Annually; since 1998 consists of three folders regularly updated; since the 4th Ed, two per year	11th Edition	April 2012
Germany	Deutsches Arzneibuch (DAB)	Updated annually	DAB 2011	2011
Portugal	Farmacopeia Portuguesa	Published every 4 years, with 3 supplements annually	9th Edition, Vol. 1,Vol. 2,Vol. 3 Supplement 9.8	2008 2010
Serbia	Yugoslav Pharmacopoeia	N/A	Translation of Ph. Eur. 3rd Ed.	1997
Spain	Real Farmacopea Española	Planned to follow the same frequency as the Ph. Eur.	4th Edition	2011
Sweden	Ph. Eur.	(see Ph. Eur.)	(see Ph. Eur.)	(see Ph. Eur.)
Switzerland	Pharmacopoea Helvetica	Annually or biannually	10th Edition Supplement 10.3	2006 2010
United Kingdom (UK)	British Pharmacopoeia	Annually	BP	2013
National:	Eastern Europe and	Central Asia		
Kazakhstan (Ph. Eur. Obs.)	The State Pharmaco-poeia of the Republic of Kazakhstan	N/A	1st Edition 1, 2 volumes	2008
Russian Federation (Ph. Eur. Obs.)	State Pharmacopoeia of the Russian Federation	Once in 5 years	12th Edition, Vol. 1	2007
Ukraine (Ph. Eur. Obs.)	The State Pharmaco-poeia of Ukraine	Bianually	1st Edition Supplement 4	2001 2011
National:	Asia			
China (Ph. Eur. Obs.) *	Pharmacopoeia of the People's Republic of China	Once every five years	9th Edition	2010
India	Indian Pharmacopoeia (IP)	Once every four years in between an Addendum	6th Edition, IP-2010 Addendum 2012 to IP-2010	2010 2012
Indonesia	Farmakope Indonesia	Updated annually by f supplement and once every 5 years as a new edition	4th Edition 3rd Supplement	1995 2011
Japan	The Japanese Pharmacopoeia (JP)	Once every 5 years since JP9; two supplements between the editions after JP12 and partial revision at any time if immediate necessity	JP16 Supplement I to JP16	2011 2012
Korea*	The Korean Pharmacopoeia	Currently revised in every 5-year term	9th Edition Supplement 7	2007 2011
National:	North America			
United States of America (Ph. Eur. Obs.)	United States Pharmacopeia (USP)	Annually, with 2 supplements per year	USP 35-NF 30 Supplement	2011 2012
National:	Latin America			
Argentina (Ph. Eur. Obs.)	Farmacopea Argentina	Undetermined, intended bianually	8th Edition* (vol.1,2,3,4)	2011

Scope Organization, region or country	Name of pharmacopoeia	Update frequency	Latest edition	Year
Brazil (Ph. Eur. Obs.)	Farmacopéia Brasileira	No defined periodicity	5th Edition, Vols 1, 2	2010
Mexico	Farmacopea de los Estados Unidos Mexicanos	Annual update	10th Edition Supplement	2011 2012

(Ph. Eur. Obs.) = Ph. Eur. Observer
* Not represented at the meeting.

Legal basis and references to other pharmacopoeias

Pharmacopoeias are referred to in legislation which puts them into force in the relevant country or region.

In Europe a regional approach is used. Ph. Eur. was created by eight Member States in 1964 and today consists of 36 Member States and the European Union (EU)**,** which are signatory to the Convention on the Elaboration of a European Pharmacopoeia. Ph. Eur. members are: Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, (the former Yugoslav Republic of) Macedonia, Malta, Montenegro, Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, United Kingdom, and the EU. In addition there are 24 observers, including 23 countries and WHO.

Figure 2. Member and Observer States of the European Pharmacopoeia

EU Directives stipulate that ″the monographs of the European Pharmacopoeia shall be applicable to all substances, preparations and pharmaceutical forms appearing in it. In respect of other substances, each Member State may require observance of its own national pharmacopoeia.″ These directives are transposed into national legislation of EU Member States, e.g. the Human Medicines Regulations 2012, 14 August 2012 (UK), the Law of Guarantees and Rational Use of Medicines (Spain), the Law for Medicines and Medical Devices (Serbia), Food, Drug, Federal and Cosmetic Act (USA), etc.

Some of the 36 member states of the European Pharmacopoeia (Ph. Eur.) Convention have decided to discontinue their own national pharmacopoeia and solely use the Ph. Eur. Examples are Sweden and Finland. Other member states of the Ph. Eur. Convention have decided to continue their national pharmacopoeia for products of solely national interest. In Switzerland, for instance, the Pharmacopoea Helvetica (Ph.Helv.) exists alongside the Ph. Eur., and the two together form the legally binding pharmacopoeia. In France, the pharmacopoeia consists of the texts of the European Pharmacopoeia and of the French Pharmacopoeia, including the ″overseas″ pharmacopoeia. Other countries, e.g. the United Kingdom, have decided to fully integrate the texts of the Ph. Eur. into their national pharmacopoeia; hence the British Pharmacopoeia (BP) contains the texts of the Ph. Eur. in addition to the national texts of the BP.

National/regional legislation often includes reference to other pharmacopoeias in case their own pharmacopoeial texts are not available. Thus the EU pharmaceutical legislation and hence the legislation of all EU Member States includes references both at the national/regional and international levels. Historic and language ties also play a role. For example the Portuguese pharmacopoeia is also accepted in the legislation from Brazil and other countries where Portuguese is an official language (Mozambique, Guinea or Sao Tomé e Princípe, for instance).

WHO's *International Pharmacopoeia* (Ph. Int.) is "ready for use" by Member States. The Ph. Int. is referred to in a number of national legislations due to its applicable status.

Table 2 presents information about legislation references in national/regional legislation as provided at the meeting, or sent to WHO by countries that were not represented at the meeting.

Table 2. Legal basis

Scope **Organization, region or country**	**Pharmacopoeia referred to in national/regional legislations**	**National/regional legislation includes reference to other pharmacopoeias**
International:		
WHO	The Ph. Int. […] is intended to serve as source material for reference or adaptation by any WHO Member State wishing to establish pharmaceutical requirements. The pharmacopoeia, or any part of it, shall have legal status, whenever a national or regional authority expressly introduces it into appropriate legislation.	Not applicable
Regional:	Europe	
European Union (EU)	Legal texts making Ph. Eur. mandatory in Europe include: • Convention on the Elaboration of a European Pharmacopoeia, and amending Protocol (following accession of the European Union) • European Union Directives 2001/82/EC and 2001/83/EC, as amended, and 2003/63/EC on medicines for human and veterinary use, stating the legally-binding character of European Pharmacopoeia texts for marketing authorisation applications.	Directive 2001/83/EC as amended: ″The monographs of the European Pharmacopoeia shall be applicable to all substances, preparations and pharmaceutical forms appearing in it. In respect of other substances, each Member State may require observance of its own national pharmacopoeia.″ ... ″In case where starting and raw materials, active substance(s) or excipient(s) are described neither in the European Pharmacopoeia nor in the pharmacopoeia of a Member State, compliance with the monograph of a third country pharmacopoeia can be accepted. ..

Scope **Organization, region or country**	**Pharmacopoeia referred to in national/regional legislations**	**National/regional legislation includes reference to other pharmacopoeias**
National:	European Union (Ph. Eur. Members)	
Croatia	Medicinal Products Act (Official Gazette No 71/07); Acts on Amendments to the Medicinal Products Act (Official Gazette No 45/09 and No 124/11); Ordinance on the Procedure and Method for Granting Marketing Authorisation for Medicinal Products (Official Gazette No 113/08); Ordinance on Special Conditions for Placing Medicinal Products Authorized in the Member States of the European Union on the Market of Republic of Croatia (Official Gazette No 10/08); Ordinance on the quality control of medicinal products (Official Gazette No 56/05)	See under "EU"
Czech Republic	Act No 378/2007 (Act on Pharmaceuticals)	"
France	National legislation (Code de la santé publique: Art. L. 5112-1). ″Overseas″ traditional pharmacopeia subject to regulatory conformities (departments: Caribbean, Guyana, Reunion Island and territories, French Polynesia, Caledonia)	See under "EU"
Germany	Medicinal Products Act (The Drug Law) –Arzneimittelgesetz (AMG) of the Federal Republic of Germany; Legal German Ordinance on the GMP implementation (Arzneimittel- u. Wirkstoffherstellungsverordnung - AMWHV) Legal German Ordinance on internal regulations in pharmacies (Apotheken-betriebsordnung)	"
Serbia	Law for medicines and medical devices - entered into force in May 2010	"
Spain	(Law of Guarantees and rational use of medicaments – 2005). Dependent on AEMPS – Department of Evaluation of Medicaments for Human Use National Formulary. Dependent on AEMPS - Department of Inspection	"
Sweden	The Swedish Government's 1977 decision that the English version of the European Pharmacopoeia should be used from 1 January 1978 For each supplement of the European Pharmacopoeia there is a Medical Products Agency provision which puts all new and revised monographs into force	"
Switzerland	Legal basis is Swiss law Art. 4, 8 and 52 of the Law on Therapeutic Products Ordinance regulating the issue of the Pharmacopoeia by Swissmedic puts the Pharmacopoeia into force	"
UK	Medicines Act 1968 (Section 99), superseded by The Human Medicines Regulations 2012 on 14 August 2012	"
National:	Eastern Europe and Central Asia	
Kazakhstan (Ph. Eur. Obs.)	Approved in 2008 by the Order of the Ministry of Health, and referred to in the Codex of the Republic of Kazakhstan "On Public Health and Healthcare System" approved on 18 September 2009	Recognition of European Pharmacopoeia, United States Ph., British Ph., German Homeopathic Pharmacopoeia by the Order of the Pharmacy Committee of the Ministry of Health (February, 2004)
Russian Federation	At present the State Pharmacopoeia 12th edition, Vol. 1 is applicable in the Russian Federation (in accordance with the Order No.73 "On the State Pharmacopoeia of the Russian Federation" of the Ministry of Health and Social Development, dated 31 January 2007).	Other pharmacopoeias do not have an official status in the territory of the Russian Federation. However, the quality standards of *The International Pharmacopoeia*, European Pharmacopoeia, USP, and BP are recognized when registering medicinal products. Other pharmacopoeias are used as a reference.

Scope Organization, region or country	Pharmacopoeia referred to in national/regional legislations	National/regional legislation includes reference to other pharmacopoeias
Ukraine (Ph. Eur. Obs.)	Status of SPU in Ukraine is defined by the law ″About medicinal products″; Article 2 ″Definition of the terms″ thereof states: ″The State Pharmacopoeia of Ukraine (SPU) is a legal act that contains general requirements for medicinal products, pharmacopoeal chapters as well as medicine quality control procedures″.	Status of other pharmacopoeias in Ukraine is not defined by law/de jure. When registering medicines in Ukraine, if related monographs are missing in the SPU, an application of standards of the European Pharmacopoeia is permitted firstly, and those of other pharmacopoeias secondarily (BP, USP, JP). Other available pharmaco-poeias are used as textbooks/reference manuals.
National:	Asia	
India	Drugs & Cosmetic Act 1949 and Rules 1945. IP is published by the Indian Pharmacopoeia Commission, the Standards Setting Institution for Drugs. It is an autonomous body under the Ministry of Health & Family Welfare.	Other national pharmacopoeia(s)
Indonesia	Act of The Republic of Indonesia Number 36 Year 2009 on Health (Revised Act of The Republic of Indonesia Number 23 Year 1992) Article105	One national pharmacopoeia applied all over the country. Legal basis also allows reference to other relevant standards such as *The International Pharmacopoeia*, US Pharmacopeia, etc., as needed.
Japan	The Japanese Pharmacopoeia (JP) was established and published to regulate the properties and qualities of drugs by the MHLW based on the provisions of Article 41, Paragraph 1 of the Pharmaceutical Affairs Act after hearing opinion of the Pharmaceutical Affairs and Food Sanitation Council.	None
Korea**	Article 51 of the Pharmaceutical Affairs Act	1. US Pharmacopeia/National Formulary; 2. The Japanese Pharmacopoeia; 3. British Pharmacopoeia; 4. Deutsches Arzneibuch 5. Pharmacopée Francaise (in KFDA notification); 6. European Pharmacopoeia (in KFDA notification)
National:	North America	
United States (Ph. Eur. Obs.)	United States Pharmacopeia (USP), National Formulary (NF) and Homeopathic Pharmaco-peia are recognized in legislation. USP in the 1938 Food, Drug and Cosmetic Act: Provisions on Definition of a drug, Adulteration, Misbranding and Drug product name	FDA Manal of Policies and Procedures (MAPP) 5310.7 notes the use of the British, Japanese, and European Pharmacopoeias during CMC review of applications. The MAPP states, however, that these compendia are not intended to be in place of or addition to the official USP-NF.
National:	South America	
Argentina (Ph. Eur. Obs.)	Ley N° 16.463/64 (Law on medicines)[1] Ordinance 21.886/56 creates the Argentine Pharmacopoeia Permanent Commission depending directly on the Health Ministry Health Ministry Resolution N° 297/96 entrusts the integration and reactivation of the Argentine Pharmacopoeia Permanent Commission to ANMAT	Brazilian Pharmacopoeia and internationally recognized Pharmacopoeias (Disp. 5743/2009)

[1] Art. 3°: The products covered by this law shall satisfy the conditions laid down in the Pharmacopoeia Argentina and, if not included in it, the conditions which arise from international standards and texts of recognized scientific value.

Scope Organization, region or country	Pharmacopoeia referred to in national/regional legislations	National/regional legislation includes reference to other pharmacopoeias
Brazil (Ph. Eur. Obs.)	Law No. 6360 of 23 September 1976 (defines the health surveillance of medicines, drugs, pharmaceutical ingredients and other products). Law No. 9782 of 26 January 1999 (defines the National Sanitary Surveillance System and creates the Brazilian Health Surveillance Agency)	ANVISA Resolution RDC No. 37, 6 July 2009, defines admissibility of foreign pharmacopoeia: German, United States, Argentinian, British, European, French, International (WHO), Japanese, Mexican and Portuguese Pharmacopoeias.
Mexico	General Health Act states that drugs and other health products are regulated by the Mexican Pharmacopoeia; Articles 195, 200, 224, 258 and 370 Regulation of health products, articles on the 2nd, 7th, 8th, 13th, 17th, 21st , 75th and 167th Mexican Official Standards: Mexican Official Standard NOM-001-SSA1-93, which establishes the procedure by which the review, update and edit the Pharmacopoeia of the United Mexican States. The Mexican pharmacopoeia is also referred to other Mexican standards.	General Health Act in Mexico states that: The quality specifications of medicine additives, drugs and medicines are those indicated in the current edition of the Mexican Pharmacopoeia. When it does not contain the information, the pharmacopoeias of other countries may be used . (Or other internationally recognized scientific literature.)

(Ph. Eur. Obs.) – Ph. Eur. Observer
* not represented at the meeting.

For which products does the pharmacopoeia provide specifications?

A large field of products is usually covered, which reflects diligence and commitment of pharmacopoeial authorities and their appointed experts to develop a comprehensive work with up-to-date scientific data. Some complexity and diversity of most pharmacopoeias results from mutual integration and interdependence, with monographs for various types of products, such as active pharmaceutical ingredients (APIs), excipients, herbal products, biologicals (vaccines, blood products), radiopharmaceuticals, dosage forms and homeopathic preparations.

It can be observed that there is an increase of finished dosage forms, which generally could be defined as the form of active ingredient which is or is intended to be dispensed or administered to the patient and requires no further manufacturing or processing other than packaging and labelling. This is in parallel to the decreasing tendency of specific national monographs for APIs within some national pharmacopoeias due to replacement with monographs from regional or international pharmacopoeias.

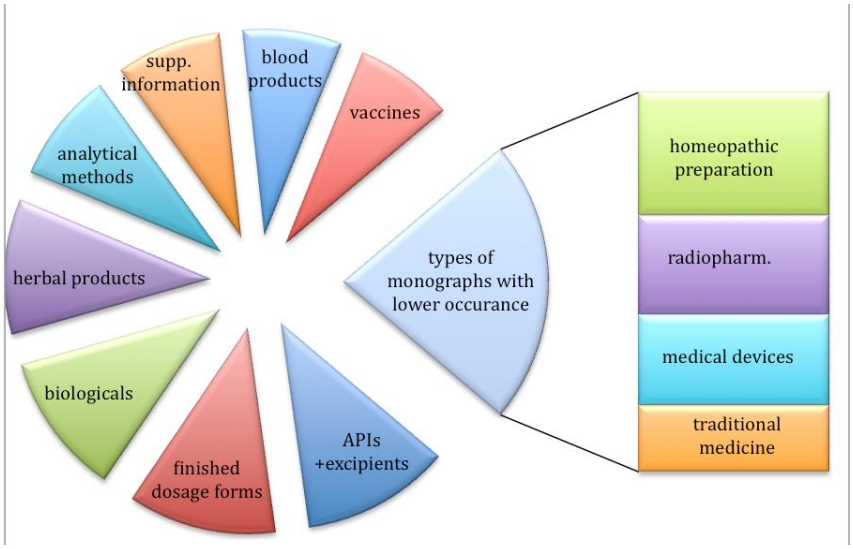
As the pharmacopoeia itself has emerged from experience of mankind gained during centuries, roots of all this valuable knowledge can still be seen in contemporary medicine as traditional medicine monographs, represented mainly in the pharmacopoeias of China, France (overseas), Japan and Ph. Eur. Likewise, homeopathic approaches are represented in pharmacopoeias, for example in Brazil, Germany and Mexico.

The pharmacopoeias reviewed at the meeting contain standards for chemical and biological drug substances, dosage forms, compounded preparations, excipients, medical devices and dietary supplements. During the current meeting some countries, such as Brazil, France, Germany, Mexico, Serbia and Switzerland, provided examples of incorporating a national formulary for hospital and/or community pharmacy preparations into their

pharmacopoeias. In Portugal, there is a non-official national formulary which is published by the Portuguese Pharmacies Association.

During the International meeting of world pharmacopoeias, there were examples of types of monographs with less frequent occurrence than other types (see Figure 2).

Figure 2. Occurrence of types of monographs in pharmacopoeias



For example, monographs for *Blood Products* were presented by Argentina (12), Brazil (20) and India (21), while monographs for *Vaccines* were presented by Argentina (21), India (57), Kazakhstan (15) and Ukraine (26). *Homeopathic preparations* described in monographs were presented mainly by France (320), Germany (120) and Mexico (558) and finally *Monographs for Traditional Medicine* were given as an example by China (2165). A total of 92 herbal, traditional herbal and homeopathic monographs are present in the British Pharmacopoeia 2012. Supplementary information is included in some of the pharmacopoeias, for example general texts, reference tables, and texts on methods of analysis, reagents, materials/containers, sutures, and references substance used in national monographs.

Detailed information as provided at the meeting or sent to WHO is summarized in Table 3.

Table 3. Number of monographs included in pharmacopoeias

Scope **Organization, region or country**	**APIs+ excipients**	**Finished dosage forms**	**Biologicals**	**General monographs + methods**	**Supple-mentary information**	**Herbal products**
International						
WHO (Ph. Int.)	441	141	N/S**	82	14	N/S***
Regional						
EU (Ph. Eur.)	1850	30	295	22	3210	N/S
National	**Europe**					
Croatia	Ph. Eur	Ph. Eur	Ph.Eur.	Ph. Eur	N/S	N/S
Czech Rep.	36	118	0	2	17	N/S
France	53	Ph. Eur.+4	5	3	N/S	115
Germany	91	N/S	N/S	N/S	N/S	N/S
Portugal	Ph. Eur.	85	Ph. Eur.	Ph. Eur.	Ph. Eur.	N/S
Serbia	Ph.Eur	Ph. Eur.	Ph.Eur.	Ph.Eur.	Ph.Eur.	N/S
Spain	3000	N/S	N/S	300	N/S	N/S
Sweden	Ph. Eur.	Ph. Eur.	Ph. Eur.	Ph. Eur.	Ph. Eur.	N/S

Scope Organization, region or country	APIs+ excipients	Finished dosage forms	Biologicals	General monographs + methods	Supple-mentary information	Herbal products
Switzerland	Ph. Eur.	Ph. Eur.	Ph. Eur.	Ph. Eur.	Ph. Eur.	N/S
UK	Ph. Eur.+171	Ph. Eur.+1431	196	incl.in finished dosage forms	73	98
National	**Eastern Europe**	**& Central Asia**				
Kazakhstan	300	77	N/S	221	N/S	26
Russian Fed.	77	16	N/S	187	18	88
Ukraine	326	74	24	79	N/S	104
National	**Asia**					
China*	733	1366	131	152	N/S	N/S
India	806	838	91	18	223	93
Indonesia	560	653	29	23	1	N/S
Iran	N/S	591	N/S	N/S	N/S	N/S
Japan	1222	542	64	N/S	39	N/S
Korea (Republic of)*	877	421	39	N/S	N/S	181
National	**North America**					
United States	1848	2454	153	300	N/S	N/S
National	**South America**					
Argentina	496	254	18	92	18	29
Brazil	284	207	51	110	N/S	58
Mexico	649	626	75	191	N/S	75

Notes: N/S – not specified in country's response
* Country not represented at the meeting, information sent to WHO.
** Part of activities of the WHO Expert Committee on Biological Standardization.
*** Part of the Traditional Medicine Programme, and published in *Quality control methods for herbal materials*, Geneva, World Health Organization, 2011.

Collaboration with and/or being part of a (different) national/regional pharmacopoeia

Pharmacopoeial authorities have collaborated at both regional and international levels for the sake of harmonization and exchange of experiences. Active and passive forms of participation occur. Active participants, such as members of Ph. Eur., can contribute their share of pharmacopoeial development, while passive forms of participation may include observational missions to benefit from the experience of other countries in specific areas and gain access to the work on quality control of medicines and methods of analysis used.

Leading world pharmacopoeias are in charge of constant progress within pharmacopoeial development, ″good pharmacopoeia practice″ and recommendation of procedures for analysis intended to serve as source material for reference or adaptation by any of their member states wishing to establish pharmaceutical requirements.

Ph. Int. provides an opportunity to comment on drafts by all world pharmacopoeias and participation in meetings, such as consultations and Expert Committees during the WHO consultation process. There are also special projects of WHO covering quality assurance of medicines worldwide, i.e. collaboration with the African Pharmacopoeia, British Pharmacopoeia, Chinese Pharmacopoeia, Council of Europe/Ph. Eur. and the Pharmacopoeial Discussion Group (PDG).

Ph. Eur. covers all national pharmacopoeias of the signatory parties to the Convention, who are members of the Ph. Eur. with emphasis on complementarity, thereby reducing duplication of work. In some member countries of the Ph. Eur. national pharmacopoeias complement the Ph. Eur. for texts of interest to one Member State only. Some member countries also republish Ph. Eur. monographs in their national pharmacopoeias. Membership and observership enables States to participate in Ph. Eur. Commission sessions even if only Members are entitled to vote. Within these sessions, each Member State is represented by its national delegation consisting of not more than three members. On all technical matters delegations cast a vote. The EU decides on behalf of EU member states in all non-technical issues of the Ph. Eur. Each Member State and observer can also propose national experts for each group of experts or working party.

The European Medicines Agency (EMA) participates in the sessions of the Ph. Eur. Commission and working parties of interest. The European Directorate for the Quality of Medicines and HealthCare (EDQM) participates in relevant committees and working parties at the level of the EMA alongside national competent authorities. In addition, annual meeting are organized between EDQM and national pharmacopoeia authorities.

Thirty-six Member States and the EU are signatory to the Convention on the Elaboration of a European Pharmacopoeia (see Figure 1). Observership to the Ph. Eur. allows for participation in the scientific work of the European Pharmacopoeia Commission. Observer examples are Belarus, Brazil, Russia, China, the United States, and WHO.

The Pharmacopoeial Discussion Group (PDG) consists of representatives of three pharmacopoeias: Ph. Eur., JP and USP. Its main activities are retrospective harmonization of general chapters and excipients monographs. In addition, Ph. Eur. and USP are running a pilot project on prospective harmonization of active pharmaceutical ingredient monographs.

MERCOSUR, as an example of intensive collaboration at the regional level, is formed by Argentina, Brazil, Paraguay and Uruguay, where texts and chapters are being discussed for inclusion in the MERCOSUR Pharmacopoeia.

Some collaborations are historically and geographically related. Traditional collaboration of the Czech Republic with the Slovak Republic results from a common history. Agreements of collaborations have been signed between countries to increase the degree of compatibility such as USP with Mexico. Ukraine has signed a collaboration agreement with USP, while intensively working with Kazakhstan. A memorandum of understanding has been signed by both the British Pharmacopoeia and Ph. Int. to use and incorporate developed monographs mutually.

Intensive collaboration with China's pharmacopoeial authorities was presented by representatives of the British and French Pharmacopoeias and USP during the meeting. France carries out collaboration with Algeria, Morocco and Tunisia mainly due to the fact that the French language used in the pharmacopoeias. Also Brazil and Viet Nam are named as collaborators with the French Pharmacopoeia. In information sent to WHO, Korean pharmacopoeial representatives mentioned bilateral memoranda of understanding with Ph. Eur. and USP.

Publication of harmonized pharmacopoeial texts within the pharmacopoeia

PDG has defined harmonization of a pharmacopoeial monograph or general chapter as follows:

> *"A pharmacopeial general chapter or other pharmacopeial document is harmonized when a pharmaceutical substance or product tested by the document's harmonized procedure yields the same results and the same accept/reject decision is reached."* (*4*).

When using a fully harmonized pharmacopoeial monograph or general chapter, an analyst will perform the same procedures and reach the same accept/reject decisions irrespective of which PDG pharmacopeia is referenced. This is called interchangeability and each pharmacopoeia will identify, in an appropriate manner, each fully harmonized monograph and general chapter.

The realization that it was important to have an independent evaluation of medicinal products before they are allowed on the market was reached at different times in different regions. In many cases the realization was driven by tragedies, such as that with sulfanilamide in the USA in 1937, and with thalidomide in Europe in the 1960s. Therefore, the urgent need to rationalize and harmonize regulation was impelled by concerns over rising costs of health care, escalation of the cost of research and development and the need to meet the public expectation that there should be a minimum of delay in making safe and efficacious new treatments available to patients in need.

Thanks to unification and interchangeability efforts of the pharmacopoeial authorities, countries have incorporated harmonized text into their pharmacopoeias, most of them from Ph.Eur, Ph. Int., USP, and PDG (i.e. Ph. Eur., JP, USP tripartite efforts).

Eastern Europe
The majority of the State Pharmacopoeia of the Republic of Kazakhstan is formed from harmonized texts (539/639), including general chapters and monographs, monographs on pharmaceutical substances, monographs on vaccines for human use and human immunoglobulins. In the Ukrainian Pharmacopoeia Supplement, there are seven harmonized monographs for finished dosage forms 4 pursuant to the *"Grant of Rights to Copy and Adapt the USP-NF "* contract, and eleven draft monographs for the 2nd Edition have already been elaborated.

Asia
Japan contributes to harmonization efforts with its counterparts – Ph. Eur. and USP – within the PDG and the Japanese Pharmacopoeia contains general tests (14), general information (11) and excipient monographs (31) as harmonized texts. The Korean Pharmacopoeia has harmonized PDG texts for General tests.

North America
USP incorporates PDG-harmonized texts in the *USP-NF***,** where 41 of 61 of excipient monographs and 28 of 35 of general chapters have been harmonized so far.

Latin America
Countries participating within MERCOSUR have included harmonized texts in their national pharmacopoeias after discussion. PDG texts are also considered in the discussions of the Brazilian Pharmacopoeia Committee. Mexico does not have a formal process for the

harmonization of information with other pharmacopoeias, but its drug monographs are consistent in their specifications with the BP, Ph. Eur. and USP in 60–100%.

Ph. Int. collaborates worldwide and has texts harmonized from various sources due to its rich collaboration. Collaboration with the British Pharmacopoeia resulted in three texts adopted in 2010, with 19 in the pipeline. Also by collaboration with PDG, 12 general methods were adopted in Ph. Int. in 2011, with more in the pipeline, for methods of analysis and supplementary information.

Interaction with stakeholders, including regulators

There are many ways how national/regional pharmacopoeial authorities interact and are influenced by stakeholders including public forums. The most common ways of interactions at the national level are between national and regional regulatory authorities, quality control laboratories and different institutions related to quality assurance of medicines. Fusion of academic, clinical and industrial fields, such as universities and other academic bodies, hospital and community pharmacies organized in expert groups, and manufacturers worldwide through their organizations, represent a platform for comprehensive and progressive discussion.

To enable harmonization and a reliable source of fluent information exchange at the global level, international organizations (e.g. UNAIDS, UNFPA, UNICEF, World Bank, WIPO, WTO, WCO), international professional and other associations, nongovernmental organizations (e.g. FIP, IFPMA, IGPA, MSF, WMA, WSMI), quality control laboratories (other than national/regional), United Nations-related organizations such as the Global Fund to Fight AIDS, Tuberculosis and Malaria, and WHO programmes including International Nonproprietary Names, Prequalification of Medicines, Medicines Regulatory Support, Medicines Safety, Traditional Medicines, Quality, Safety and Standards and specific disease programmes, are all stakeholders in collaboration.

Specific harmonization issues are discussed with regional and interregional harmonization groups (e.g. ASEAN, GCC, ICH, PANDRH, SADC, etc.). To ensure discussion and a pragmatic approach for everyday life, annual science and standard symposia are organized, as well as public forums, as an unbiased outside view on particular issues.

Strategy for the future

Strategies of the individual pharmacopoeias differ for geographical and economic reasons and depending on the level of integration to respective regional international systems. From the commitment to establish comprehensive, updated editions with highly compatible standards at a national or regional level, up to progressive intentions in order to harmonize intensively with emphasis on increase of quality assurance of medicines all around the world, those directions were determined by representatives during the meeting.

International

Ph. Int. commits to fulfilling the mandate of WHO given by its Member States and responds to the needs of the latter. As an international body, it also responds to the needs of quality control laboratories for post-marketing surveillance and maintains the international applicability of Ph. Int. specifications. Keeping the costs of analysis in mind, especially in the case of developing countries, Ph. Int. provides standards for major public health needs.

Regional

European Union

Ph. Eur. supports innovation and flexibility without losing the aim of a pharmacopoeia (i.e. to provide official, recognized and technically sound quality standards), e.g. PAT, NIR and acceptance criteria for large sample sizes. It also remains at the forefront in the biofield (e.g. P4Bio) and constantly increases harmonization with pharmacopoeias by collaboration, i.e. as part of PDG, and maintains observers within other pharmacopoeial institutions worldwide.

Ph. Eur. Member States Sweden and Finland continue to cooperate and to be active in the elaboration of the Ph. Eur.

Croatia is currently preparing a publication of a new edition of the Croatian Pharmacopoeia.

The Czech Republic would like to complete a national formulary, mainly in the field of paediatrics by cooperation with a chamber of paediatricians; assessment of stabilities in the pharmacopoeia formularies for small-scale products and products prepared in pharmacies have also been mentioned as a future plan by Czech representatives, i.e. establishment of a new group of experts from hospital pharmacies and certified laboratories.

France presented its strategy for the future at both the national and European levels. Publication online (and revisions: REACH, DCF), defines new policy and reinforces the code of practices in line with the new French Public Health Law; it defines the work programme based on both interest of patients or professionals (paediatric, ophthalmic and homeopathic preparations) and conforms to regulation and national strategy (French overseas territories). As a key player within the Ph. Eur., France would like to contribute its share of specific topics such as biological products, cell and tissue, allergenic products, antiseptic preparations, paediatric preparations, traditional herbal preparations (TCM) and collaboration with OMCLs work programme (MMS) and P4 procedures.

In addition to its contributions to the Ph. Eur. Germany focuses on particular technical issues in terms of pharmaceutical analysis such as identification of materials by the evaluation of analytical fingerprints, use of non-destructive spectroscopic methods, imaging techniques for the intact pharmaceutical preparations, trace analysis of impurities and simplified analytical identification tests for certified substances.

As a country collaborating closely with the Ph. Eur. Portugal focuses on its future plan to update national texts, to tighten the links with Portuguese-speaking countries and with stakeholders (regulators, manufacturers of APIs and manufacturers of medicines).

Serbia will prepare its national addition to Ph. Eur., update national ″Magistral Formularies″ and continue cooperation with the Ph. Eur. as a member.

Spain plans to follow the timetable of publication of the in-force Ph. Eur. successive editions (simultaneous translation), to work with internal Spanish groups that support the work of the experts and specialists in European and international groups and continue its efforts to cooperate with the work of the Ph. Eur. and international groups (groups of experts, working parties).

Switzerland focuses on participation in the activities of the Ph. Eur. in the framework of the legally binding mandate of the Ph. Eur. Convention.

Introduction of the quality standards of the SP RF 12th edition (Vols 1-5) in the territory of the Russian Federation, development of new quality standards for medicinal products and review of the old ones, will help to upgrade the national regulatory system. Plans for the future also include harmonization of the SP RF monographs with the corresponding monographs of the leading world pharmacopoeias. This will be assisted by participation of the Federal State Budgetary Institution "Scientific Centre for Expert Evaluation of Medicinal Products" of the Ministry of Health of the Russian Federation in the work of the WHO Expert Committee on Specifications for Pharmaceutical Preparations, work of the EDQM (as observer) and work of the WHO Working Group on Good Pharmacopoeial Practices.

The United Kingdom (UK) representatives presented their priorities at an international level by working together (world pharmacopoeias) through acknowledging the roles of the national authority, acknowledging regional roles and commercial activity. Intensive contribution and collaboration within the Ph. Eur. (expertise, advice, comments on drafts, laboratory support, UK Government support) were also mentioned. National activities of the BP will focus on the Annual BP and BP (Vet) Publications, British Approved Names Supplements, increase in New Formulated Preparation Monographs (licensed and unlicensed), Supplementary Chapters for BP and BP (Vet), Red Tape Challenge, Stakeholder Co-operation (manufacturers, practitioners, pharmacies, etc.) and Tailored Publications.

National within regions

Asia

Japan's tendencies for internationalization of its pharmacopoeia are based on prompt publication and further improvement of the JP English Edition and Home Page. Building up of the frameworks for international information exchange among pharmacopoeias should also be intensified. For its next revision JP commits itself to follow-up of the revision of ″General Rules for Preparations ″ in JP16: general quality tests for preparations would be newly set, to revise containers and storage and to create a new framework for monographs of drugs, whose manufacturing processes are different, including impurities (including residual solvents), process-related substances, impurities in biotech-products and tests for preparations.

China provided information to WHO stating that the country is committed to more cooperation with other world leading pharmacopoeias.

India, in terms of sharing of information among pharmacopoeias, would like to focus on resources, working in pockets where there is a need for sharing information and providing commitment to monitoring, harmonization with leading pharmacopoeias and also providing quality medicines through harmonized drug standards and monitoring quality of medicines through an effective regulatory system.

Indonesia's plans are to publish a new edition of the Indonesian Pharmacopoeia every five years, to publish the supplement annually for the existing pharmacopoeia and to publish the pharmacopoeia in an English version.

Korea informed WHO that it aims to include in its pharmacopoeia all medicines which are relevant from the viewpoint of health care and medical treatment, to revise it in timely fashion in part, if necessary, for efficient application, to follow international harmonization, to ensure transparency regarding the revision of the Korean Pharmacopoeia, to render the

document publicly available and to include up-to-date analytical methods in a timely fashion and prepare reference standards.

Eastern Europe
Introduction of the State Pharmacopoeia of the Republic of Kazakhstan standards in a pharmaceutical area, further harmonization with Ph. Eur. and USP and development, and edition and revision of its own monographs, were shared as a future strategy for Kazakhstan.

Ukraine would like to transform the Ukraine status from observer of the Ph. Eur. Commission to membership, support the world leading pharmacopoeias to implement harmonized standards in developing countries, to facilitate the free movement of high-quality medicines and develop pharmacopoeial educational programmes and expansion of possibilities for visiting scientist programmes.

Latin America
The priorities of Argentina's Pharmacopoeial Commission are strengthening of regional harmonization through joint development of reference standards and harmonization of general methods and monographs in order to establish similar quality standards within the region.

Brazil commits to continuing its integration with the MERCOSUR Pharmacopoeia and aligning the Brazilian Pharmacopoeia with public health needs and with public policy development in Brazil.

Mexico wants to stay tuned to the needs of the health authority and users, to maintain its current pharmacopoeia, continue promoting the approach of users to participate in the development of monographs and establish closer communication with colleagues in other parts of the world.

North America
The strategy of the US Pharmacopeial Convention (USP) focuses on creating monographs in ways that rely on both the traditional donor model as well as on research and development in its own laboratories. In support of the second approach, USP created the *Medicines Compendium* (MC), a freely available, online-only compendium of public standards for medicines approved in any country. The MC monographs provide performance tests for critical quality attributes and acceptance criteria, a source-independent Reference Procedure and one or more Acceptable Procedures submitted by manufacturers. The MC strives to make available reference materials for all possible impurities associated with a particular monograph, and to expand approaches to include USP-NF, where many monographs are missing and more need updating. USP is also strengthening its ability to develop impurity reference materials independently through synthetic capabilities. In addition, USP is working on standards with allied activities in support of manufacturers, regulatory bodies and others. Examples include a ″global comparator product″, as well as emphasis on biological medicines standards in support of new, biosimilar and interchangeable biological products. USP is working on spectral imaging approaches that allow field approaches to assure identity. These latter efforts align with the more elaborate laboratory testing approaches in a pharmacopoeial monograph or a private specification.

In conclusion it was agreed during the meeting to focus on acceleration of international harmonization between world pharmacopoeias, and also that an international bank of

harmonized texts for substances and finished dosage forms of the most common vital medicines should be performed. There should be a build-up of the frameworks for international information exchange among pharmacopoeias, an introduction of new techniques: analytical fingerprints; non-destructive spectroscopic methods and imaging, and lastly maintenance of the international applicability of Ph. Int. specifications.

Individual presentations, the full report and conclusions are to be found on the web site (*3*).

4. References

1. Kopp, S. *The International Pharmacopoeia* – a Myth or Reality? International Pharmacy Journal. 2006, 20 (2).

2. Index of Pharmacopoeias http://www.who.int/medicines/areas/quality_safety/quality_assurance/resources/index-of-pharmacopoeias16032012.pdf.

3. International meeting of world pharmacopoeias http://www.who.int/medicines/areas/quality_safety/quality_assurance/resources/qas_worldpharmmeeting/en/index.html.

4. Harmonization – Pharmacopoeial Discussion Group (PDG): http://www.usp.org/usp-nf/harmonization.

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