

Revision Process for Global/National Pharmacopoeias

This article describes the revision process and the resulting publication of proposed and official updates for pharmacopoeias around the world.

J. MARK WIGGINS AND JOSEPH A. ALBANESE

The first article of this series about compendial activities in the bio/pharmaceutical industry stressed that compliance with requirements published by pharmacopoeias around the world is a legal and regulatory requirement in those countries and regions in which the pharmacopoeia is applicable (1). The second article provided an end-to-end compendial framework to aid in understanding many of the challenges with ensuring compliance (2). One significant factor that makes compliance challenging is the multiple pharmacopoeias around the world and the lack of broad harmonization of the requirements and standards they each contain. Subsequent articles explored the history of pharmacopoeias and the current global situation (3), with consideration of the potential benefits of compendial harmonization and a description of current activities to achieve global pharmacopoeia standards (4, 5).

Another challenge is the significant volume of new and revised requirements, which are published by the pharmacopoeias as both proposed and official changes. It is essential for bio/pharmaceutical companies to monitor these periodic updates to ensure ongoing compliance. The surveillance process used by the industry is driven by the revision process and publication schedules of the pharmacopoeias. Designating pharmacopoeias as either "global" or "national" can help give visibility to some of the differences between them, and can, in turn, assist individual companies in focusing their compendial work on those activities that help ensure compliance with pharmacopoeial requirements.

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A Practical Guide to Pharmacopoeia Compliance: A Series

In this series of articles, the authors provide an understanding about the need for pharmacopoeia compliance and practical guidance to assist those who perform this work to establish effective processes, partnerships, and tools to maintain appropriate and timely compliance across the bio/pharmaceutical industry to the benefit of patients.

The following articles can be found within this ebook and online at www.BioPharmInternational.com/compendia:

- Why Pharmacopoeia Compliance is Necessary
- Why Pharmacopoeia Compliance is Difficult
- A Brief History of Pharmacopoeias: A Global Perspective
- Global Pharmacopoeia Standards: Why Harmonization is Needed
- Harmonization Efforts by Pharmacopoeias and Regulatory Agencies
- Revision Process for Global/National Pharmacopoeias
- Surveillance Process for Industry: Monitoring Pharmacopoeia Revisions

Upcoming articles in this series will include the following:

- Monograph Development: Why and When to Participate
- Monograph Development: How to Participate; How to Harmonize
- A Practical Approach to Pharmacopoeia Compliance
- A Case Study in Pharmacopoeia Compliance: Excipients and Raw Materials
- Pharmacopoeia Compliance: Putting it All Together; What is on the Horizon

DEFINING GLOBAL AND NATIONAL PHARMACOPOEIAS

In the second article of this series (2), brief definitions were provided for "national" and "global" pharmacopoeias.

- National pharmacopoeias form the legal requirements in their individual countries and are important for ensuring access to medicines for patients in these specific markets.
- Global pharmacopoeias form the legal requirements in their country/region and are acceptable to regulatory agencies well beyond the geographical boundaries covered by the pharmacopoeia, ensuring access to medicines for patients at a global level.

It is helpful to consider these designations in more detail (see **Sidebar** pp. 20–21). Throughout these articles, the *European Pharmacopoeia* (*Ph. Eur.*), *British Pharmacopoeia* (*BP*), and *United States Pharmacopeia–National Formulary* (*USP–NF*) are considered global pharmacopoeias, based on their acceptance by regulators around the world. Many other important pharmacopoeias are considered national.

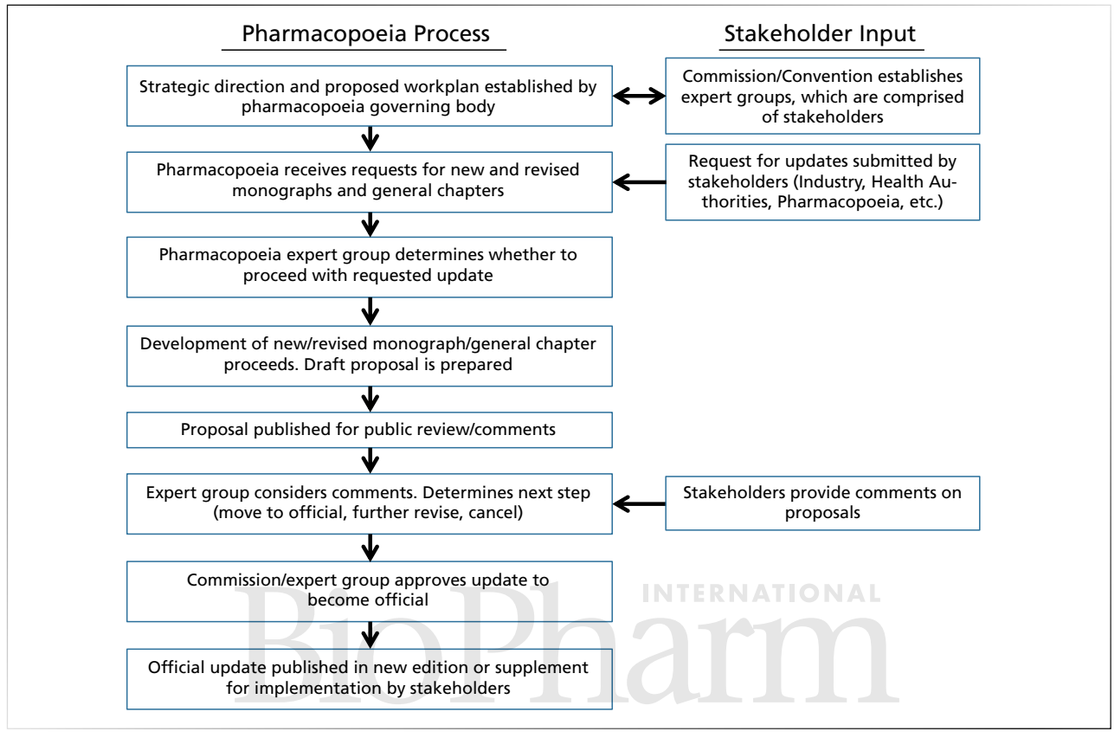
REVISION PROCESS FOR GLOBAL PHARMACOPOEIAS

In their article (6), Schwarzwalder and Bishara made the critical point, "... pharmacopoeial requirements are not static, and continued compliance demands that companies in this regulated industry be alert to changes." The article continues, "(a) program for reviewing pharmacopoeial proposals and implementing changes is needed to ensure continued compliance."

Surveillance activities used by bio/pharmaceutical companies are triggered by the publication of new and revised pharmacopoeial requirements. The publication schedule, in turn, is driven by the pharmacopoeia revision process. The ongoing revision of pharmacopoeias can be initiated in several ways. For example, pharmacopoeia changes can be driven by a significant technology update that requires a general chapter to be revised. Changes could be started to reflect a new International Council for Harmonization (ICH) guidance (e.g., Q3D) with impact to both existing general chapters and to monographs for many materials. Pharmacopoeial updates may be driven by collaborative efforts to achieve harmonization, as with the activities of the Pharmacopoeial Discussion Group (PDG), which is comprised of representatives from the *Ph. Eur.*, *USP*, and the *Japanese Pharmacopoeia* (*JP*). Pharmacopoeial evolution can be sparked by industry with the submission of a new or revised monograph. With so many possible avenues for change, the situation clearly demands that a company have a process for monitoring and staying up to date with the continuous revisions in the pharmacopoeias. But obviously, monitoring is not enough, since impact assessment and change control are needed to enable ongoing compliance with the current requirements. These considerations will be discussed in later articles.

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Figure 1. Pharmacopoeia revision process.



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The revision process used by global pharmacopoeias includes internal steps taken by the responsible organization and authorities, and also has steps that connect with external stakeholders (e.g., the bio/pharmaceutical industry and health authorities) that may be impacted by the changes (7, 8). **Figure 1** shows the process steps followed to generate a proposal for a new or revised monograph or general chapter, and the subsequent steps to move the proposed update to official status. At the outset, the governing body of the pharmacopoeia—called the Commission for *Ph. Eur.* and *BP*, and the Convention for *USP*—defines its strategic direction and proposed workplan for the duration of the cycle, based on its own governing rules. For *Ph. Eur.*, this is a three-year cycle, coinciding with the publication of each new edition. The activities of the *BP* Commission are reported annually, with a triennial review to provide assurance that they are operating effectively. For *USP*, the Convention is on a five-year cycle. The Commission or Convention establishes expert groups or committees that further refine the direction, focus areas, and specific workplans, which are used to identify, prioritize, and pursue key issues and gaps in compendial coverage (9). These expert groups are typically comprised of volunteers from industry, academia, healthcare, and government agencies, to ensure that a broad representation of stakeholders contribute to the process. The expert groups review suggestions received for new or revised items as possible updates to the pharmacopoeias. Suggestions for new general chapters or monographs and revisions to existing general chapters or monographs, with appropriate justification for the request, may come from various stakeholders such as industry, academia, healthcare practitioners, and trade organizations, or may come from the pharmacopoeia expert groups or staff themselves. Proposals specifically for harmonized general chapters and excipient monographs may also come as a result of the work of the PDG.

Within the overall context of pharmacopoeia revisions, it is useful to realize that industry can influence this process through active collaboration and communication with the pharmacopoeias to make proposals for new and updated requirements. This influence will be explored in a later article that looks at the monograph submission process. Additionally, having a company's subject matter experts participate on an expert group is another excellent way to participate and influence the direction of new and revised pharmacopoeial requirements.

FIGURES COURTESY OF THE AUTHORS

The request for a new or revised monograph or general chapter is reviewed by the appropriate pharmacopoeia staff and expert group to determine if it should proceed as a proposal for public review and comment. For *Ph. Eur.*, input is obtained from the pharmacopoeia authorities in each European member country on whether to add the requested update to the workplan. In progressing the work to develop the update, the pharmacopoeia expert group and staff may be assisted by advisory working parties or expert panels with technical knowledge on the particular subject. Additional information may be sought from the original submitter of the request, from other manufacturers, additional interested parties, or from specialists with knowledge in that particular area. Often, laboratory work is performed by the pharmacopoeias, regulatory agencies, industry, or academia to support the proposal by verifying the suitability of analytical procedures and qualifying physical reference standards needed for the proposal.

A draft of the proposal is prepared and published by the pharmacopoeia, usually through an on-line forum for public review and comment by stakeholders. The expert group considers any comments received and determines the appropriate next step in the process, which may be a recommendation to move the proposal forward as an official change, to make further revision to the proposal with possible re-publication in the forum (if changes are significant), or to cancel the proposal. Responsibility for adoption or approval of the proposal to move it to official status is given to the decision-making body of the pharmacopoeia. For *Ph. Eur.*, the decision is made by the Commission and requires unanimous agreement. For *USP*, the decision is made by the expert group based on majority vote.

Suggestions for new or revised monographs or general chapters may come from industry, academia, healthcare practitioners, and trade organizations.

Once adopted, the new or revised monograph or general chapter is published in the next edition or supplement to the pharmacopoeia and becomes official on the date specified for the update. It is at this point that companies must comply with the updated requirements. It is also at this point that a request for further revision to a monograph or chapter—or to any of the official requirements in the pharmacopoeia—may be submitted by a company or other stakeholder, with appropriate justification for the requested revision. This request would start the pharmacopoeia revision cycle over again from the beginning. While these ongoing updates provide an opportunity for advocacy, more importantly they stand as the fundamental reason why a company must monitor pharmacopoeia publications to remain compliant with the current requirements.

PUBLICATION SCHEDULE FOR GLOBAL PHARMACOPOEIAS

As noted above, the pharmacopoeia revision process includes two stages where information is made available to stakeholders:

- Draft proposals for new and revised monographs and general chapters
- Updates to official requirements.

This information is provided by the pharmacopoeias through two types of publications and online postings:

- Proposals are communicated through a pharmacopoeia forum, which provides stakeholders the opportunity to comment on the new or revised item
- Official updates to general chapters and monographs are published in new editions and supplements to the pharmacopoeia.

All stakeholders are expected to implement the updated official requirements in the timeframe specified by the pharmacopoeia.

Proposed updates in pharmacopoeia forums. The forum publications for global pharmacopoeias, typically available on-line and in English only, contain proposals for new and revised monographs and general chapters that are provided for public review and comment. The forum publications for *Ph. Eur.*, *BP*, and *USP* occur at a set frequency: four times per year for *Ph. Eur.* and *BP* and six times per year for *USP* (**Table I**). Having visibility to the publication schedule is beneficial to industry for planning the workload and resources

Table I. Publication schedule for pharmacopoeia forum (proposals).*

Pharmacopoeia	Forum publication	Media type	Frequency (Months)
European Pharmacopoeia (*Ph. Eur.*)	*Pharmeuropa*	Online	4 per year (January, April, July, October)
British Pharmacopoeia (*BP*)	*British Pharmacopoeia Forum*	Online	4 per year (January, April, July, October)
United States Pharmacopeia (*USP*)	*Pharmacopeial Forum*	Online	6 per year (January, March, May, July, September, November)
Japanese Pharmacopoeia (*JP*)	*Japanese Pharmacopoeia Forum*	Hard copy⁺	4 per year (March, June, September, December)

* Other pharmacopoeias do not have a regular/consistent schedule for publication of proposed changes.
⁺ JP Forum is published in Japanese and English. Some of the proposals are also published online in English.

needed for the review process. The expectation is the same for each of the pharmacopoeias to their stakeholders: to review those proposals with potential impact and provide any comments, along with scientific rationale and supporting data regarding issues and concerns with the proposal. Comments are typically expected within 90 days from the date the forum is published.

Official updates in pharmacopoeia new editions/supplements. New editions and supplements to the pharmacopoeias are published to provide updated official requirements for monographs, general chapters, and other content. These updates become official on a set date, typically six months from the date of publication, although this timeline can be different for national pharmacopoeias. A company needs to be compliant with the new and revised general chapters and monographs by the specified official date. While it is generally allowed that the updated requirements may be implemented early, it must be understood that implementing the requirements late does not meet the regulatory expectation of compliance with "current" pharmacopoeial requirements.

The publication schedules and format (hard copy and/or electronic) for new editions and supplements are unique for each pharmacopoeia (**Table II**). The *Ph. Eur.*, published simultaneously in both English and French as official languages, is on a three-year cycle; a new edition is published every three years with two supplements provided later in the first year, followed by three supplements published in each of the second and third year of the cycle (for a total of one new edition and eight supplements during the three-year cycle). The *Ph. Eur.* is available in both print/hard copy and on-line formats. In the print version, the supplements are non-cumulative, whereas the supplements are integrated in the electronic version, making it completely cumulative.

A new edition of *BP* is published yearly in English, available in print and on-line formats. The *BP* does not publish supplements during the year for content that is specific to the *BP* but does update the on-line publication (not the hard copy version) to reflect the updates made to the *Ph. Eur.*, as these updates are incorporated into the *BP* content.

For *USP*, a new edition is provided yearly in English, with a Spanish edition available for Spanish-speaking pharmaceutical scientists and professionals. The *USP* publishes updates to official requirements in two supplements to the new edition every year. The *USP*43–*NF*38, which was scheduled for publication in November 2019, will be the last edition available in print/hard copy or on a USB flash drive. Future supplements and editions will not be printed. Starting with the first supplement to *USP*43–*NF*38, which will be published in February 2020, only the on-line format will be available, and it will contain all current *USP–NF* content (10).

Other types of pharmacopoeia updates. The pharmacopoeial processes allow for other approaches and timelines for the publication of proposed and official changes. These allowances can be especially important for revisions that need to be put in place quickly, for example, to address safety concerns related to the requirements contained in a general chapter or monograph. The "Guide for the Work of the *European Pharmacopoeia*" provides for the publication of rapid revisions, as well as corrections of errors in *Ph. Eur.* text (7). The *Ph. Eur.* may also publish minor revisions, which are justified and necessary, but not considered controversial and do not, therefore, require prior publication in their forum as a proposal. While perhaps not controversial, these minor revisions often still have impact, and a company may find it challenging to implement the changes quickly, after they are seen for the first time as official updates.

USP's "Rules and Procedures of the Council of Experts" specify processes that can be used to make official revisions to the *USP–NF* more quickly than through their standard process (8,11,12). These accelerated processes include the publication of interim revision announcements (IRAs), revision bulletins (RBs), and errata, which are posted on the *USP* website on a regular (monthly) schedule. IRAs are first published as proposals in the forum, given a 90-day notice and comment period, then posted as official text on the *USP* website and incorporated into the next

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Table II. Publication schedule for new editions/supplements (official updates).

Pharmacopoeia	Official publication	Media type	Official language (Translation)	Frequency (Publication date)	Notes
European Pharmacopoeia (*Ph. Eur.*)	Main Edition	Online and hard copy	English and French	New edition every 3 years (Publish: July. Official: January)	
	Supplements	Online and hard copy	English and French	8 supplements over 3-year cycle (Publish: October, January, July)	
British Pharmacopoeia (*BP*)	Main Edition	Online and hard copy	English	New edition every year. (Publish: August. Official: January.)	Updates are made to the *BP* online publication (not the hard copy version) to reflect *Ph. Eur.* supplements.
	Supplements	N/A	English	No supplements are published	
United States Pharmacopeia (*USP*)	Main Edition	Online	English (Spanish)	New edition every year (Publish: November. Official: May)	Final hard copy publication of *USP* occured in November 2019. Only online publication available after that date.
	Supplements	Online	English (Spanish)	2 supplements per year (Publish: February, June)	
Japanese Pharmacopoeia (*JP*)	Main Edition	Hard copy	Japanese (English)	New edition every 5 years	Free online PDF versions of the official *JP* edition and supplements are available on the health authority website in both Japanese and English.
	Supplements	Hard copy	Japanese (English)	2 supplements published in year 2 and 4 of 5-year cycle	
Chinese Pharmacopoeia (*ChP*)	Main Edition	Hard copy	Chinese (English)	New edition every 5 years	
	Supplements	Hard copy	Chinese	2 supplements over 5-year cycle (No English translation)	
Indian Pharmacopoeia (*IP*)	Main Edition	Hard copy	English	New edition every 4 years	
	Supplements	Hard copy	English	2 supplements (addenda) published over 4-year cycle	
State Pharmacopoeia of the Russian Federation (*SP RF*)	Main Edition	Online	Russian	New edition published but not on a regular cycle. (No English translation.) Publication of supplements unknown.	Free online version of the official *SP RF* edition is available on the health authority website in Russian (only).
Korean Pharmacopoeia (*KP*)	Main Edition	Hard copy	Korean (English)	New edition targeted every 5 years. Publication of supplements unknown.	Free online PDF version of the official *KP* edition is available on the health authority website in English.
Brazilian Pharmacopoeia (*FBras*)	Main Edition	Hard copy	Portuguese (English)	New edition published but no defined periodicity. Publication of supplements unknown.	Free online version of *FBras* may be available on the health authority website in Portuguese and English

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Detailed Consideration of Global and National Pharmacopoeias

Further discussion of global and national pharmacopoeias is useful in providing context for this series of articles. Differences are revealed between the pharmacopoeias designated as global, compared with those designated as national. These differences impact the surveillance and other processes used by the bio/pharmaceutical industry to ensure compliance with pharmacopoeia requirements. The definition for a national pharmacopoeia is straightforward, and the understanding is facilitated by the historical context provided earlier in this series. The national pharmacopoeias were developed to support the health of the population in that country through consistent standards for medicines. The national pharmacopoeias in Japan, China, India, Brazil, Russia, and Korea are among those published around the world that must be considered for compliance in these specific countries.

The definition for a global pharmacopoeia may not be as readily apparent and warrants further explanation. There are no specific literature or compendial references for the designation of a global pharmacopoeia. Rather, the definition is proposed by the authors, based on many years of practical experience dealing with the challenges of surveillance and compliance with pharmacopoeial requirements. Simply put, the designation as a global pharmacopoeia is based on the acceptance of the pharmacopoeia by regulators at a global level. In particular, the compendial standards published in the *European Pharmacopoeia* (*Ph. Eur.*), *British Pharmacopoeia* (*BP*), and *United States Pharmacopeia–National Formulary* (*USP–NF*) are accepted by regulators in many countries around the world to help support global access to medicines. Confirmation is provided in **Table I** (see page 21), which shows regulatory acceptance of *Ph. Eur.*, *BP*, and *USP* for more than 70 specific countries, based upon a regulatory intelligence database query.

It is straightforward to suggest that *Ph. Eur.* should be considered a global pharmacopoeia, recalling that it was established to provide harmonized standards that help ensure access to medicines for citizens throughout the countries of Europe—truly an international pharmacopoeia. Compliance with *Ph. Eur.* requirements is mandatory in those European countries—currently 38—which are signatories to the Convention on the Elaboration of a *European Pharmacopoeia*. Looking at the broader global picture, it has been recently noted that *Ph. Eur.* is used in over 100 countries worldwide (1).

It is, perhaps, more difficult to argue that *BP* should be considered a global pharmacopoeia. As one of the original signatories to the Convention, compliance with *Ph. Eur.* requirements is mandatory in the United Kingdom (UK). This will not change in any Brexit outcome, since the Convention was established within the Council of Europe, rather than the European Union. In publishing the *BP*, there is an obligation to include the entire content of the *Ph. Eur.*, including monographs and general chapters, to ensure alignment with *Ph. Eur.* requirements. The *BP*, however, also includes requirements in addition to those in *Ph. Eur.*; most notably, *BP* contains many monographs for specific drug products containing small-molecule active ingredients. BP requirements, including drug product monographs, are accepted by regulators around the world, providing quality standards that are applicable in the UK, and also with wide international reach. These standards form an inherent part of established medicines legislation in Commonwealth countries and are used in more than 100 countries globally (2). Similarly, *USP* standards are legally recognized in the United States and elsewhere and are used in more than 140 countries around the world (3). Clearly, *USP* requirements are accepted by regulatory agencies well beyond the geographical boundaries of the US. This near-global acceptance by regulators supports the designation of *USP* and *BP*, along with *Ph. Eur.*, as "global" pharmacopoeias. In practical terms for global drug product registrations, the chemistry, manufacturing, and controls/regulatory group within a company would typically reference compliance with standards in *USP* and/or *Ph. Eur.* for excipients, drug substances, and general chapters, while also referencing compliance with *BP* and/or *USP* monographs for drug products.

In considering which pharmacopoeias should be designated as global, it is relevant to mention the *International Pharmacopoeia* (*Ph. Int.*) published by the World Health Organization. As noted earlier in this series of articles, despite the inclusion of "international" in its title, the *Ph. Int.* was not intended to be a legal pharmacopoeia in any country unless adopted by the pharmacopoeial authority of that country. With the understanding that compliance with *Ph. Int.* is not widely required by regulatory agencies around the world, *Ph. Int.* would not be considered a global pharmacopoeia by the authors' definitions, even though its original intention was to serve as an international standard to support the global availability of medicines.

It is recognized that other pharmacopoeias—those designated as "national"—may be accepted beyond their own geographical boundaries as well. For example, the *Japanese Pharmacopoeia* (*JP*) is also accepted by regulators in countries outside Japan. This is due, in part, to the long-standing participation of *JP* representatives in the harmonization work of the Pharmacopoeial Discussion Group. In some ways, *JP* fits squarely between the "national" and "global" pharmacopoeia designations, since many of their processes are more closely aligned with those of the global pharmacopoeias. The *JP* also has historical importance for the pharmaceutical markets in Japan and other Asian countries; their International Strategic Plan from 2015 includes the vision of maximizing the common health benefits to other countries and regions by positioning *JP* as one of the reference pharmacopoeias in Asian countries (4). However, countries that accept *JP*, other than Japan, would also accept *Ph. Eur.*, *BP*, or *USP*, and it is one of these global pharmacopoeias that would usually be filed in product registrations in these countries. At a practical level, *JP* might only be referenced by a company in their drug product registrations for Japan. Similarly, compliance with the *Chinese Pharmacopoeia* (*ChP*) might only be included in the registration for China, even though *ChP* may also be accepted in other countries.

The designation of *Ph. Eur.*, *BP*, and *USP* as global pharmacopoeias is a practical consideration, which can help address some of the challenges that a company faces in complying with the various pharmacopoeias, while aligning and simplifying the information listed in drug product registrations around the world. Still, the value of national pharmacopoeias should not be underestimated because they are critical to supporting access and ensuring quality of medicines in their respective countries.

Detailed Consideration of Global and National Pharmacopoeias (cont.)

Table I. Regulatory acceptance of "global pharmacopoeias" in countries around the world.

European Pharmacopoeia		*British Pharmacopoeia*	*United States Pharmacopeia*
European Union*	Algeria	Algeria	Algeria
Austria*	Argentina	Argentina	Argentina
Belgium*	Australia	Australia	Australia
Bosnia and Herzegovina*	Brazil	Brazil	Brazil
Bulgaria*	Canada	Canada	Canada
Croatia*	Chile	Chile	Chile
Cyprus*	China	China	China
Czech Republic*	Colombia	Colombia	Colombia
Denmark*	Costa Rica	Costa Rica	Costa Rica
Estonia*	Egypt	Egypt	Egypt
Finland*	Guatemala	Guatemala	Guatemala
France*	Hong Kong	Hong Kong	Hong Kong
Germany*	India	India	India
Greece*	Indonesia	Indonesia	Indonesia
Hungary*	Iraq	Iraq	Iraq
Iceland*	Israel	Israel	Israel
Ireland*	Jordan	Jordan	Jordan
Italy*	Kenya	Kenya	Kenya
Latvia*	Lebanon	Lebanon	Lebanon
Lithuania*	Malaysia	Malaysia	Malaysia
Luxembourg*	Morocco	Morocco	Morocco
Macedonia*	New Zealand	New Zealand	New Zealand
Malta*	Nigeria	Nigeria	Nigeria
Montenegro*	Panama	Panama	Panama
Netherlands*	Peru	Peru	Peru
Norway*	Philippines	Philippines	Philippines
Poland*	Republic of Korea	Republic of Korea	Republic of Korea
Portugal*	Saudi Arabia	Saudi Arabia	Saudi Arabia
Republic of Moldova*	Singapore	Singapore	Singapore
Romania*	South Africa	South Africa	South Africa
Serbia*	Tunisia	Thailand	Tunisia
Slovak Republic*	United Arab Emirates	Tunisia	United Arab Emirates
Slovenia*	Vietnam	United Arab Emirates	United States
Spain*		United Kingdom	Venezuela
Sweden*		Venezuela	Vietnam
Switzerland*			
Turkey*			
Ukraine*			
United Kingdom*			

* Signatory to the European Pharmacopoeia Convention.

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3. *USP*, "Legal Recognition of *USP* Standards," *USP.org*.
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available official publication. If circumstances require a more rapid publication of official text, a revision bulletin is posted on the *USP* website with the official date indicated. Errata are published to correct content in the *USP* that does not accurately reflect the intended requirements as approved by the experts, and may address inaccuracies in chemical formulas, mathematical equations relevant to analyses, or inaccurate descriptions of apparatus or materials used in analytical tests. The *USP* also publishes compendial notices to inform stakeholders of the changing status of monographs and general chapters, for example, to modify general chapter titles, appendix titles, or references to external resources that may be listed throughout the pharmacopoeia. These processes for accelerated revisions do not always require publication in the forum and allow revisions to become official prior to the next edition or supplement. There is another process for *USP* pending monographs to allow development of new or revised monographs for articles awaiting approval by FDA (13). *USP* also publishes stimuli articles, which present initial thinking of the experts in their development of new or revised general chapters or other standards and provide additional time for comments from stakeholders. The wide array and frequent use of these other approaches to notify stakeholders of proposed and official updates makes routine (monthly) monitoring of the *USP* website an important component of a company's surveillance process to remain in compliance with current requirements.

REVISION PROCESS AND PUBLICATION SCHEDULE FOR *JP*

Shifting focus from the global to the national pharmacopoeias, special consideration should be given to *JP*, because it does not fit as easily into the global or national designations. Because it is primarily required in Japan only, the *JP* is a national pharmacopoeia according to the authors' definitions. The revision process and regular publication schedule for *JP*, however, more closely align with those of the global pharmacopoeias, making it simpler for a company to include *JP* in their surveillance activities. As with the global pharmacopoeias, the *JP* revision process includes steps that are internal to the organization and steps that connect with external stakeholders, with communication of proposed and official updates occurring on a regular basis. **Table I** shows that proposed updates are published four times per year in the *JP* forum on an established schedule. The *JP* forum is published in a hard copy/print version only, although some of the proposed revisions are also posted on the *JP* website for review and comment. The *JP* forum is provided in both the Japanese and English languages within the same print copy, but the entire content is not exactly the same in each publication due to delays in translation of some of the proposals. This translation timing may make it difficult for a company to provide a timely response to revisions published in the *JP* forum. **Table II** reveals that official *JP* updates are published in a new edition every five years, with two supplements published during the five-year cycle between editions. Partial revision to official *JP* requirements may also be made at any time on the *JP* website, if necessary.

The revision process and regular publication schedule for *JP* more closely align with those of the global pharmacopoeias.

The new *JP* editions and supplements are published in hard copy/print versions, first in Japanese (the official language) and subsequently in English. Free, on-line PDF versions of the official *JP* edition and supplements are available on the *JP* website, in both Japanese and English, although the English version may not be the most current edition. The English translation may take up to 12 months for completion, but this delay is taken into account in establishing the official date, which is usually set at 18 months after the official publication. Experience has shown, however, that compliance for companies located in Japan is expected sooner. This situation creates the potential for inconsistencies in the procedures and documentation for a multi-national company regarding updated *JP* requirements if there are manufacturing sites both inside and outside of Japan. Because of this, some companies may implement new *JP* requirements based on the official Japanese version, which provides extra time to complete the necessary change control activities. The benefits for a company to translate from the Japanese to enable implementation of updated *JP* requirements and the earlier opportunity to respond to *JP* proposals make it important for the compendial affairs group in a company to have a strong connection with their local contact group in Japan, if available. Compliance with compendial requirements in Japan is also made more difficult by the publication (not on a regular schedule) of official compendia other than *JP*. Examples of these include *Japanese Pharmaceutical Excipients*; *Japanese Pharmaceutical Codex*; Japan's *Specifications and Standards for Food Additives*; *Requirements for Antibiotic Products of Japan*; and *Minimum Requirements for Biological Products in Japan*. The health authorities in Japan expect compliance with these additional compendial requirements if standards do not otherwise exist in the official *JP*.

REVISION PROCESS AND PUBLICATION SCHEDULE FOR OTHER NATIONAL PHARMACOPOEIAS

Looking at the revision process and publication schedules for other national pharmacopoeias, it is apparent that there are differences from the global pharmacopoeias and from each other. These differences, in particular the irregular publication schedules and the need for translation, pose challenges for industry surveillance activities and necessitate partnership with a company's local contact group, if available, in these countries to help with compliance. Differences between the pharmacopoeias have been explored in the International Meetings of World Pharmacopoeias convened by the World Health Organization (14, 15), which have focused on ways to achieve international harmonization among the many pharmacopoeias. One outcome of these discussions has been the publication of *Good Pharmacopoeial Practices* (*GPhP*), which defines approaches and policies in establishing pharmacopoeial standards (16). One key consideration contained in the *GPhP* document is the assurance of an open and transparent process throughout the development and revision of pharmacopoeial standards. This process calls for engaging stakeholders in the process by making workplans available and providing adequate and timely public notification with allowances for commenting. While the revision processes for national pharmacopoeias typically follow similar steps as previously described, there is not always a similar level of transparency as seen with the global pharmacopoeias. National pharmacopoeias do not publish their proposed revisions for public comment at a predetermined time; it typically happens in an ad-hoc fashion. The lack of a regular schedule for notification of proposals contributes to the challenge for industry in monitoring the national pharmacopoeias.

The *Chinese Pharmacopoeia* (*ChP*) commission, for example, publishes items for comments on its website when a sufficient number of new and revised monographs and general chapters have progressed through their development process. These proposals are published in Chinese only. Comments on first draft items typically receive a 90-day commenting period, whereas items that are second or subsequent drafts typically get only 30 days for commenting. Many large multi-national companies find it difficult to meet the commenting deadlines for *ChP* since the proposals must first be translated into English to enable assessment of the potential impact. It is important, therefore, for the compendial affairs function in a company to have a strong connection to the local contact group in China, if available (e.g., regulatory affairs, quality, etc.) to perform the monitoring, identification, and translation of items with potential impact. If needed, the local group can also translate the company's comments from English to Chinese so a response can be provided back to the pharmacopoeial authority.

For the *State Pharmacopoeia of the Russian Federation* (*SP RF or Russian Pharmacopoeia*), proposed updates are not available on a regular schedule, and when they appear, they are in Russian only, with a comparatively short timeframe to submit comments. The company's local contact group in Russia can help monitor and translate the items with potential impact.

For the *Indian Pharmacopoeia* (*IP*), proposals for new and revised requirements are also posted on the commission's website on an ad hoc basis. Even though they are published in English, the irregular publication schedule for these items again makes it helpful to have a connection with the local contact group in India to assist in monitoring the website. The commenting period allowed for *IP* proposals also seems to be irregular and often quite short compared to the global pharmacopoeias, which makes it difficult to respond to the proposals. For many of the other national pharmacopoeias, there may be even less transparency in their public notification and commenting processes.

For national pharmacopoeias, the governing commission's workplan typically coincides with the publication cycle. The publication schedules for official updates (15) also reveal differences between the national pharmacopoeias (**Table II**), with translation from the local language being another complicating factor for compliance. A new edition of *ChP* containing official updates is published every five years in the Chinese language. The *ChP* commission provides an English transla-

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tion, but for the 2015 edition, there was a significant delay in the availability of the English version, which made it difficult for multi-national companies to comply with the updated requirements. For the *ChP* 2020 edition, there are indications that the English translation will be available more quickly after the Chinese version, which will be helpful in the implementation activities for industry.

A new edition of the *Russian Pharmacopoeia* is also targeted every five years, but the actual publication has not strictly adhered to this intended schedule. These official updates to the *Russian Pharmacopoeia* are provided on the commission website in Russian only; an English translation is not available. The challenges with publication schedules and translations again make it critical to the success of a company's compendial vigilance program to have a strong connection with their local contact group to provide access to speedy translations of proposed and official items for assessment. The urgency for receiving the translation can be reduced as some pharmacopoeias (e.g., *Russian Pharmacopoeia*) allow a delayed implementation timing due to the lack of the information in English. However, this is not the case with all national pharmacopoeias (e.g., *ChP*) where a very short time may be provided for compliance with the updated requirements following publication in the local language. In the case where implementation follows a short timeline, connection with the company's local regulatory group (or other identified function) to provide the translation is critical to ensure on-time compliance. Additional information about the pharmacopoeias in India, Korea, and Brazil is provided in **Table II**.

The irregular publication schedules of national pharmacopoeias and the need for translation pose challenges for industry surveillance activities.

CONCLUSION

The revision processes used by the pharmacopoeias, and their associated schedules for publication of proposed and official updates reveal some similarities, but also many differences between global and national pharmacopoeias. Pharmacopoeial revision activities are inextricably bound to the surveillance activities carried out by the bio/pharmaceutical industry. The next article in this series will take a closer look at the industry processes to monitor the significant volume of changes published in the pharmacopoeias and to remain compliant with the current requirements.

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