Health Sciences Authority | April 2011
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HSA Connects

HSA Connects is a regular communication update of present services available and future developments in the regulatory field for our industry clients.

In this issue, we will highlight new pro-enterprise initiatives undertaken by HSA's Health Products Regulation Group (HPRG). In addition, we will focus on selected topics from the HPRG Joint Regulatory Workshop held in January this year.

HSA turns 10 in 2011!

An overview of HPRG's partnerships and initiatives in the past years

2011 marks an especially exciting year for the Health Sciences Authority (HSA) as we are celebrating our 10th year as a protector for national health and safety. Established on 1 April 2001, our capabilities are built on the foundation of the 5 well-established former national agencies that came together to form HSA. Our 10th Anniversary theme "Transforming through Synergy" underscores HSA's aim to move into our second decade with an emphasis on innovative transformation through better synergies of our unique and diverse range of scientific expertise.

Over the last 10 years, HSA has undergone significant transformation – strengthening professional expertise, putting in place organisational systems, growing significantly in international standing and fostering closer industry linkages.

HSA's HPRG has worked hard to progressively strengthen a robust framework that enables consumers to have safe and timely access to health products while taking into account industry's needs for greater transparency and flexibility.

While the implementation of any new regulatory framework can be challenging, HPRG, with our industry partners worked effectively together to enable the successful implementation of the Health Products Act in 2007, followed soon after by the Health Products (Medical Device) and Health Products (Cosmetics) Regulations.

Over the years, we have also inked Memoranda of Understanding with many established health agencies around the world. In April 2009, HSA achieved a significant milestone when we signed the ASEAN Sectoral Mutual Recognition Agreement on GMP Inspection of Manufacturers of Medicinal Products. With the signing of this agreement, regulatory agencies in the ASEAN region will accept Singapore's HSA GMP inspection reports and outcomes for medicinal products. This may potentially allow faster access of medicinal products manufactured in Singapore to the ASEAN market.

HSA has also had the honour of hosting a number of major conferences and training programmes in the past years. We ended the year 2010 with the successful organisation of the 14th WHO International Conference of Drug Regulatory Authorities (ICDRA). The pre-ICDRA meeting "Effective collaboration: the future of drug regulation" was opened to industry and other stakeholders, and proved to be an excellent platform for drug regulators, industry and NGOs to network, exchange ideas, challenge viewpoints and better understand one other. Another recent successful meeting was the inaugural HPRG Joint Regulatory Workshop conducted earlier this year. You may read more about this Workshop on pages 4 and 5 of this newsletter.

In 2010, HPRG set up a Service Management Office (SMO) to focus on pro-enterprise initiatives and improve communication with external stakeholders. The newsletter that you are now reading, "HSA Connects", represents one of SMO's initiatives to provide important updates and announcements to industry, so that you can stay connected and well-informed of the latest regulatory news. Past issues of HSA Connects are available on the **Industry Newsletter page on the HSA website.**

Through various interactive platforms, you have shared with us your honest feedback. In response to your feedback, HPRG has planned/implemented a series of initiatives which optimise regulatory control and enhance service delivery, while keeping pace with changes in the business environment. The table on page 3 provides a glimpse into some of these initiatives. Details of these pro-enterprise initiatives are being shared with industry in an email communication series in March and April. Look out for this email series in your inbox.

We thank you for your constructive feedback that has been valuable to us as we continue to refine our regulatory framework. We are also very encouraged by the strong industry participation and support for our training programmes. As we progress into our second decade, we look forward to your continued partnership with us in safeguarding public health by ensuring that health products available in the Singapore market meet the necessary standards.

HSA Connects

Initiative	Impact and Benefits
Review of Rules and Regulations	
Inclusion of Vitamin K in multivitamin / mineral preparations for adults (subject to conditions) (From 1 Dec 2010)	Allows companies to import multivitamin products containing Vitamin K without the need for reformulation
Revision of criteria and requirements for verification route (applicable to medicinal products) (From 1 Apr 2011)	Allows more companies to benefit from faster approval timelines of 60 working days, compared to 180 working days for the abridged route
Transparency	
Publishing of legislation administered by HSA (including subsidiary legislation) on the HSA website (Since Apr 2010)	Facilitates industry's easy access to information
Sharing of GCP inspection metrics / findings with industry through communication sessions and the HSA website (Since Dec 2010)	Enhances transparency and raises awareness on common GCP inspection findings
Compliance Costs	
Removal of requirement to submit approved package insert from the country of origin for new drug application submission (From 1 Apr 2011)	Reduces the regulatory burden of obtaining the English translated package insert for submission to HSA
Exemption of locally-manufactured solely-for-export Chinese Proprietary Medicine (CPM) from product listing (Since Feb 2011)	• Reduces time and resources spent on product listing process • Facilitates product launch in the intended overseas market(s)
Customer Responsiveness	
Revision of target processing timelines for clinical trial amendment applications (From 1 Apr 2011)	Reduces regulatory processing timelines for clinical trial amendment applications from 30 working days to 15 working days or fewer, translating to enhanced operational efficiency in conducting clinical trials
Consolidation of product enquiry forms and streamlining of enquiry process (From Quarter 2, 2011)	Offers convenience by having a single contact point and streamlined process
Pro-Enterprise Orientation	
Set-up of Service Management Office	Focuses on service-related initiatives and improved communication with industry stakeholders
Inaugural HPRG Joint Regulatory Workshop 17-20 Jan 2011 at Grand Copthorne Waterfront Hotel	• Provides a platform for information exchange • Enables HSA to gain better understanding of industry's needs • Provides timely update on regulation and guidance changes

HPRG Joint Regulatory Workshop

The inaugural **HPRG Joint Regulatory Workshop** was held at the Grand Copthorne Waterfront Hotel from 17 – 20 January 2011. Over the 4 days, participants had the option to attend five different workshops covering a wide spectrum of topics including the new drug registration guide, updates on the medical devices regulatory framework, good clinical practice inspection findings, cosmetics submission requirements and the latest updates in good manufacturing practice and international harmonisation activities.

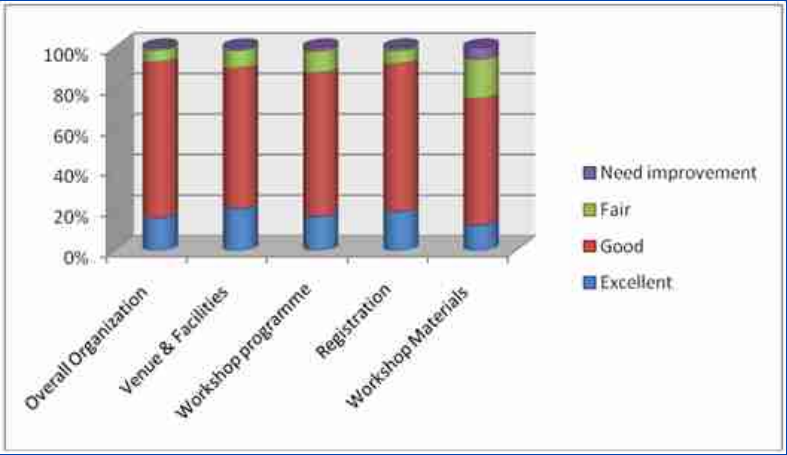
This is the first time HPRG has pooled its resources and consolidated expertise to run a comprehensive training programme for the industry. In alignment with HSA's ongoing pro-enterprise initiatives, the organising committee's aim was to provide a single run of training workshops at the same time in order to make it easier for companies to schedule their participation, and also for HPRG to more efficiently deploy its expertise rather than spread such commitments throughout the year.

Many participants found the sessions to be informative and helpful to their work. Ms Leow Kwee Foong (GlaxoSmithKline Pte Ltd) felt the workshop was a good platform to share initiatives, issues faced with registration and recommendations for improvement. Ms Cynthia Tan from Merz Aesthetics Asia Pacific shared that there is room for improvement on time-keeping, but nonetheless enjoyed the workshop.

The interactive question-and-answer sessions gave participants the opportunity to clarify their questions and provide honest feedback. It was also an excellent platform for us to understand industry's needs and expectations, and gain insight into how we can facilitate regulatory processes without compromising public safety.

To better meet the needs of industry, the organising committee will be analysing the valuable feedback provided by participants, and work on enhancing the contents and logistics management for the next workshop industry.

Close to 700 industry participants and HSA officers attended the HPRG Joint Regulatory Workshop. This was how participants rated the event:



Revision of Guidance on Medicinal Product Registration in Singapore

As the regulatory environment continues to evolve to meet changes to the pharmaceutical industry, the Guidance on Medicinal Product Registration in Singapore has also undergone a timely revision to reflect HSA's current regulatory thinking and process.

While many of the changes made to the 2009 version of the Guidance were for clarifying the registration processes, the Pharmaceutics & Biologics Branch (PBB) and Generics & Biosimilars Branch (GBB) are pleased to announce the following changes:

Re-format of the Guidance Document

The main Guidance document has been re-formatted to a modular approach to simplify access to the information you need for registration of your products into one part of document instead of different locations throughout. Here is an overview of the different modules of the revised Guidance:

Chapter A – General Overview
Chapter B – Registration Process
Chapter C – New Drug Application Submission
Chapter D – Generic Drug Application Submission
Chapter E – Biosimilar Product Submission
Chapter F – Post-Approval Process
Chapter G – Major Variation Submission
Chapter H – Minor Variation Submission
Chapter J – Submission of PRISM Application

Verification Evaluation Route

With the recent implementation of two new evaluation routes for Generic Drug Applications (GDAs), the GDA verification evaluation route under the CECA scheme in September 2010 and the GDA verification evaluation route in January 2011, the regulatory requirements have been added to the revised Guidance under Chapter D.

Changes have also been made to the current New Drug Application (NDA) verification evaluation route to facilitate registration of products under this route.

1. Choice of Primary Reference Agency

In the revised Guidance, the choice of the primary reference agency will now be based on quality aspects instead of clinical aspects. The quality aspects for the proposed drug product for Singapore should be the same as that approved in the primary reference agency.

2. Eligibility Criteria for Subsequent Strength of Currently Registered Product

For subsequent strengths of a currently-registered product (NDA-3) submitted via the verification route, the eligibility criteria has been expanded to allow submission if the product has been evaluated and approved by at least one of HSA's reference agencies within two years of submission to HSA. Currently, the product would need to be evaluated and approved by at least two of HSA's reference agencies and submitted within three years from the date of approval by the chosen primary reference agency.

Biosimilar Products

A chapter on registration of biosimilar products has been introduced in the revised Guidance under Chapter E.

Minor Variation Application (MIV) Requirements

While changes have been made to give greater clarity on the documentary requirements for MIV applications, we are pleased to highlight the following:

1. To facilitate responses to your MIV inquiries and in moving towards a greener environment, all inquiries can be emailed to **HSA_MedProd_Registration@hsa.gov.sg** using the new form (Appendix 14 of the revised Guidance) in Microsoft Word format.

2. A new checklist for variations to a Plasma Master File has been added to the Guideline on MIV Applications for Biologics, which is Part D in Appendix 16 of the revised Guidance.

3. From 1 July 2011, only consequential changes related to a main change can be submitted as one MIV-1 application. A consequential change is regarded as a change that is unavoidable and is a direct result of another change.

The revised Guidance on Medicinal Product Registration in Singapore will be effective 1 April 2011 and may be downloaded from the **HSA website**. A bound hardcopy guidebook can also be purchased for S$22 from HSA [11 Biopolis Way, #11-01 Helios, Singapore 138667] from 1 April 2011.

Useful Tips:

• A thermometer that allows the recording of minimum and maximum temperature would help to alert whether or not the storage conditions of your warehouse was appropriate for the products stored within, both overnight and during weekends.

• The thermometer should be subjected to periodic calibration to ensure its accuracy and precision in monitoring the storage temperature, and should cover its intended operating range. A trained personnel should review the calibration report to ensure that it is traceable to a national or international standard, and determine the suitability of its use as a routine monitoring device.

• If a digital thermometer is used, its degree of accuracy should be ±0.5ºC

Cold Chain Management – Revision of HSA Guidance Notes on Good Distribution Practice (GDP)

Over the last few years, there has been a rapid growth in the number of temperature-sensitive products being marketed in Singapore, thus triggering the need for a better understanding of the importance of cold chain management. A 'break' in the cold chain, either during transportation, storage or distribution, could adversely affect the safety, efficacy and quality of these products. For instance, a 'break' in the cold chain for products such as vaccines and biologicals, could result in the irreversible denaturation of its proteins, and potentially cause serious health problems to patients.

Recognising the industry's need for clearer guidelines on cold chain management, we have revised the HSA Guidance Notes on GDP. The revised document may be downloaded from the **HSA website.**

From now till end May 2011, any gaps related to cold chain management that were identified during GDP audits would be issued as recommendations. With effect from 1 Jun 2011, companies are expected to comply with the cold chain management requirements. For more details on the implementation timelines, please visit the **HSA website**.

Update on the Use of Vitamin K as an Ingredient in Health Supplements

HSA had initiated a review on the use of Vitamin K in health supplements, in response to industry requests.

Additional Information

Presently, Vitamin K is allowed as an ingredient for health supplementation by overseas regulatory bodies such as the USA, Canada, Australia, UK and the EU.

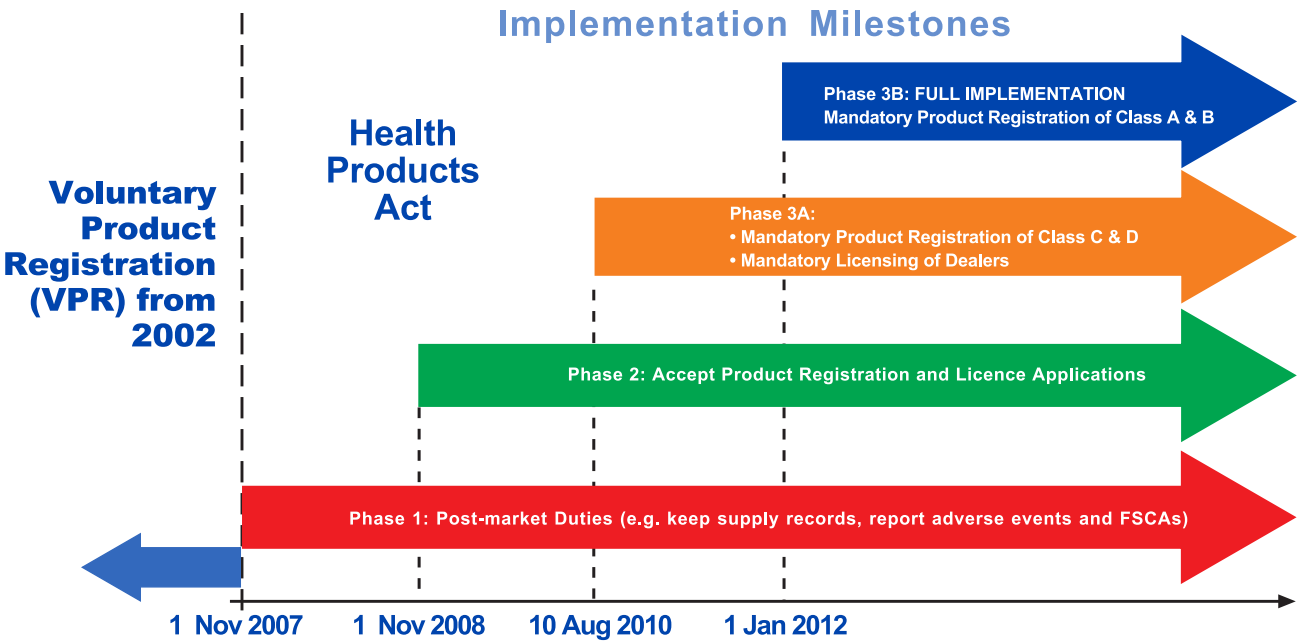
In the past, preparations containing Vitamin K were subject to drug registration as Vitamin K was often used clinically for the prevention or treatment of Vitamin K deficiency in newborns or in patients with malabsorption syndromes, as well as for reversing excessive anti-coagulation effects in the case of anti-coagulant overdose. As Vitamin K was used for therapeutic purposes, it was not allowed as an ingredient in Health Supplements. Following our review and in consultation with HSA experts, Vitamin K1 (phylloquinone, phytomenadione, phytonadione) and Vitamin K2 (menaquinone, menatetrenone) may now be included as an ingredient in Health Supplements, subject to the following conditions:

Conditions for use	Limited to oral dosage forms of multi-vitamin/mineral preparations for adults
	Maximum daily limit of Vitamin K is 120mcg
	Must be labeled with the cautionary statement, or words with similar intent: "Consult a health care professional prior to use if you are taking a blood thinner such as warfarin"
	Vitamin K-containing preparations intended for children will not be allowed until further review on its suitability in this target group has been concluded

These changes, which took effect from 1 December 2010, have been updated in the Guidelines for Health Supplements available on the **HSA website**.

Implementation milestone for Class A and B devices

In line with HSA's mission to safeguard public health and safety, our Medical Device Branch (MDB) implemented the medical device regulatory framework in November 2007. A phased approach to implementation was adopted to allow the Singapore medical device industry adequate time to prepare the necessary documentation and minimise impact on business and market supply.



The next and final milestone (Phase 3B) of the phased implementation plan will take effect from 1 January 2012, as has been extensively communicated to the medical device industry.

This means that in order for Class A and B medical devices to be imported and supplied after 1 January 2012, they must meet one of the following criteria:

i. Listed on the Class A and B Transition List
ii. Listed on the Singapore Medical Device Register (SMDR).
iii. Authorised via one of the other Authorisation Routes. Please refer to the guidance documents on the **HSA website**

Criteria to qualify for Class A and B Transition List

1. Application(s) must be received by HSA by **31 August 2011.**
2. Class B medical devices must qualify for the abridged evaluation route

The Class A and B Transition List will be published on HSA website by **31 December 2011.** Please ensure that applications are submitted with the correct risk classification to avoid rejection of the application. As in all our previous notices, there will be no refunds for rejected applications. Once the devices are approved after evaluation, they will be removed from the Transition List and listed on the SMDR. Devices which are withdrawn or rejected will be removed from the Transition list, and the import and supply are required to be halted.

HSA Connects

Product Registration – Class A Medical Devices

The new Class A MEDICS platform, which is specially catered for Class A applications, has been enhanced to facilitate the registrant in their submission of Class A applications. It features

- Streamlined submission process, requiring less documents to be attached
- More user friendly system

Please refer to the application guide on the **HSA website** for detailed guidelines on the application for product registration of Class A devices.

Class A exempted products

Class A products which are of very low risk are exempted from product registration. Some examples are non-sterile bandages, walking sticks and plasters. The description / intended purpose for which the products are allowed for Class A exemption are listed in GN22. If the products have additional medical/therapeutic claims, product registration is required. The revised guidance document is available on the **HSA website**.

Dealers' licence registration and GDPMDS Certifications will still be required for companies dealing solely with Class A exempted products.

Requirement for	Class A Products	Class A Exempted Products
Product Registration	✓	✗
Dealer's Licence	✓	✓
GDPMDS Certification	✓	✓

HSA remains committed to communicating openly and sharing in a timely manner, the latest updates on the medical device regulatory framework. As the Phase 3B implementation milestone draws nearer, we would encourage the medical device industry to be familiar with the regulatory requirements and begin preparing for the necessary submissions.

Upcoming Events

The 18th ASEAN Consultative Committee for Standards and Quality (ACCSQ) Pharmaceutical Product Working Group (PPWG) meeting will be held in Singapore from 7 – 10 June 2011 at the Grand Copthorne Waterfront Hotel.

Established in 1999, the key objective for ACCSQ-PPWG is to develop harmonisation schemes of pharmaceutical regulations of the ASEAN Member countries to complement and facilitate the objective of ASEAN Free Trade Area, particularly, the elimination of technical barriers to trade posed by regulations, without compromising on drug quality, efficacy, and safety.

This is an excellent platform for regulators and industry from the ASEAN Member Countries to discuss technical guidelines, regulatory requirements and look at ways of harmonisation applicable to the ASEAN pharmaceutical industry.

Details of registration and agenda will be made available shortly.

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