

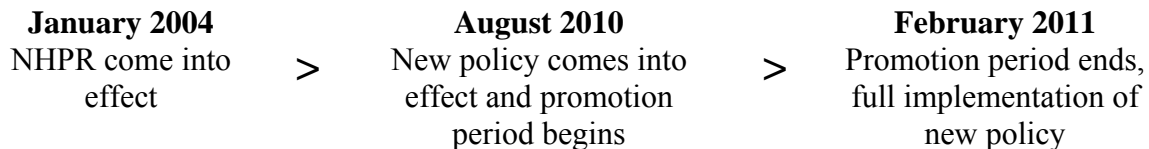
# Report from the NHPD Workshop – June 2, 2010

By: Ashleigh Hampton

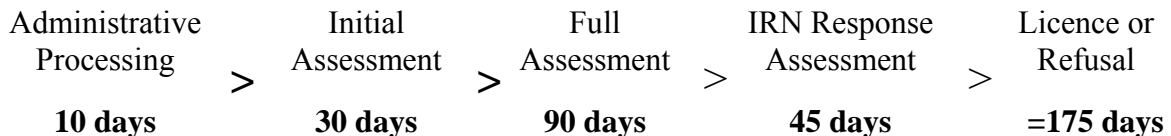
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## Summary

- It has been proposed that products in queue awaiting product licences be issued an Exemption Number (EN) and therefore are deemed legal for sale
- Initial assessment will take place prior to the issue of a submission number, but a full assessment will be completed after the issue of the EN – safe and efficacious products of high quality will then receive an NPN following full assessment
- Products which are classified as higher risk for safety will not be issued an EN
- New NHPD performance targets will hopefully be met such that a product will get a licence before an EN is issued
- If the NHPD cannot meet their internal performance target and the product is in queue for 180 days, then an EN will be issued allowing the product to be sold legally, provided there are no significant safety concerns associated with the product
- Full compliance is proposed to take effect Feb 1<sup>st</sup>, 2011



## Non-traditional applications, traditional applications, homeopathic applications and amendments



- the total time for a decision (licence or refusal) will be **175 days** (if internal performance standards are met)
- Provided that the above targets are met, a submission is filed August 1, 2010 should potentially **receive an NPN before Feb 1, 2011** (August 1 + 175 days falls in the month of January)
- Submissions filed in September or later potentially will have neither an EN or an NPN by Feb 1, 2011 and will not be legal for sale while in queue, based on proposed NHPD internal standards

## Applications referencing pre-cleared information only

Administrative Processing	>	Review against pre-cleared information	>	Licence or Refusal
<b>10 days</b>		<b>50 days</b>		<b>=60 days</b>

- Includes compendial applications, labeling standards, applications referencing abbreviated labeling standards, PCI amendments, the total time for decision (licence or refusal) will be **60 days**
- Provided that the above targets are met, a submission is filed August 1, 2010, should potentially receive an NPN by **October 2010**

Note: The annual report for ARR should be filed based on a **whole-product basis**, not an ingredient basis – the NHPD will deal with the ingredient specific issues themselves

## NHPD Regulatory Proposal

Speaker: Matthew Bown

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- UPLAR is a proposed solution allowing the legal sale of products awaiting a license until the NHPD is able to fully review the application
- There is a much higher volume of NHPs to be licensed than drugs (39000 NHPs vs 12200 drugs)
- The new regulations would provide a voluntary exemption from the prohibition against sale without a license – these products would be issued an exemption number (EN) which will be immediately posted on the NHPD website will remain there regardless of whether the product is fully licensed or refused
  - A product that has not fully been licensed but is legally allowed to be sold, will be listed as valid under the EN# heading on the NHPD website
  - A product which has been refused (i.e. did not receive an NPN) will be listed as invalid
  - When a product becomes licensed, the EN number will remain visible on the NHPD website, but it will be indicated that the product is licensed
- It is proposed that UPLAR be a temporary solution to the long lengths of time a product waits in queue before it can be legally sold – UPLAR will be repealed 30 months after it comes into force
- Products that are presently in queue, and have been in queue for 180 days or more, will receive an EN following the acceptance of UPLAR
  - For all other products, 180 days after an acknowledgement letter (submission number) has been received, the NHPD will provide the product with an EN until a full evaluation of the evidence can be performed – at this time the product is legal for sale in Canada
- Products which will not be eligible for ENs:

- Sterile products for ophthalmic use
- Prohibited substances
- Products making schedule A claims
- Products for use in children under the age of 12
- Products for use in pregnant or breastfeeding women
- Contains an ingredient that has been subject to recall or stop sale
- The products issued ENs will be treated like licensed products with regards to
  - Site licensing requirements
  - GMP
  - Record Maintenance
  - ARR requirements
  - Labeling and Packaging requirements
- During the period of time that a product carries a valid EN, the Minister has the power to
  - Order a stop sale
  - Request additional safety information
  - Suspend or cancel the exemption number
- Sections of the NHP regulations that do not apply to products carrying a valid EN
  - Amendments, notifications and fundamental changes
  - Suspension for false/misleading statements in the PLA
  - Site information prior to commencing sale
  - NPN for product recall
  - NPN on product label
  - NPN on small package label
  - All others apply
- Products issued a valid EN may be suspended if the applicant does not follow the regulations
- Site information must be provided prior to sale, unless the product is already for sale when the EN is issued
- The product can be recalled even if it is issued a valid EN
- The product must be labeled with the EN
- August 1, 2010 is the earliest these regulations can come into effect, provided they are accepted
- Currently, and up to June 6, the draft is available in the Canada Gazette I and comments and feed back are encouraged (30 day consultation period ending June 6) – next step will be formal adoption and publication in Canada Gazette II in the summer, if change is accepted

### **Management of PLAs for NHPs**

Speaker: Sara O'Connor

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- NHPD's Application Management Policy – comes into effect the day the regulations are adopted, or in the near future if UPLAR is not accepted
- There will be 2 main application categories:

- Pre-cleared information – applications containing only pre-cleared information (e.g. compendial, labeling standards, PCI amendments)
- Non-PCI – applications needing full assessment (e.g. non-traditional applications, traditional applications, homeopathic applications, Non-PCI amendments)
- eIRN will no longer be issued – if the application has a critical deficiency then a refusal will be issued immediately
- MIs and NMIs will have to be present in the NHPD ingredient database prior to submission – submit an ingredient issue form to get it in the database, if it is not already – the turnaround for this is estimated by the NHPD to be 4 weeks
  - The applicant must provide the information to support the addition of the ingredient to the NHPD ingredients database including evidence that the product meets schedule 1 (is an NHP), and that NMIs have excipient purposes which is also in the ingredient database
- Initial assessment of the application will occur before the issue of the submission number – all pre-PLA preparation must be complete – all ingredients must be present in the ingredient database
- Proposed performance targets which the NHPD will strive to meet to generate licensed products as opposed to issuing ENs to products in queue – If the NHPD cannot make these targets in 180 days, then an EN will be issued
  - For non-traditional applications, traditional applications, homeopathic applications and amendments:
    - Administrative processing for PLA completeness is proposed to take 10 days
    - Initial assessment will take an additional 30 days (so far 40 days to get a submission #)
    - Full assessment of the application is proposed to take 90 days (IRNs will be issued as needed)
    - Assessment of applicant response to IRN is proposed to take 45 days and then a refusal or license is proposed to be issued
      - Total time for license (provided only 1 IRN is issued): 175 days
  - For Pre-cleared information (compendial applications, labeling standards, applications referencing abbreviated labeling standards, PCI amendments):
    - Administrative processing for PLA completeness is proposed to take 10 days
    - Review against pre-cleared information is proposed to take 50 days
      - Total time for license: 60 days
- Automatic extensions for IRNs will not be issued, extensions may still be granted depending on the circumstances
- Refusals older than 6 months should not be referenced as they are generally out of date
- New Initiatives and Process Improvements
  - The NHPD stressed the use of the new finished product specifications Form

- Also mentioned the use of *The Evidence Assessment Template* to be used with the *Evidence Criteria* document (Both were published on the NHPD website in Nov 2009)
- Safety and Efficacy Review Process
  - The NHPD will try to make improvements in
    - Indicating claim wording more likely to be licensable to applicant
    - Creating PCI for safety of common ingredients
    - Developing an issues management
    - Reduction of duplicate reviews
    - Expert consultation to leverage expertise and resolve long standing issues (Soy, CLA, picolinate)
    - Clairimails – emails to clarify small discrepancies noticed on application review
- New online components available this summer
  - Upgraded NHPD ingredients database
  - New and improved ePLA
  - Submission builder
  - Smart form for company management
  - Single ingredient monograph rules will be built into ePLA
- In the future the NHPD hopes to
  - Formalize a separate stream for PCI
  - Have the ePLA as the only acceptable form
  - Develop and improve training and guidance
  - Use webinars and other interactive approaches as guidance
  - Continue with communication with BEEP
- If UPLAR is adopted: Phase 1
  - The NHPD will notify all applicants and licensees informing them of the new Regulations and this notice will outline eligibility criteria
  - Fax-back form will be attached to the notice which the applicant can fax back requesting the issue of an EN – this form must be received by the NHPD within 30 days of issuance – upon receiving the fax-back form the NHPD will post the appropriate EN info on the website, including company name, brand names, Dosage form, EN status (Valid, not valid, product licensed) and status date
  - As PLAs are processed, the database is updated
- If UPLAR is adopted: Phase 2
  - Each day within 30 months of UPLAR, new PLAs will be eligible for an EN, provided they have met the 180 day queue
  - The same rules as Phase 1 apply regarding fax back and notifications
- The NHPD hopes to deal with amendments within 190 days

### **The NEW NHP Compliance and Enforcement Policy**

Speakers: Stephanie Collins and Christine Zaczynski

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- The existing compliance policy was implemented in 2004 and was adopted to provide a reasonable transition time for industry to come into compliance with the product licensing requirements for the NHP regulations
  - Two approaches:
    - Risk-based approach
    - Product category approach: priority 1-6
  - Key areas of consultation:
    - Risk criteria
    - Regulatory validation
    - Product categorization
    - Implementation
    - Outreach
  - In the 2009 workshop feedback was provided by Stakeholders and it was agreed that the current high risk factors (e.g. adulteration, schedule A claims) need some clarification
    - Lack of a product license is considered a risk and the existing product categories need to be reviewed
    - Backlog elimination and performance targets should be linked to initiation of compliance actions for products without a product license
    - For high risk products a full suite of compliance and enforcement tools should be used, including stop sale, recall and public communications
- The Program Advisory Meeting
  - The NHPD wanted to further develop key areas of a new policy based on what was heard from the stakeholders in 2009
- The New NHP Compliance and Enforcement Policy
  - Purpose: The new C&E Policy will replace and supersede the existing compliance policy and compliance guide
    - The policy outlines and informs stakeholders of Health Canada's approach to compliance and enforcement
  - Scope:
    - The policy applies to issues of non-compliance with the NHP regulations and the FDA
    - The policy does not apply to NHPs use in clinical trials involving human subjects
    - NHP-UPLAR: an annex would be added to the policy for the length of time the NHP-UPLAR are in place
  - Decision Making Structure:
    - Health Canada's Risk-Based Decision Making Framework → Policy 0001 : Compliance and Enforcement Policy → NHP C&E Policy
    - Compliance and Enforcement – Policy 0001
      - The inspectorate's foundation document is its compliance and enforcement policy

- This policy provides the inspectorate with guiding principles for the fair, consistent and uniform application and enforcement for relevant acts and regulations
  - The goal is to increase transparency by providing the industry with a clear description of the inspectorate's role in delivering a national compliance monitoring and enforcement program – [www.hc-sc.gc.ca/hpfb-dgpsa/inpektorate/compliance\\_enf\\_policy\\_tc\\_e.html](http://www.hc-sc.gc.ca/hpfb-dgpsa/inpektorate/compliance_enf_policy_tc_e.html)
- Key differences between the old policy and the new policy:
  - Risk Criteria: The policy will clarify instances of non-compliance based on their potential level of risk
  - Regulatory Violations: Will set out the expectations for all products to have been issued a product license (or EN#) to be made available for sale
    - Will identify instances of non-compliance that are not in the scope of the current policy
  - Product Categorization: The policy will not outline product categories as many factors are to be considered
- Key Policy Positions
  - It is the responsibility of the regulated party to ensure that NHPs being sold, advertized, manufactured, packages, labeled, imported, distributed or stored comply with the FDA and the NHP regulations
  - The primary objective of the compliance and enforcement approach is to manage the risk to Canadians and use the most appropriate level of intervention to ensure that the regulated party brings the product or activity into compliance
- Identified Non-Compliance by HPFBI (Health Products and Food Branch Inspectorate)
  - HPFBI is generally made aware of potential non-compliance via complaints and/or referrals
  - HPFBI aims to prioritize work according to the potential level of risk to health that a non-compliance may pose
  - HPFBI may request that a risk assessment be conducted by the NHPD
  - Level of risk can increase or decrease with any instance of non-compliance given the circumstances
  - There are 3 levels of risk: Higher risk (those that may pose a risk to health) and lower
    - Higher risk products are required to have a more formal risk assessment
    - Examples of higher risk products include
      - unlicensed products which are sold/imported
      - unlicensed site conducting activities
      - Advertising of labeling for schedule A diseases
      - Products out of specification or adulterated
    - Examples of non-compliance:
      - Items which may cause a risk:
        - Labeling contraventions

- Products sold/advertised in a misleading manner
    - GMP contraventions
  - Items which pose a lower risk: technical labeling violations
- Enforcement Approach
  - The objective is to mitigate the risk using the appropriate level of intervention, prioritize enforcement according to the potential level of risk to health that a non-compliance may pose
  - Some instances may require immediate risk management actions
  - Compliance is normally achieved through a cooperative approach between the regulated party and HPFBI
  - In addition to health risk, there are a number of factors which will be considered in determining the appropriate risk management steps, including, but not limited to:
    - Likelihood of reoccurrence and effectiveness
    - Public confidence
    - Properties and resources
    - Intent
    - Compliance history and cooperation
- Ways to enforce compliance
  - Company initiated:
    - Voluntary stop sale, voluntary product recall, product detention, product disposal, consent to forfeit
  - Health Canada initiated:
    - Warning letter, regulatory stop sale, product detention, customs activities, public communications, letters to trade associations, product seizures, prosecution
    - Tools under the NHP regulations:
      - Product License: safety information request, stop sale, intent to suspend, suspension, cancellation
      - Site License: intent to suspend, suspension
  - Triggers for a more detailed assessment:
    - Health hazard evaluation
    - Health risk assessment
    - New PCI information
    - Revisions to PCI
    - Product classification
    - New scientific information
    - Information from program partners (e.g. ADR, recalls)
    - Foreign product alerts
- The NHPD process for compliance and enforcement
  - Compliance promotion → compliance monitoring → compliance verification → Investigation (in cases of possible non-compliance) → prosecution (in cases of non-compliance)

### **Annex to the NHP Compliance and Enforcement Policy**

- In the event of implementation of the proposed regulations

- The annex provides clarification on the C&E approach for exempt products
- The regulations apply to exempt products with some exceptions
- The regulations (UPLAR) will be in effect for 30 months following its adoption
- Changes
  - Exempted products will be legally allowed to be sold and imported
  - Recall reporting will take place and labeling with EN is required within a reasonable amount of time
  - Site information must be provided upon request
- Compliance and Enforcement Considerations
  - An EN is obtained provided that
    - none of the specified risk criteria have been met
    - The marketed NHP for which the EN has been issued should be consistent with the information upon which the EN is assigned
    - Exempt NHPs have not been fully assessed for safety, quality and efficacy
  - Instances of non-compliance will be identified throughout the review
- Enforcement procedures
  - Safety assessment, stop sales, additional suspension measures in NHP-UPLAR

**Implementation of the NHP Compliance and Enforcement Policy - Speakers:**

Stephanie Collins ([Stephanie-collins@hc-sc.gc.ca](mailto:Stephanie-collins@hc-sc.gc.ca)) and Christine Zaczynski ([Christine.zaczynski@hc-sc.gc.ca](mailto:Christine.zaczynski@hc-sc.gc.ca))

- The compliance and enforcement policy is anticipated to come into effect late in August 2010
- Once in effect, a compliance promotion period will commence – this involves outreach as well as a phased approach to the new policy
- Full implementation of the policy will begin 6 months after it comes into force (this length of time was discussed during our Plenary discussion – that overall it seems very short and it was proposed that the NHPD give more time to implement the changes through the entire industry and across the country)
- The compliance promotion period is an opportunity to transition into the new compliance and enforcement position regarding product licensing requirements
- It is also an opportunity to enhance awareness of other requirements
- All other parts of the policy still continue to apply to compliance and enforcement identified, as they do with the existing policy
- Compliance promotion principles:
  - The ultimate goal is compliance
  - Education is critical
  - Regulated parties must be educated about the relevant sections of the regulations, but they must also be informed of the consequences for non-compliance
  - A comprehensive implementation strategy can result in a higher level of compliance and enhance safety

- During the 6 months following the releases of the policy, compliance promotion will include:
  - Phasing in changes to product licensing regulations
  - Outreach and education including
    - Workshops
    - communications materials (Fact sheets, webinars, letters)
    - C&E stakeholder bulletin
    - Outreach and product authorization market survey initiate
  - During this period, C&E in response to unauthorized products will focus on compliance promotion and education
  - Regulated parties that make an effort to come into compliance with the product licensing requirements will not be a high priority for enforcement unless they meet the risk criteria
  - Once the compliance promotion period has elapsed, products without an NPN (or EN) may be subject to compliance and enforcement activities

#### Outreach and product authorization market survey initiative

- Retail survey will be issued to determine compliance with product licensing requirements
  - This will focus on compliance promotion
  - It will not be linked to enforcement activities unless a risk to health is identified
  - Opportunity to educate retailers of the requirements
  - When unauthorized products are identified, the distributors/manufacturers/importers will be contacted and informed of actions that may be taken after the compliance promotions period has elapsed and requested to come into compliance
- Full compliance is proposed to take effect Feb 1<sup>st</sup> 2011.