Business Engagement Assessment	
Title of Proposal	***Variations processing review - Composite Coordination Collection***
Lead Regulator	*Medicines and Healthcare Products Regulatory Agency (MHRA)*
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Date of assessment	*12 January 2014*	Commencement date	*1 Nov 2013*
Estimated net annual saving to Business in England:	*£25m*	Stage of assessment	*Draft*
Price base year	*2013*	Is this directly applicable EU or other international legislation?	*No*
Does this include implementation of Red Tape Challenge commitments?	*Yes*		

Brief outline of proposed change in regulatory action

Composite Coordination Collection (CCC) (One stop shop) is a new process to coordinate assessment and processing of applications to change (vary) a medicines marketing authorisation (MA). The document that the MHRA regulates by law that contains this information is called the Summary of Product Characteristics (SmPC). MHRA processes thousands of changes per year to medicines SmPCs, and these are assessed by different parts of the MHRA. In the past this resulted in companies waiting for different assessors to complete work before all changes were completed.

The new CCC process is particularly useful when a company wants to change different parts of a document it owns called the Company Core Data Sheet (CCDS). This periodically has to be brought into line with the Summary of Product Characteristics (SmPC) held by MHRA. It can simultaneously require other changes that impact on the SmPC, including to the medicine label and patient information leaflet. Estimated savings in this BEA are based on the changes to the CCDS only as this is the area of greatest impact. CCC is currently being piloted and when evaluated later in 2014 MHRA will evaluate uptake and assessment of impact. The estimated savings may be greater if other process changes have been included.[1]

The new process was designed to reduce burden and not introduce any new burden in the process.

The multiple, separate submissions that industry previously had to submit could relate to:

- safety variations
- clinical variations extending the use of the product
- eg new indications or posology
- quality variations
- Patient information and labelling

In addition MHRA has used this opportunity to update guidance relating to grouping of variations[2] which has clarified a number of issues for industry. This certainty allows them to submit applications in the knowledge that they should be approved and allow a “right first time” approach.

In total this BEA responds to 7 issues raised by trade associations following the medicines Red Tape Challenge in 2012 (listed in full in the next section). MHRA is grateful to a number of trade associations, coordinated by the Association of the British Pharmaceutical Industry (ABPI), who developed a preliminary assessment of the issues and cost savings that formed the basis of this BEA.

[1] At the time of writing, the proposed CCC approach is now broader than core label (CCDS) updates that form the basis of the estimates in this BEA as it covers e.g. Article 61(3) label/PIL changes which will also have a significant impact, particularly for over-the-counter and generics sectors.

[2] http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Marketingauthorisations/Variationstolicences/QualityAuditReportofNewTIANotifications/index.htm

Why is the change proposed? Evidence of the current problem?

Issues with changes (variations) to medicines marketing authorisations were the most common issue reported in the medicines Red Tape Challenge.

As an example, in relation to CCDS changes which the CCC will help to resolve, one company said

> *A co-ordinated variation approach would allow one approval date and a single SmPC label change following a global CCDS change rather than multiple staggered assessments and approvals. At present, different components of the update are managed separately, with different approval dates and timelines which adds significant complexity, delay and cost updating of SmPCs and delay in the implementation and communication of what may be important safety changes to patients.*

Detail on each proposal raised by industry

Proposals 1 - 5 have been resolved by updating MHRA guidance and clarifying how to submit requests for grouping to MHRA. Some of these were based on misconception of regulatory requirements.

Proposal 1: MHRA should follow a coordinated approval process for SmPC updates as following EU work sharing procedures (e.g. paediatric, PSUR/pharmacovigilance). MHRA has clarified that it already allows this.

Proposal 2: Grouping of variations should be allowed where the meaning of the change is similar (rather than identical) due to differences in formulation/presentation/strength. MHRA has clarified that this is acceptable for routine cases eg for

- a product range: eg change in shelf life/storage where study matrixing is relevant
- powder for solution for injection, directly related changes to active substance and finished product

(complex products/scenarios requiring distinct substantive data should be sent to variation queries@mhra.gsi.gov.uk)

Proposal 3: MHRA should implement processes to ensure a 14 working day response timeframe is adhered to for requests for groupings. MHRA has confirmed that no change is needed but is able to confirm that 85% of replies are sent < 5 days.

Proposal 4: MHRA should publish up to date examples of groupings already agreed to allow subsequent applicants to follow the same rationale This has been done.

Proposal 5: MHRA should automatically accept CMDh acceptable grouping. MHRA has confirmed that 75% of grouped variations already have no prior MHRA approval. The company provides justification for the grouping based on CMDh guidance, published examples or previous similarly agreed groupings. Of the remainder, most could be similarly justified by the company rather than submitting an approval request. Advice on grouping should be sought for only the more complex cases.

The following are resolved by the new CCC proposal

Proposal 6: PIQU assessments should be accepted as 'group-able' with other variations. MHRA has confirmed that certain Article 61(3) notifications which would otherwise be notified to the agency, may be submitted within a relevant variation where the company is amending its product information.

Proposal 7: MHRA should follow a co-ordinated variation approach for a CCDS update to the SmPC MHRA has addressed Proposals 6 and 7 by the CCC scheme.

Which types of business will be affected? How many are affected?

There are currently 950 holders of MAs issued by MHRA. All of them are likely to benefit from the proposal and these benefits will be on-going rather than one-off. The proposal is not expected to impose any costs on any sector.

Not all holders of a MHRA MA are based in the UK as the industry is global, with some having a single European head office. BIS statistics suggest that there are 385 UK businesses in this sector (of which 230 are micro and 65 medium sized). *Manufacturers of pharmaceuticals, medicinal chemicals and botanical products (SIC 244)*

How will the change impact these businesses?

The proposal directly affects these business. The proposal seeks to **reduce the burden of regulation on business** while keeping risks to public health to a minimum. A co-ordinated variation approach would allow one approval date and a single SmPC label change following a global CCDS change rather than multiple staggered assessments and approvals

MHRA expects the proposal to have a positive effect on the UK economy. The proposal will benefit from reduced administrative burdens and opportunity costs from time saved. No impacts on Civil Society Organisations (CSOs) are expected.

Initial feedback from industry on the revised groupings guidance has been very positive.

Scale of impact

The expected amount of savings is currently estimated to be £25 million per year.

The estimated cost to industry of changes to CCDS is estimated to be £49,782,60per annum, and trade association research suggests about £24,900,080 per annum could be saved by the new CCC process.

1) Estimated total cost to industry per annum

Estimate a cost to industry of £49,782,600 per annum based on 2,835* X £16,000 average cost per CCDS change (assuming 1 change per year) = £45,360,000 + man hours 2,835 X 26 hrs per CCDS change X £60 per hour = £4,422,600), note: this excludes variation submission costs.

* MHRA estimate 5670 safety variations affecting section 4.8 (National or UK as RMS in MR/DC) which were validated since January 2012 (a period of nearly 2 years). To get yearly data: 5670/2 = 2,835

2)) Estimated savings per annum of a coordinated review/ approval approach

By allowing a coordinated review/approval for variations arising from a single CCDS, industry estimate a saving to industry in excess of approximately £24,900,080 per year based on 1,418** X £16,000 average additional cost per CCDS change (assuming 1 change per year) = £22,688,000 + man hours 1,418 X 26hrs per CCDS change X £60 per hour = £2,212,080), note: this excludes variation submission costs.

** MHRA estimate 2,835 safety variations validated during 2012 included changes to section 4.8. However, if MHRA are only providing one approval for an average of 2 variations per CCDS then this figure would half, 1,418.

NB: As part of our engagement exercise, we ask firms to comment particularly on this section. Please also comment if you have identified any other benefits or costs and provide a clear description and quantification of them where possible.

Business Engagement

MHRA has introduced the CCC approach following 3 subgroup meetings of the Medicines Industry Liaison Group in 2013 that was established to consider this issue. All relevant sectors were represented in membership. The proposal has therefore been developed with industry support and engagement.

The Agency would like the pharmaceutical industry to comment on any aspect of this Business Engagement Assessment, particularly with a view to quantify costs and benefits of the proposal. The deadline for comments is 30 January 2014 and a final Business Engagement Assessment will be published shortly thereafter. Please send comments to Stephen.fawbert@mhra.gsi.gov.uk

Impact on small businesses

No disproportionate impact on small and micro businesses has been identified.
Given that this measure is of permissive nature, we expect that businesses will only take advantage of the opportunities offered by the new proposal if the associated benefits outweigh costs. Small businesses are therefore expected to switch to the CCC regime only if they find the net benefit of doing so to be positive.