THE PROPOSED RECLASSIFICATION OF JOINT REPLACEMENT IMPLANTS: REGULATORY IMPACT ASSESSMENT SUBMITTED BY THE ASSOCIATION OF BRITISH HEALTH-CARE INDUSTRIES (ABHI) TO MHRA

An independent report on the European Commission proposed directive for reclassification of certain total joint replacement prostheses

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1. Introduction

The Medical Devices Directive (93/42/EEC) classifies joint replacement implants in Class 2B. The proposed reclassification directive reclassifies hip, knee and shoulder joint replacements as Class 3. This assessment determines the impact of the proposed change. The assessment is based on a survey of manufacturers performed by ABHI and Eucomed in the period from mid-August to mid-September 2003.

This assessment was requested by the MHRA in their letter to ABHI dated 18 July 2003 in which they state: "As you are aware, there is a Commission proposal for a Directive on the reclassification of hip, knee and shoulder joint replacements. MHRA will be preparing a Regulatory Impact Assessment on the proposal and we would like some facts and figures on the effect the proposed directive would have on industry."

2. Definitions and Abbreviations

Manufacturer: As defined in Article 1.(f) of EC MDD
Class 2B file: Technical file produced in compliance with the requirements of Annex II.3.3 of the EC MDD
Class 3 file (or design dossier): Technical file produced in compliance with the requirements of Annex II.4 of the EC MDD
Significant change: Change to the "approved design" which would require notified body approval under Annex II.4. Significant changes include design changes, process changes and line extensions (in other words the addition of a larger or smaller size to an existing product range).
EC MDD: EC Medical Devices Directive (93/42/EEC)

3. The Current and Proposed Legislation

The current legislation is the EC MDD. This directive classifies joint replacement implants in Class 2B. The applicable decision rule is rule 8 (Annex IX, 2.4). The Directive provides a choice of conformity assessment options for class 2B devices (see Article 11), namely either "Full quality assurance" (Annex II excluding section 4) or "Type-examination" (Annex III with Annex IV, V or VI).

The proposed legislation is the Commission proposal for a directive on the reclassification of hip, knee and shoulder joint replacements (7 July 2003). This proposal classifies these joint replacements as Class 3. The conformity assessment options for class 3 devices are different from class 2B devices, namely "Full quality assurance" (Annex II, but in this case including section 4) or "Type-examination" (Annex III with Annex IV or V).

Today, under the current legislation, most manufacturers of joint replacement implants are following the Annex II option. These manufacturers under the proposed legislation will be obliged to upgrade from the requirements of Annex II without section 4 to Annex II with section 4. The most significant requirements of section 4 are the following:

1) the technical file (now called a "design dossier") must be approved by the manufacturer's notified body before the product can be placed on the market and
2) all "changes to the approved design" must be approved by the same notified body before these changes can be implemented.

It is obvious that the requirements of section 4 are onerous, both in terms of the time taken for dossier review and in terms of cost. This assessment quantifies the time and cost involved by obtaining actual quantitative data from manufacturers.

4. Scope of Assessment

It should be noted that the obligation to meet the requirements of the proposal resides principally with the manufacturer of the devices themselves. This being so, the question arises as to which manufacturers should be included in this survey. A narrow interpretation of the MHRA request might be to include UK manufacturers only. But the number of UK manufacturers is small, considering the industry as a whole, as indeed is the number of manufacturers, who manufacture in the UK. Instead we have taken the view that the matter of importance is not who manufacturers the product or indeed where it is manufactured, but rather whether the product is supplied to the UK market. Since most manufacturers, wherever they are located, supply products to the UK market, we have included all manufacturer in our analysis.

5. The survey instrument for Manufacturers

The survey instrument for manufacturers consisted of 9 questions most of which had to be answered separately for hips, knees and shoulder joint replacements. The questions covered existing class 2B technical files, existing class 3 design dossiers and existing design changes. It also included questions on the estimated effort and cost involved in converting existing class 2B files to class 3 files. A copy of the instrument is provided in Attachment 1.

The instrument was sent by Eucomed to Eucomed members on 13 August. A total of 16 replies were received. These replies were analysed and the data was summarized using appropriate statistical techniques. The data presented is in each case the mean of the replies received.

6. Results of Manufacturers' Survey:

Table 1 -15 gives the results of the survey of manufacturers. It can be seen that:

- Each manufacturer has 56.6 class 2B files in total and produces 10.5 new class 2B files per year (table 1).

- Each manufacturer made 51.1 significant changes in total to these class 2B files last year (table 2).

- Each manufacturer has 3.3 class 3 design dossiers in total and produces 0.6 new class 3 design dossiers per year (table 3).

- Each manufacturer takes 104 days to prepare a single class 3 design dossier and each manufacturer estimates that it takes his notified body a further 100 days for review and certification for which the manufacturer is charged 7,840 Euros (table 4).

- Each manufacturer submitted 0.6 change notification requests to his notified body with respect to these class 3 design dossiers last year (table 5).

- Each manufacturer takes 15 days to prepare a single change notification for a change to a class 3 design dossier and each manufacturer estimates that it takes his notified body a further 62 days for review and certification for which the manufacturer is charged 3,330 Euros (table 6).

- Each manufacturer takes 19.6 days to prepare and convert a single class 2B file to a class 3 design dossier and each manufacturer estimates that it takes his notified body a further 80.2 days for review and certification for which the manufacturer is charged 8,730 Euros (table 7).

From these results the total time and total cost for a single manufacturer can be obtained by multiplying the quantity of files, dossiers or significant changes by the time taken or by the cost for each. In this way it can be seen that:

- The total once-off impact per manufacturer of converting all existing class 2B files to class 3 design dossiers is 1,110 days of manufacturer time and a further 4,540 days of notified body time for which the manufacturer is charged 494k Euros (table 8).

- The total annual impact per manufacturer of new class 3 files (which would have been class 2B files) is 207 days of manufacturer time and a further 845 days of notified body time for which the manufacturer is charged 92k Euros (table 9).

- The total annual impact per manufacturer of change notifications is 757 days of manufacturer time and a further 3,160 days of notified body time for which the manufacturer is charged 171k Euros (table 10).

- The total annual impact per manufacturer of new class 3 files and change notifications is 964 days of manufacturer time and a further 4,007 days of notified body time for which the manufacturer is charged 263k Euros (table 11).

- The total time required by notified bodies to handle the additional workload from a single average manufacturer is 4,540 days for conversion of existing files, 845 days for processing of new files and 3,162 days for processing of file changes (table 12).

The combined impact on all manufacturers can be determined by multiplying the average manufacturer data (tables 8 and 11) by the total number of manufacturers, which is assumed to be 20 (see discussion section below). In this way it can be seen that:

- The total once-off impact of converting all existing class 2B files to class 3 design dossiers for all manufacturers is 22.2k days (61 years) of manufacturers time, 90.8k days (249 years) of notified body time and 9.9 million Euros to be paid by manufacturers to notified bodies (table 13).

- The total annual impact associated with all new class 3 files (which would have been class 2B files) and all changes to existing files for all manufacturers is a 19.3k days (52.8 years) of manufacturers' time, 80.1k days (219 years) of notified body time and a further 5.3 million Euros to be paid by manufacturers to notified bodies (table 14).

Similarly the total impact on all notified bodies can be determined by multiplying the notified body data in table 12 by the same factor (20) as shown in table 15.

Assuming that the workload from the 20 manufacturers was shared equally between the main notified bodies, of which it is estimated that there are 10 (see discussion below), then it follows that each will have the workload shown in table 12 multiplied by a factor of 2.

7. Accuracy of results and assumptions

Manufacturer indicated that they process 511 changes per year, but we have estimated that only one tenth of these are significant changes requiring notified body approval (see table 2). This is because it is believed that manufacturers will lump changes together when submitting change approval applications to notified bodies, as a cost saving measure. In this way it is estimated that manufacturers will submit slightly less than one change approval application per existing file per year. Based on manufacturer experience this would appear to be a reasonable estimate.

The present number of large manufacturers (those having at least 8% worldwide market share) is six. The total number of manufacturers with greater than 2% market share is probably 20. Thus a value of 20 manufacturers is probably a good estimate.

At least 45 notified bodies are designated under the EC MDD and listed in the Official Journal of the European Communities. Based on our survey data it is estimated that only about 10 of these have a significant share of the joint replacement market. This is considered a reasonable estimate.

It is difficult to estimate the accuracy of the notified body involvement data, namely the time taken and the cost. The data presented is derived from the manufacturers and is based on first-hand experience. For this reason it should be accurate. On the other hand, manufacturers may over-estimate, because they recall previous time and cost over-runs. To validate the manufacturer data, estimates were obtained directly from notified bodies. These estimates were smaller than the manufacturer data, but may be under-estimates for two different reasons:
1. Because notified bodies cannot accurately forecast how much work will be involved for any given file (their times and costs normally increase, if any unforeseen difficulties arise) and
2. Because, when estimating the time taken, notified bodies count only work days whereas manufacturers count and are interested in total turn-around time.

Taking these points into account it is believed that the data provided is accurate to within a factor of 2 for both time taken and cost.

Manufacturers have indicated that the notified body cost for conversion of class 2B files is greater than the notified body cost for new files (8,730 Euros compared with 7,840 Euros). This is unlikely to be correct, since the number of notified body days is less for conversion than for new files (80 compared with 100). Consequently, the cost of conversion is likely to be an over-estimate. A better value for the cost of conversion might be 6,270 Euros, in other words a 30% reduction.

8. Discussion and non-quantified impacts

The time taken is also time during which a new product cannot be sold. Thus the proposed directive would lengthen the development process and would delay the return on investment. Even if it turns out in a given case that the actual time taken is less than the forecasted time, it is unlikely that product launch can be brought forward since short-term scheduling changes are normally not possible. Thus the proposed directive would have an additional cost impact, namely as a result of the increased development time, which for the moment has not been quantified.

The notified body workloads calculated above are very large and it is questionable whether notified bodies with their existing resources will be able to cope with them. Some notified bodies have indicated that they have the necessary resources, but it is not clear whether they have estimated accurately the anticipated workload. Others have indicated that they intend to acquire additional resources, but, additional resources may not be readily available. The supply of suitably qualified labour (to review files, etc) is not elastic and the availability of experienced reviewers with the necessary knowledge of this specialized subject (orthopaedic joint replacement) is undoubtedly scarce.

Not all notified bodies are designated for the assessment of class 3 products. To cater for the needs of existing joint replacement customers such notified bodies will need to obtain the necessary class 3 designation. This will only be forthcoming if they acquire the necessary additional expertise. Alternatively, their customers will need to transfer to other notified bodies. In both cases extra cost and effort will be involved.

Since the transition period (TP) of the proposed directive for Annex II products is 2 years, the work of conversion of existing files must be performed during this two-year period. During this period the annual work associated with new files and changes to existing files will go on. This being the case the annual workload and cost in the first four years per manufacturer for all files is as shown in the table below:

Year	Manufacturer	Notified Body	Notified Body
	Days	Days	Euros
Yr 1 (TP)	1,518	6,277	510k
Yr2 (TP)	1,518	6,277	510k
Yr 3	964	4,007	263k
Yr 4	964	4,007	263k

9. Conclusion

The anticipated impact of reclassification on both manufacturers and notified bodies will be very large. The impact will be of two types.

The first will be the time taken and cost related to the conversion of existing class 2B technical files, of which each manufacturer has on average 56.6, to class 3 design dossiers. This will be a once-off event, which will take place during the transition period of the proposed directive. It will require on average per manufacturer:

- 1,110 days of manufacturer time
- 4,540 days of notified body time
- 494k Euros to be paid to the notified body for review and certification

The second will be the time taken and cost associated with the processing of new design dossiers (which would have been class 2B files) and change notifications to existing files. This will be an annual event and will require on average per manufacturer:

- 760 days of manufacturer time
- 3,160 days of notified body time
- 171k Euros to be paid to the notified body for review and certification

Since the number of large manufacturers is 20, the total impact is obtained by multiplying the above figures by 20. Since there are only 10 large notified bodies, the impact on each is obtained by multiplying the above figures by 2.

Notified bodies have assumed either that they will be able to manage the additional workload with existing resources or that they will be able to readily acquire the necessary additional resources. Both these assumptions are likely to be false, given the scarcity of experienced reviewers.

Other non-quantified costs and considerations also need to be taken into account.

The accuracy of the survey data has been estimated and it is possible that the notified body data presented here is on the high side (possibly by a factor of 2). Even if this were true, it does not adversely affect the main conclusion, which is that the impact of the proposed directive on both manufacturers and notified bodies will be very large.

10. List of Attachments

1: Survey Instrument for manufacturers

11. Appendices

Appendix 1: Results of Manufacturers' Survey

Table 1 gives the number of existing class 2B files per manufacturer per year and the number of new files per manufacturer per year.

Table 1: Number of existing class 2B files and number of new class 2B files per year for a single manufacturer

	Hip	Knee	Shoulder	Total
Existing Files	40.4	12.3	3.9	56.6
New files per year	4.8	4.1	1.7	10.5

Table 2 gives the number of significant changes made to these class 2B files last year. It has been estimated that significant changes represent one tenth of all changes recorded in the survey (see discussion section).

Table 2: Number and type of significant changes made last year to existing class 2B files

	Hip	Knee	Shoulder	Total
Design change	3.2	2.0	0.7	5.9
Process change	10.3	8.3	5.0	23.6
Line extensions	7.0	12.0	2.6	21.6
Total	20.5	22.3	8.3	51.1

Table 3 gives the number of existing class 3 design dossiers per manufacturer and the number of new class 3 design dossiers per manufacturer per year.

Table 3: Number of existing class 3 dossiers and number of new class 3 dossiers per year for a single manufacturer

	Hips	Knees	Shoulders	Total
Existing dossiers	2.3	0.7	0.3	3.3
New files per year	0.4	0.2	0.0	0.6

Table 4 gives the time taken by each manufacturer for preparation of a single design dossier, the time taken for notified body review and certification of this design dossier and the cost of notified body review and certification per design dossier. The hip, knee and shoulder data is combined.

Table 4: Time taken and cost per single class 3 design dossier

	Days	Euros
Time taken by manufacturer	104	
Time taken by notified body	100	
Cost of notified body review		7,840

Table 5 gives the number of change notification requests submitted by the manufacturer relating to these existing class 3 design dossiers last year.

Table 5: Number of change notification requests made to existing class 3 files last year by a single manufacturer

	Hips	Knees	Shoulders	Total
Changes	0.4	0.2	0.0	0.6

Table 6 gives the time taken for preparation of a single change notification request by the manufacturer in days, the time taken for notified body review and certification of this change notification in days and the cost of notified body review and certification in Euros. The hip, knee and shoulder data is combined.

Table 6: Time taken and cost per single change notification to existing class 3 dossier

	Days	Euros
Time taken by manufacturer	15	
Time taken by notified body	62	
Cost of notified body review		3,330

Table 7 gives the time taken to convert (upgrade) a single existing class 2B file to a class 3 design dossier, the time taken for notified body review and certification and the cost of notified body review and certification in Euros. The hip, knee and shoulder data is combined.

Table 7: Time and cost of conversion of a single file from class 2B to class 3

	Days	Euros
Time taken by manufacturer	19.6	
Time taken by notified body	80.2	
Cost of notified body review		8,730

Table 8 gives the total time taken and notified body cost to convert all existing files from class 2B to class 3 per manufacturer. The data is obtained by combining the data from tables 1 and 7. The total number of files per manufacturer is 56.6.

Table 8: Once-off impact of converting all existing class 2B files to class 3 for a single manufacturer

	Days	Euros
Total time taken by manufacturer	1,110	
Total time taken by notified body	4,540	
Total notified body cost		494k

Table 9 gives the total annual time taken and notified body cost for new design dossiers per year (files would have been class 2B) for a single manufacturer. The data is obtained by combining the data from table 1 and 7. The time taken is in addition to the time taken had the files remained class 2b files. The total number of new class 3 files per annum is 10.5.

Table 9: Annual impact of all new class 3 files (which would have been class 2B files) for a single manufacturer.

	Days	Euros
Total time taken by manufacturer	207	
Total time taken by notified body	845	
Total notified body cost		92k

Table 10 gives the total annual time taken and cost for significant changes to class 3 dossiers (which would have been class 2B files) for a single manufacturer. The data is obtained by combining the data from table 2 and 6. The total number of changes is 51.1.

Table 10: Annual impact of all significant changes for a single manufacturer

	Days	Euros
Total time taken by manufacturer	757	
Total time taken by notified body	3,162	
Total notified body cost		171k

Table 11 gives the total annual impact on an average manufacturer. The data is obtained by combining the data from tables 9 (new class 3 files) and 10 (changes).

Table 11: Total annual impact on a single manufacturer (new files and changes)

	Days	Euros
Total time taken by manufacturer	964	
Total time taken by notified body	4,007	
Total notified body cost		263k

Table 12 gives the total time required by notified bodies to handle the additional workload of a single manufacturer, which consists of the conversion of existing files, the processing of new files and the processing of file changes. This data is taken from tables 8, 9 and 10.

Table 12: Impact on notified bodies as a result of the work from a single manufacturer

	Days
Time taken for conversion of existing class 2B files	4,540
Time taken for processing of new files	845
Time taken for processing of changes	3,162

Table 13 gives the total time taken and notified body cost to convert all existing files from class 2B to class 3 for all 20 manufacturers. The data is obtained by multiplying the data in table 8 by a factor of 20.

Table 13: Total once-off impact of converting all existing files for all 20 manufacturers

	Days	Euros
Total time taken by manufacturer	22.2k	
Total time taken by notified body	90.8k	
Total notified body cost		9.9m

Table 14 gives the total annual impact on all 20 manufacturers. The data is obtained by multiplying the values in table 11 by a factor of 20.

Table 14: Total annual impact on all 20 manufacturers (excludes once-off impact)

	Days	Euros
Total time taken by manufacturer	19.3k	
Total time taken by notified body	80.1k	
Total notified body cost		5.3m

Table 15 gives the total time required by notified bodies to handle the additional workload from all 20 manufacturers, which consists of the conversion of existing files, the processing of new files and the processing of file changes. This data is obtained by multiplying the data in tables 12 by a factor of 20.

Table 15: Impact on notified bodies as a result of the work from all 20 manufacturers

	Days
Time taken for conversion of existing class 2B files	90.7k
Time taken for processing of new files	16.9k
Time taken for processing of changes	63.2k