BRITISH GENERIC MANUFACTURERS ASSOCIATION

Response by the British Generic Manufacturers Association (BGMA) (interest group registration 52609045913-87) to the general report on Experience acquired as a result of the application of the Paediatric Regulation (SANCO/d5/fs/(2012)1251190)

The British Generic Manufacturers Association (BGMA) represents the interests of UK-based manufacturers and suppliers of generic medicines and promotes the development and understanding of the generic medicines industry in the UK. Our 25 members account for around 90% of the UK generics market by volume. Generic medicines are launched when the patent on a medicine produced by a research-based pharmaceutical (or originator) company expires. When a patent expires, generic manufacturers can produce equivalent versions that contain the same active ingredient. Generics are tested by the medicines regulator (MHRA) to the same standards of safety and efficacy as the originator product. The high number of generic manufacturers helps ensure that generic medicine prices are much less than that of the originator version under patent protection. In 2011, if all medicines had been reimbursed at the average brand price (instead of the price for the generic version), the NHS drugs bill would have been £10.25bn higher.

Competition from generics also stimulates the research-based pharmaceutical industry to develop new medicines (as generics capture the bulk of the market after patent expiry). Furthermore, in keeping medicines affordable for the Department of Health, this allows further investment in other healthcare priorities, and promotes innovation in the development of new medicines.

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INTRODUCTION

The British Generic Manufacturers Association (BGMA) welcomes the opportunity to be able to respond to European Commission's public consultation on Experience acquired as a result of the application of the EU Paediatric Regulation.

The BGMA fully supports the intention of the Paediatric Regulation to ensure that more safe and effective medicines are made available for children through a system of obligations and reward. We do, however, have significant doubts about the appropriateness of the incentives introduced by the Regulation, in particular their burden / reward ratio; and the effectiveness of the Regulation.

1. A CHANGE OF CULTURE: NOWADAYS PAEDIATRIC DEVELOPMENT IS AN INTEGRAL PART OF PRODUCT DEVELOPMENT

Consultation item No 1: Do you agree that the Paediatric Regulation has paved the way for paediatric development, making it an integral part of the overall product development of medicines in the European Union?

The Paediatric Regulation may have made it the norm for originator companies to assess paediatric uses for new innovative medicines during their development, but it has not created conditions to drive investigation of potential paediatric uses of well-established products, arguably the area of greatest need. Further, the cost to payers of the incentives prescribed by the Regulation is disproportionately high when compared with the costs to the industry of carrying out PIPs. We comment further on these issues below.

2. HAS THE REGULATION DELIVERED IN TERMS OF OUTPUT? TOO EARLY TO JUDGE

Consultation item No 2: Do you agree with the above assessment?

We know of no data either specific to the UK or relating to the EU which quantifies the amount of off label use. Unless the Commission has access to data of this type of which we are unaware, we shall never be able to judge the success of the Regulation in reducing off label use. If this is the case, the argument that it will take a decade to judge the Regulation's success is not true: there will never be a time to judge without these data.

However, the fact that 500 PIPs have been approved does suggest that there may be sufficient data to judge the success of the Regulation in terms of whether the Paediatric Committee's decisions have properly focused work on developing medicines to deal with paediatric conditions for which licenced medicines are not available; and whether focused provision of EU funding for research has led to the development and authorisation of off-patent medicines for children.

3. THE PUMA CONCEPT: A DISAPPOINTMENT

Consultation item No 3: Do you share this view? Could you give specific reasons for the disappointing uptake of the PUMA concept? Is it likely that PUMA will become more attractive in the coming years?

Clearly, the Commission's proposition that the PUMA concept has been a disappointment is true. It does not provide an adequate commercial incentive for manufacturers to develop products licenced for paediatric use in the off-patent market. Prices are frequently too low and data exclusivity in substitution or INN markets is an ineffective tool to create true incentives. Different branding and reimbursement regimes may be required to ensure that there is a proportionate and effective incentive.

4. WAITING QUEUES? NO EVIDENCE OF DELAYS IN ADULT APPLICATIONS

Consultation item No 4: Do you agree that, generally speaking, the paediatric obligations have no impact on timelines in adult development, as there is no evidence for delays in marketing authorisation applications for reasons of compliance with the paediatric obligation? If you feel that there is an impact, practical examples would be appreciated.

We have no relevant experience that would enable us to comment.

5. MISSING THE POINT? PAEDIATRIC DEVELOPMENT IS DEPENDENT ON ADULT DEVELOPMENT, NOT PAEDIATRIC NEEDS

Consultation item No 5: Do you have any comments on the above?

We believe that the Commission's analysis is correct so long as such a blunt incentive as an extension to the SPC is used. A more focused economic instrument would, in our view, be effective in driving the development of needed medicines for children.

6. THE BURDEN/REWARD RATIO —A BALANCED APPROACH?

Consultation item No 6: Do you agree with the above?

ANALYSIS OF THE ECONOMIC IMPACT OF THE REGULATION

Whilst the European Commission outlines in the consultation document that it will assess the economic impact of the EU Paediatric Regulation in 2017, we note that Article 50.4 of the Regulation provides that "Provided that there are sufficient data available to allow robust analyses to be made, the provisions of paragraph 3 *[the economic impact]* shall be fulfilled at the same time as the provisions of paragraph 2" *[the current general report]*. We contend that the information presented below shows that sufficient data are available for that economic impact to be made now.

THE BURDEN-REWARD RATIO

The "reward"—more accurately, the incentive—of extending the originator company's SPC means that the NHS and other European public health systems have to wait a further six months before the onset of a generic market, delaying the significant cost savings that this creates.

Looking purely at the UK market, Losartan (brand name Cozaar™) received a paediatric extension. We estimate the cost to the NHS of delaying generic entry for Losartan for six months to be £32million. The more recent patent extension of Atorvastatin (brand name Lipitor™) from November 2011 to May 2012 is estimated to have cost the UK NHS £160 million.

Furthermore, because the extension of exclusivity is for the product as a whole and not just the paediatric use, the cost benefit ratio for manufacturers is disproportionately high. The originator of Losartan received a financial benefit of £32m at a cost of some £1 – 2m for the conducting the trial. As mentioned, a similar SPC extension for Atorvastatin cost the NHS over £160million. In the case of Atorvastatin, the branded manufacturer was rewarded with £215m of sales by receiving the SPC extension. The cost to the NHS and financial benefit for the manufacturer is wholly out of proportion to the cost of gaining the SPC extension. This also suggests that the marginal cost of undertaking and implementing the PIP for an NCE is not, as the Commission suggests, "a considerable additional burden".

Indeed, since September 2009, we note that the following SPC extensions have taken effect in three year period. In this period, these patent extensions have cost the NHS a total of £284 million in savings to the drugs budget. Our calculations for the cost to the NHS in each instance are conservative estimates intended to outline the cumulative cost of the Regulation.

INN name	Brand name	Annual brand value (£)	Date of original SPC patent expiry	Sales for originator during additional SPC extension period (£)	Cost to NHS (£)
Losartan, Tablets	Cozaar™	£85,960,000	September 2009	£42,980,000	£32,235,000
Anastrozole, Tablets	Arimidex™	£67,080,000	August 2010	£33,540,000	£25,155,000
Valsartan, Capsules	Diovan™	£49,170,000	May 2011	£24,585,000	£18,438,750
Valsartan, Tablets	Diovan™	£860,000	May 2011	£430,000	£322,500
Latanoprost, Ophthalmic Solution	Xalatan™	£55,480,000	July-2011	£27,740,000	£20,805,000
Atorvastatin, Tablets	Lipitor™	£429,930,000	November 2011	£214,965,000	£161,223,750
Montelukast (all forms)	Singulair™	£70,971,264	August 2012	£35,485,632	£26,614,224
Total cost to NHS from September 2009 to present					£284,471,724

We have listed the cost to the NHS over a three year period. This strongly suggests that the Regulation will deny the NHS the opportunity to make significant cost savings in the next five years up to 2017 – the date that the European Commission states that it will carry out an economic analysis if it feels that there are not sufficient data available to carry out a robust economic assessment now.

As stated above, we feel that these data, taken with that across other EU Member States that the consultation may provide, gives the Commission an opportunity to consider whether SPC extension is the right tool for proportionately encouraging paediatric work to be conducted.

We believe that an assessment on proportionality and output at this time is vital as from an EU-wide perspective, the delaying of generic entry for all medicines granted a paediatric extension over the next five years, whether they are granted a paediatric indication or not, is very likely to cost billions of pounds. This

means that public health systems like the NHS will have less money directly to invest in children's medical care as well as other priorities.

And importantly, for this taxpayer saving forgone, we do not appear to be seeing new formulations for children or many totally new uses for unmet clinical need. Indeed, most paediatric medicinal versions have the same or similar uses as for adults.

A MORE PROPORTIONATE WAY TO ACHIEVE THE SAME BENEFITS

Our view is that rewarding through a SPC extension is a blunt instrument and that a scheme more tailored to the research performed and the paediatric formulation developed should be considered. We believe that different branding and reimbursement regimes may be required to ensure that there is a proportionate and effective incentive.

Though partially a matter for the member states, this could include an enhanced system of tax credits or bespoke reimbursement regimes, or direct grants. Medicines that may only be used in very low volumes, and are likely to be uneconomic to develop under 'normal' pricing arrangements, could be reimbursed at higher levels to takes into account their societal value.

Whilst the European Commission has committed to reviewing the economic impact, including the incentives and costs involved with the EU Paediatric Regulation, in 2017, we hope that it will consider this and other ways to achieve the same output in a way that allows European public health systems the opportunity to maximise savings through generic competition.

7. ARTICLES 45/46: THE HIDDEN GEM OF THE PAEDIATRIC REGULATION

Consultation item No 7: Do you agree that Articles 45/46 have proved to be an efficient and successful tool for gathering and compiling existing paediatric data and making it available to the competent authorities and subsequently, via databases, to the interested public?

We support these provisions and welcome the benefits they bring.

8. LOST IN INFORMATION: HEALTHCARE PROFESSIONALS NOT AS RECEPTIVE AS EXPECTED

Consultation item No 8: Do you agree that healthcare professionals may not always be as receptive to new scientific information on the use of particular products in children as might be expected? Do you agree that this problem has to be addressed primarily at national level? How could healthcare professionals be more interested and engage in paediatric clinical research?

We believe that adequate information is available to healthcare professionals to enable them to take informed judgements. We believe that national guidance on prescribing and dispensing may be required.

9. CLINICAL TRIALS WITH CHILDREN: NO SPECIFIC PROBLEMS DETECTED

Consultation item No 9: Do you have any comments on developments in clinical trials with children following the adoption of the Regulation and in view of the above description?

We have no direct experience here.

10. UNNECESSARY EFFORTS? NON-COMPLETED PAEDIATRIC INVESTIGATION PLANS

Consultation item No 10: Do you have any comments on this point?

We have no direct experience here.

11. SOPHISTICATED FRAMEWORK OF EXPERTISE ACHIEVED

Consultation item No 11: Do you agree that the Paediatric Regulation has contributed substantially to the establishment of a comprehensive framework of paediatric expertise in the European Union?

We have no direct experience here.

12. ANY OTHER ISSUE?

Consultation item No 12: Overall, does the implementation of the Regulation reflect your initial understanding/expectations of this piece of legislation? If not, please precise your views. Are there any obvious gaps with an impact on paediatric public health needs?

No comment.

FURTHER INFORMATION

Should the Commission wish to discuss anything in the response including our ideas for developing more proportionate incentives, please contact BGMA Director-General Warwick Smith on +44 20 7457 2065 or warwick.smith@britishgenerics.co.uk.

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