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# Challenges and Priorities For the Next Five Years

## The Response of the PHG Foundation to the Consultation by the MHRA

## Introduction

The PHG Foundation is the successor body to the Public Health Genetics Unit. Its purpose is to enable and foster the responsible and evidence based application of biomedical science for the benefit of human health. Among its specific objectives is the fostering of a social and regulatory environment receptive to the application of biomedical science for health, but at the same time imposing an appropriate, equitable and proportionate regulatory burden. We submit the following response to some of the questions posed in the consultation proposal.

## Specific Questions

### 4. How should we best communicate the benefit-risk balance associated with medicines and medical devices?

We feel that it is important for the MHRA to clarify its methodology for weighing risks and benefits of products as far as it is practically possible. The question as to when a product is sufficiently 'safe' - when, that is, the associated benefits outweigh the risks to an extent that warrants its licensing - lies at the heart of the decision making of the MHRA. A clear methodology facilitates transparency of the rationales offered in support of decisions and produces a clear and consistent set of tools to aid in the decision-making process.

An instructive parallel is the major methodological document of the Health and Safety Executive, '*Reducing Risks, Protecting People*', which details a fairly well developed 'Tolerability of Risk' approach to health and safety decision making. A similar effort could be undertaken by the MHRA to provide detailed reasoning regarding the appropriateness of using a quantitative approach to weighing costs and benefits, the ways in which societal concerns should influence regulators, and so forth.

### 9. What are your views on the technological advances to which the Agency will need to respond in the coming years?

We have a particular interest in the development and evaluation of genetic and molecular biomarkers, which are becoming increasingly important as diagnostic and predictive tools and fall under the remit of the MHRA as medical devices. We note that their regulation is governed by the European Directive on In Vitro Diagnostic Devices and that the regulatory focus is directed at ensuring analytical validity, reliability and safety rather than on clinical validity and utility. We believe that in the future, as more complex molecular and other biomarkers are developed, a framework for the evaluation of clinical performance will be needed.

Believing that the health of the public is best served by ensuring that innovation remains unhampered as much as possible, we do not advocate the establishment of a licensing regime for biomarkers on the basis of new standards or thresholds of performance. Nevertheless, there may be an argument for imposing a requirement upon manufacturers of biomarker devices to provide full disclosure of information and evidence relating to their clinical test performance.

We therefore encourage the MHRA to look at issues that surround the labelling of biomarkers, particularly those that predict disease or the risk of disease, and to consider how all relevant information regarding test performance might be made available in the public domain. This will enable all those with an interest, whether reimbursers and commissioners or physicians and patients, to have access to the available evidence.

We note in particular that evidence of statistical association between the biomarker and the disease in question does not in itself entail that the biomarker will be an effective clinical test, and suggest that this can only be demonstrated following evidence from studies that determine the sensitivity, specificity, positive and negative predictive values, and likelihood ratios of the biomarker as it relates to disease in specified populations and for specified purposes. It is only right that those who use or wish to consider the use of such tests are made aware of the available evidence so that they can judge for themselves whether the claims made by the manufacturer are substantiated by the evidence.

**10. What are your views on how the balance is currently struck between supporting research and innovation, and taking a precautionary approach to prevent harm?**

We take the view that the demands of precaution in the healthcare sector are unclear, for overly restrictive regulation may be as detrimental to public health as the more obvious dangers of overly permissive regulation. A carefully prepared methodology, as discussed in conjunction with question 4, is fundamental to many 'balancing exercises' undertaken by the MHRA and will assist with determinations such as deciding how lay and expert opinion are to be combined in regulatory decision-making, and what it means to take a 'precautionary' approach in this arena.

**11. Do you have a view on the proposal to move to earlier, conditional licensing of medicines?**

We believe that a clarification of the demands of reasonable precaution could help to bolster the case for conditional licensing made by Sir David Cooksey.

## PHG Foundation

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