June 2017

PAGB position on EU Exit

PAGB's overarching position is that when the United Kingdom leaves the European Union there should be no fewer over-the-counter/self care products available in the UK and those products should be no less safe than they are today.

PAGB considers it vital that there remains effective proportionate regulation for over-the-counter medicines, self care medical devices and food supplements after the UK leaves the EU.

Priorities

PAGB's priorities are, therefore, to:

- **Ensure no additional regulatory barriers are introduced**
- **Agree an ongoing partnership/collaboration with the EU27 and continued participation in regulatory structures and processes**
- **Ensure appropriate mutual recognition agreements are in place to allow over-the-counter/self care products manufactured in the UK to continue to be exported to the EU and vice versa**
- **Ensure the UK continues to participate in EU pharmacovigilance systems to protect public health**
- **Ensure a simple, streamlined transition process to any new arrangements with adequate timescales**
- **Expand opportunities for self-regulation for over-the-counter products to deliver improvements in availability, access and choice for people in the UK, whilst ensuring sufficient regulatory alignment with the rest of the EU.**

Over-the-counter medicines, self care medical devices and food supplements are rightly highly regulated products. This is imperative to protect public health. Regulation of these products in the UK must continue to be sensible and proportionate, without becoming overly burdensome.

Since the EU referendum on 23 June 2016, PAGB has worked with its member companies and stakeholders to examine the implications and probable impact of the UK's exit. It is our view that to protect public health and ensure the supply of safe and effective medicines and self care products to the British people, it is vital that the UK maintains a close partnership with the EU, through continued participation in EU regulatory and pharmacovigilance structures and processes and through access to the single market. Mutual recognition arrangements between the Medicines and Healthcare products Regulatory Agency (MHRA) and European Medicines Agency (EMA) should be put in place to avoid unnecessary duplication.

We would like the UK to be a 'trusted partner' of the EU and for the two parties to work closely together to achieve, as far as is possible, a frictionless border. We would like to see a customs union agreement to minimise the additional time and administrative burden that would result from a hard border. In the meantime, it is vital the UK works to invest in improvements to its customs infrastructure to reduce the impact of any future additional burdens and, more

PAGB, Vernon House, Sicilian Avenue, London, WC1A 2QS 020 7242 8331 info@pagb.co.uk www.pagb.co.uk

importantly, to ensure the UK does not become, or be perceived to be, a customs weak-spot and an entry point for counterfeit products, falsified medicines or parallel trade, which would in turn undermine the UK's ability to be a trusted partner of the EU.

PAGB and its member companies are committed to working with Government departments and agencies, including MHRA, to ensure negotiations over the terms of the UK's departure and any future arrangements take our concerns into account and ensure appropriate measures are put in place to mitigate the risks we have identified to public health and the continued availability of medicines and other self care products in the UK.

This paper outlines an overview of PAGB's concerns for the regulation of over-the-counter medicines (including traditional herbal medicines), self care medical devices and food supplements. Further details and case study examples are being developed to explore these issues in more detail.

We have also considered the possible opportunities that exist to improve access to over-the-counter/self care products after the UK has left the EU.

Concerns

PAGB has identified a number of concerns that need to be considered and addressed in any future arrangements.

The consumer healthcare industry faces many of the same challenges being articulated by our colleagues in the prescription pharmaceutical medicines, medical devices and food sectors. PAGB is working closely with colleagues in the trade associations for those industries and is supportive of issues raised by those sectors.

Over-the-counter medicines

Over-the-counter medicines are medicines that can be bought from a pharmacy or other retail outlet without a prescription. These are well known and trusted medicines, such as Anadin, Beechams, Calpol and Gaviscon, that people in the UK use every day.

These medicines help people to self care for self-treatable conditions which don't require consultation with a doctor, thereby reducing pressure and costs on GPs and the NHS.

The continued availability of these medicines to the public is, therefore, of paramount importance.

Over the last 40 years, the UK has worked closely with the other European nations to build a system of effective medicines regulation that has ensured that the over-the-counter medicines available are appropriately safe and well regulated. Withdrawing from this effective system presents a number of challenges which will need to be addressed.

The issues raised in this section relate to medicinal products, including traditional herbal medicinal products (THM) with a traditional herbal registration (THR). As with all medicinal products, there are requirements from EU law to ensure the quality and safety of THMs on the

PAGB, Vernon House, Sicilian Avenue, London, WC1A 2QS 020 7242 8331 info@pagb.co.uk www.pagb.co.uk

market in any EU Member State, but there are additional complexities for THMs because the regulatory framework for these products is a hybrid of the Traditional Herbal Medicinal Products Directive (2004) and Implementing Commission Decisions.

There needs to be an agreement for an ongoing partnership/collaboration between the UK and the rest of Europe in relation to medicines regulation. Ideally the UK should continue to be involved in the development of EU medicines guidelines and processes but, if this is not possible, the UK must agree to unilaterally accept EU standards. Clarity on this is required quickly to minimise uncertainty.

The timeframes for the development and manufacture of OTC medicines are such that companies are making decisions now about how to license and where to manufacture products.

Guidance published by the EMA and EU Commission is clear that "as of the date of the withdrawal of the UK from the Union, medicinal products manufactured in the UK will be considered imported medicinal products"[1,2]. As such, the commercial framework for our industry will be very different in 2019 to the current situation. The arrangements that are put in place from 'Day One' (the first day after the UK has left the EU) have the potential to impact the availability of self care products on UK shelves, therefore Marketing Authorisation holders in the UK urgently need guidance and a flexible approach from MHRA.

Key areas of concern which will need to be addressed and clarified before Day One are:

Access to medicines

- Regulatory processes are established in the EU to ensure the quality and safety of medicines on the market in any of the Member States. If the UK is not a member of the EU or the EEA and these processes are not recognised, vital links in the supply chain will be broken. Ingredients can cross the border up to four times in the manufacturing process, therefore systems must be in place to ensure that this can continue without the need for Border Inspection Post Personnel (BIPP) checks and tariffs. This underlines why appropriate mutual recognition agreements are important. If mutual recognition agreements are not in place, the UK will need to unilaterally recognise EU and EEA procedures.
- There are medicines on the market in the UK that have licences issued by the EMA via the centralised licensing procedure or the decentralised licensing procedure. In order for these medicines to continue to be available in the UK after it leaves the EU, mutual recognition procedures will need to be in place or have national licences simultaneously granted by the MHRA.

[1] EU Commission/EMA Questions and Answers related to the United Kingdom's withdrawal from the European Union with regard to the medicinal products for human and veterinary use within the framework of the centralised procedure: http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2017/05/news_detail_002757.jsp&mid=WC0b01ac058004d5c1

[2] CMDh Questions and Answers related to the United Kingdom's withdrawal from the European Union with regard to national authorised medicinal products for human use: http://www.hma.eu/fileadmin/dateien/Human_Medicines/CMD_h_/BREXIT/CMDh_361_2017.pdf

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- Due to uncertainty over the nature of the final EU Exit deal, and the need to be prepared in advance of Day One, companies are already questioning the usefulness of Scientific Advice Meetings with MHRA and are moving away from using MHRA as a Reference Member State (RMS), a Concerned Member State (CMS) or a rapporteur in licensing applications. This means new products which are available in the EU will not be made available in the UK unless a mutual recognition agreement is put in place, as a national licensing scheme is likely to add complexity and unnecessary additional regulatory burden. As a minimum, MHRA must respect decisions made in the EU and adopt them in the UK with minimal or no additional assessment.
- Current EU legislation specifies that a Marketing Authorisation holder has to be established in an EU country in order to market a medicine in the EU. Once the UK leaves, any UK Marketing Authorisation holder currently exporting to the EU will no longer be able to do so unless they are also established in another EU country. Equally an EU Marketing Authorisation holder could not supply to the UK. As a minimum, the UK will need to continue to recognise Marketing Authorisation holders based in other EU countries, or a number of self care products currently on the shelves in the UK will disappear.
- It will be important to ensure that for both retrospective and future supply of medicines, the reference product for a licence application can continue to be in the EU (for a UK submission) and in the UK (for an EU submission) to prevent products being withdrawn from either market.
- OTC medicines are subject to clinical testing requirements and should continue to be. The UK should recognise and meet Good Clinical Practice and accept studies which meet Good Clinical Practice from the EU and globally.
- Unnecessary regulatory divergence should be avoided and mutually recognised roles, standards and testing procedures agreed to ensure trade with the EU can continue effectively and products can be imported without retesting or re-release. Where standards cannot be mutually agreed, other solutions must be sought, for example, if separate EU and UK tests must be carried out, it may be possible for the same testing facility to carry out both tests, or carry out a test that can be recognised for both UK and EU purposes.

Patient safety

- We believe it is important for MHRA to retain its status as an equal partner on the Pharmacovigilance Risk Assessment Committee (PRAC) of the EMA. As an absolute minimum for patient safety MHRA must be guaranteed observer status and commit to reviewing and reflecting PRAC assessments in the UK.
- The UK is currently part of the EU pharmacovigilance surveillance system, EudraVigilance, which manages and analyses information on suspected adverse reactions to medicines which have been authorised in the EEA. The EMA operates the system on behalf of the EU medicines regulatory network.

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- Access to this data is a critical patient safety issue both for the UK and the EU27. If information is not shared about adverse events in a systematic way to allow patterns and trends to be identified potential problems with medicines will not be identified. The UK has invested in the updates necessary to be ready for the new EudraVigilance system which launches in November 2017. There is not time to build a new UK based system by March 2019 nor would a UK system provide the same level of public safety as it would cover a much smaller population.
- Global pharmacovigilance structures are not recorded consistently or to a high enough standard to replace the level of protection afforded by the EU system and are therefore not a viable alternative.
- As a minimum, a partnership arrangement must be agreed to facilitate the sharing of pharmacovigilance information between the UK and the EU27 and the UK should align with EU timetables for Periodic Safety Update Reports (PSURs) and Periodic Benefit:Risk Evaluation Reports (PBRERs).
- The Falsified Medicines Directive aims to protect the public from fake medicines. It should be applied in the UK and the UK should continue to link into the European database.

Qualified persons

- A qualified person (QP) is required to release medicines as batches are produced. QPs are highly trained individuals who need extensive experience to effectively carry out their vital role. There are not enough QPs in the UK and due to the years of training required, it will not be straightforward to recruit more. The UK should seek mutual recognition agreements for quality testing and batch release in the EU. As a minimum, the UK will need to accept products QP tested and released within the EU without additional QP release in the UK.
- Qualified Persons Responsible For Pharmacovigilance (QPPVs) have a critical role. Ensuring that there are enough QPPVs available is vital for public safety. Currently QPPVs for EU registered products must reside in the EU and must hold an EU qualification. The UK should ensure mutual recognition agreements are in place with the EU for QPPV and EU and UK qualifications are mutually recognised.
- There is potential that QP and QPPV roles will have to be duplicated in the UK and the EU unless mutual recognition is put in place.

Supply chain (quality)

- Currently, there are legally binding quality standards for all medicinal products in States which are members of the European Pharmacopoeia (“Ph. Eur.”). A country does not have to be in the EU to be a member of the European Pharmacopoeia Commission therefore PAGB believes the UK should remain a member and continue to apply Ph.Eur. standards to help facilitate approvals across the EU and to ensure the continued safety of products available to the UK public.
- The UK must maintain alignment with EU guidelines and standards, such as Good Manufacturing Practice and Good Distribution Practice, to ensure the continued availability of medicines on the shelves. Introducing new requirements which could lead to divergence between the UK and EU would result in current processes having to be revised. Any level of divergence from current agreed EU guidelines will lead to a duplication of processes and additional testing at the border.

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- Certificates of suitability (CEPs) are currently issued by the European Directorate for the Quality of Medicines and Healthcare (EDQM), a Directorate of the Council of Europe. By certifying suitability centrally, the need to review the same information repeatedly across different products is removed. This is important, particularly for OTC medicines as the specific substances within medicines can change frequently. It needs to be ensured that CEPs will continue to be recognised in the UK and that CEPs can continue to be generated and approved for ingredients made in the UK for export to the EU.

Supply chain (trade)

- The safety check and quality standards that medicines are subject to are relied on globally. This means that ongoing collaboration and input into EU standards, such as Good Manufacturing Practice and Good Distribution Practice, is vital for international trade. As a minimum, the UK would need to align with these standards.
- Having assessed the possible impact on supply we can see that non-tariff barriers caused by additional regulatory requirements on either side of a "hard" border without mutual recognition would delay the availability, and increase the cost, of OTC products to the public.
- With regards rules of origin and tariffs, the UK should, as a contingency, seek to adopt the EU schedule of commitments at the World Trade Organisation (WTO) as soon as possible to minimise the risk of controversy and delay in the future.

Self care medical devices

Self care medical devices are products intended to help people self treat ailments or symptoms and which achieve this effect by a physical mode of action in or on the body. Unlike medicines, they do not achieve their principle effect by pharmacological, immunological or metabolic means. Registrations for self care medical devices relate to the product as a whole, so some regulatory requirements are specific to this category of medical devices.

For self care medical devices, there are similar challenges to medicines in relation to ensuring checks and balances are in place via a system of Authorised Representative and notified bodies which all interconnect at an EU level.

Medical Devices Regulation

- The Medical Device Regulation (2017) marks the gold-standard for regulation and should be implemented in full in the UK in line with the timeline defined in the Regulation.
- The current regulation in force in the UK (Medical Devices Regulation 2002) implements European Directives published in the 1990s and therefore does not take account of significant developments in the MedTech industry in recent years. Significant changes to the current legislation are needed ensure safety and to restore public confidence in these products. Implementing the Medical Device Regulation, which has been carefully developed over a number of years, is the most effective way to ensure appropriate regulation of these products in the UK.

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- Learning from the shortcomings of the 2002 Regulation, the Medical Devices Regulation (2017) introduces more scrutiny, stricter clinical requirements, greater surveillance and vigilance, and improved transparency and traceability. It is a ready-made solution to the shortcomings of the existing regulation.
- Furthermore, failure to adopt the Medical Devices Regulation would leave the UK vulnerable to regulatory divergence at a time when the global trend is for regulatory convergence (Turkey, Switzerland and Australia already use the European system as this is widely acknowledged to be the gold standard in MedTech regulation).
- CE marking is used to indicate a device's conformity with the Medical Devices Regulations. The CE mark is widely recognised, including beyond the EU and the EEA. Not only could divergence from the EU standards make trade with the EU more difficult but could also have a negative effect on global trade. It will be important for the UK to continue to recognise CE marks granted in any of the EU27 states and for a CE or equivalent mark granted in the UK to be recognised by the EU27.

Notified Bodies

- UK notified bodies make a significant and highly regarded contribution to the European medical devices framework and perform conformity assessments for many UK and EU27 manufacturers. UK notified bodies must continue to be able to operate within the existing European network to enable the regulatory network to continue to function effectively, thereby ensuring that the products on the market meet safety requirements.
- Notified Bodies can start to apply for designation under the Medical Devices Regulation in November 2017. PAGB believes UK notified bodies must continue to play a full role in the European medical devices network to enable manufacturers to plan for conformity assessment under the Medical Devices Regulation.

Patient Safety

- In the interests of public safety, the UK should continue to participate in the Eudamed (European Databank on Medical Devices) system of market surveillance and transparency for medical devices.

Food supplements

Food supplements may contain vitamins, minerals and other ingredients such as herbs, amino acids, amino sugars, enzymes and essential fatty acids that the body needs in very small amounts to work properly. Most of them cannot be manufactured by the body and need to come from the food we eat. Where people do not obtain enough of these nutrients from their diet, a supplement can be beneficial. They incorporate a range of end products from the wider food industry and will be affected by the same issues as the more general food industry, as well as having their own specific regulatory structure.

UK structures

- Responsibility for food legislation has been separated across three Government departments, DEFRA, the Department of Health and the Food Standards Agency.
- All three departments have experienced staffing cuts in recent years leaving them under-resourced and lacking the expertise required to deal with a repatriation of food regulation from the EU.

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- All food legislation relating to consumer safety and nutritional standards (but not agriculture and security of supply) should become the responsibility of one organisation, ideally the FSA. This needs to be sufficiently staffed and the current knowledge gaps addressed.

Imports

- The majority of food supplements are manufactured outside the UK and imported as finished products; those that are manufactured in the UK rely on imports of ingredients from a wide range of countries, in the EU and also from China, Australia, a number of African nations and the USA.
- If there is a 'hard Brexit', we expect that WTO trade tariffs will apply on imports. The global average import duty for food supplements is 12.8% with a minimum of 0% and a maximum of 150%. Tariffs on raw materials and finished products will vary by substance, for example products of animal origin (POAO) average at 40%. This means the cost of importing raw materials/ingredients and finished products will increase, so the price to the consumer will increase and/or it may no longer be commercially viable to manufacture or market products in the UK.
- Additional import tariffs and checks would put additional pressure on Border Inspection Post Personnel, therefore additional resources must be provided to reduce delays at the border. We would like to see mutual recognition agreements to avoid duplication and tariff free trade on food supplements between the UK and EU.
- There may be risks from accepting imports from the USA as these do not necessarily meet the standards set out in EU law and can contain substances which are currently prohibited by the EU (GMO's, growth hormones in meat and POAO, minerals which are not permitted for use in food supplements in the EU, such as germaninum, which is highly toxic, or vanadium, for which there is little safety data. These products from the USA should continue to be banned in the UK.

Exports

- As above, in a 'hard Brexit' scenario, it is expected that WTO trade tariffs will apply on exports which may make manufacture in the UK unviable.
- A 'hard Brexit, would also mean exports to the EU would be subject to border checks and companies would have to prove that products comply with all relevant legislation. This would require a paper trail of some significance, and would slow down the process of getting products, or raw materials, across the border into the EU. This is of particular concern in relation to products of animal origin such as gelatine, collagen, fish oils, glucosamine, whey products and amino acids which are all found in food supplements.
- The potential for the EU to set maximum and minimum levels for vitamins and minerals in food supplements (and fortified foods) once the UK has left the union could also impact negatively on UK export capabilities.

Divergence from EU law

- The majority of UK food law devolves from the EU; therefore, if UK companies wish to continue to trade with the EU they will need to ensure their products comply with EU regulation.
- For example, the legislation sets out the vitamins and minerals (including their chemical forms) which are permitted for use in food supplements.

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- From Day One these lists could diverge – if the EU adds or removes a substance there will be no guarantee that the UK will follow suit. Likewise, if the UK makes an amendment to allow a substance that is not permitted for use in the EU, any product containing that substance would not be eligible for export to the EU.
- If at all possible, the UK should maintain a list that mirrors the EU listing of vitamins, minerals and their sources that are permitted for use in food supplements
- With regard to maximum permitted levels, it would be appropriate for the current UK practice of adhering to the levels established by the 2003 Expert Group on Vitamins and Minerals (EVM) to continue. This would include the use of the established advisory statements alongside the 11 key nutrients if these used at higher levels. These standards are national and would not apply to the wider EU.
- Mutually recognised standards and testing procedures should be agreed to avoid unnecessary duplication.

Complexity

- There are multiple pieces of overlapping, interrelated, and sometimes contradictory legislation with which food supplements need to comply.
- The core legislation for food supplements is “hybrid legislation” which consists of EU Directives, Regulation(s) and Implementing Commission Decision(s).
- Much of this legislation also refers to other pieces of relevant legislation within the forum of food law; for example the Food Supplements Directive 2002/46/EC refers to EU labelling legislation as well as the food hygiene legislation and general food law. The EU Food Information for Consumers Regulation refers to general food law, additives legislation and food contact materials legislation.
- Unpicking this will be a lengthy and difficult process and will have to be done accurately or it could threaten public health.

Labelling

- The food industry has undergone several years of substantial change to the regulation of food labelling as old legislation was repealed and new legislation came into place.
- PAGB would like to see continued alignment with EU labelling regulations for food supplements. Work undertaken on behalf of DEFRA in 2010 indicated that costs for relabelling range from £2,430 to £3,860 per stock keeping unit (SKU), depending on the size of the company and the complexity of the packaging. Costs have since increased as a result of inflation and the value of sterling. Therefore, for a company with an average of 100 SKUs the cost for relabelling would run into the hundreds of thousands of pounds, meaning divergence from the EU rules is not economically viable.

PAGB, Vernon House, Sicilian Avenue, London, WC1A 2QS 020 7242 8331 info@pagb.co.uk www.pagb.co.uk

Opportunities

PAGB has reviewed and considered every area of regulation relating to over-the-counter medicines, self care medical devices and food supplements to look for opportunities where the UK could do things better outside of the EU. We have identified some areas where there could be opportunities for the UK to diverge from the EU position, but these are limited in scope. While these would be welcome changes, in many cases alignment with the EU position is preferable in the short-term and, therefore, the priority must be ensuring appropriate action is taken to mitigate the negative impact of the EU's withdrawal from the EU on the industry, as outlined above.

Over-the-counter medicines

- MHRA has been a leading agency in the reclassification of prescription-only medicines to over-the-counter, whether pharmacy or general sales list medicines. We would like to see MHRA continue to lead the way on reclassification. We would also welcome the introduction of a period of exclusivity for reclassified products, as is the case in the USA.

- PAGB would like to see a simplified process for registering over-the-counter medicines in the UK, particularly where they have already been assessed and registered in the EU.

- We would like to explore the scope for introducing more user-friendly language, more comprehensible names and labelling for our products.

- We would like to see the removal of the sunset clause which requires a Marketing Authorisation to lapse if the product has not been marketed for three years.

Self care medical devices

- PAGB has not identified any areas where it would be beneficial for the UK to diverge from the new Medical Devices Regulation, which we believe represents the gold-standard of regulation in this area and is, therefore, the right approach for the United Kingdom.

Food supplements

EU Exit affords the UK an opportunity to review and consolidate what is a complex area of law.

- We would like to see a principle-based approach to health and nutrition claims to allow greater innovation in the industry and improve consumer understanding. Specifically
  - We would like to see a useful degree of flexibility in wording to genuinely improve consumer understanding of individual claims and health issues generally.
  - We would like to see a reassessment of restrictions that currently prohibit nutrition claims which are capable of substantiation, for example "sugar reduced by 20%".
  - We would like to see requirements tailored so that communications with healthcare professionals are dealt with differently to communications with consumers, allowing for greater depth and detail. If claims can be scientifically substantiated, industry should be able to make these in communications with healthcare professionals.

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- We would like to see a change to the new claims process to allow for greater innovation in the UK when making new claims or dealing with claims which are currently stalled within the current system ("on hold" claims).

- We would like to see labelling information anchored in consumer understanding to allow labels to be adapted to reflect the fact that consumer understanding varies between different nutrients. Specifically:
  - We would like to see labelling considered as a whole with an emphasis on clarity of information rather than limiting the assessment to a restrictive interpretation of "field of view".
  - We would like the prohibition on additional information for consumers in allergen labelling to be removed, allowing boxed information about allergen content of food to appear on label.

- We would like to retain the use of currently approved additives in food supplements, and in particular the continuance of the use of technologically necessary additives in food supplements for infants and young children. There is no evidence that these additives are harmful and restricting their use will result in products being removed from the market with no alternative available. This would undermine an important public health message.

- We would like to see restrictions on novel foods rescinded as consumer safety can be ensured through the prohibitions and requirements of the Food Safety Act.

For further information, please contact:
PAGB, Vernon House, Sicilian Avenue, London, WC1A 2QS
info@pagb.co.uk
020 7242 8331
www.pagb.co.uk