

# Medicines and Healthcare products Regulatory Agency

## International Strategy



2017

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## Current Position

The Agency currently has a wide network across the globe with many interactions and collaborative activities with international partners, stakeholder and customers. These different interactions by the Divisions and Centres are driven by the variety of different needs of those respective areas. As such, different approaches may be required to ensure that the interactions are beneficial and that the Agency objectives, to ensure effective medical products are available to the public and are of appropriate quality and are acceptably safe, are met.

## Environment

In the current environment, it is appropriate to consider the Agency's International interactions and set in place a robust International Strategy to maintain our regulatory standing across the landscape for the benefit of UK public health, to enhance our brands and reputation and finally to align to wider strategies that are focused on ensuring that the UK remains an attractive place to do business.

While there may be some overlaps, this strategy is not aimed to duplicate the work being undertaken and resultant recommendations emerging from the Brexit negotiations. This strategy focuses on the international partnerships (current and future) and the value that can be exchanged, and that results from, these partnerships.

To underpin this overarching strategy, Divisions and Centres have developed international activity matrices and in some cases, Divisional or Centre specific international strategies. These more detailed documents will drive the specific activities for each area. However, this document will provide the glue that holds together and co-ordinates our overall approach to our current and future international interactions, with particular emphasis on those that would be most effectively delivered collaboratively, and to present a justified approach to prioritisation and resource allocation.

## The need for international partnerships

The fundamental driver for our international work is public health and our commitment to ensure we protect and safeguard the public. Our work also contributes to the UK Life Sciences agenda; it provides support to developing countries and provides opportunities for commercial growth.

The supply chain, regulatory system and standard setting processes are unquestionably international activities. Innovative capabilities can be enhanced by collaboration, nationally and internationally. International partnerships and contractual arrangements bring a number of benefits, not only do they enable the exchange of information, they have potential to bring funding into the UK, they contribute to our strong reputation that the UK is a place to do business with (and in) and upskills our work force. Collaborative work programmes supports manufacture of high quality medical products, but also enable opportunities for harmonisation and burden reduction.

From our partner's perspective, we provide knowledge, skills and experience and can support them while they develop and grow their own regulatory infrastructure, particularly important for countries with developing regulatory systems. This in turn contributes to the delivery of high quality medical products into the supply chain from these important markets.

## Our vision

The following is from the Agency's Corporate Plan:

***“Vision, scope and partnerships:*** *The strategic priorities proposed under Theme 1 reflect our commitment to maximising the Agency's public health impact both within the UK public health and healthcare systems and through our active engagement with European and global regulatory networks. In particular, there is a renewed focus on establishing strong, effective and purposeful partnerships, as highlighted under ‘cross-cutting themes’.*”

## Strategic questions

To achieve our vision, we must consider the strategic questions that need to be addressed by the Agency or by Divisions/Centres:

- *Who are our most important international partners and what do we need from each other in order to succeed?*
- *How will we work with international partners to ensure the supply of safer medicines and medical devices?*
- *How will we influence internationally to enhance the quality and standard of medical products in the global supply chain?*
- *What do we need to do to continue to be recognised internationally as a leader and a strong strategic partner?*
- *What do we need to do to maintain our global influence to ensure we maximise our public health impact?*

## Underpinning principles

In order to develop an aligned International Strategy, all areas of the Agency must be aligned to the following principles:

- *Work together (recognising our different needs) as a joined up, united organisation to ensure we maintain our position as an influential leader, whether in regulation, patient safety, standards, science, research or innovation.*
- *Continue to enhance our scientific and technical capacity and capabilities to increase our international reputation for the purposes of public health and Life Sciences.*
- *Share information, experience and knowledge with our international partners to improve the quality of the products available in the global supply chain.*
- *Allocate sufficient time to build and foster international relationships.*
- *Prioritise resource to ensure safe and effective medical products are available to the public.*

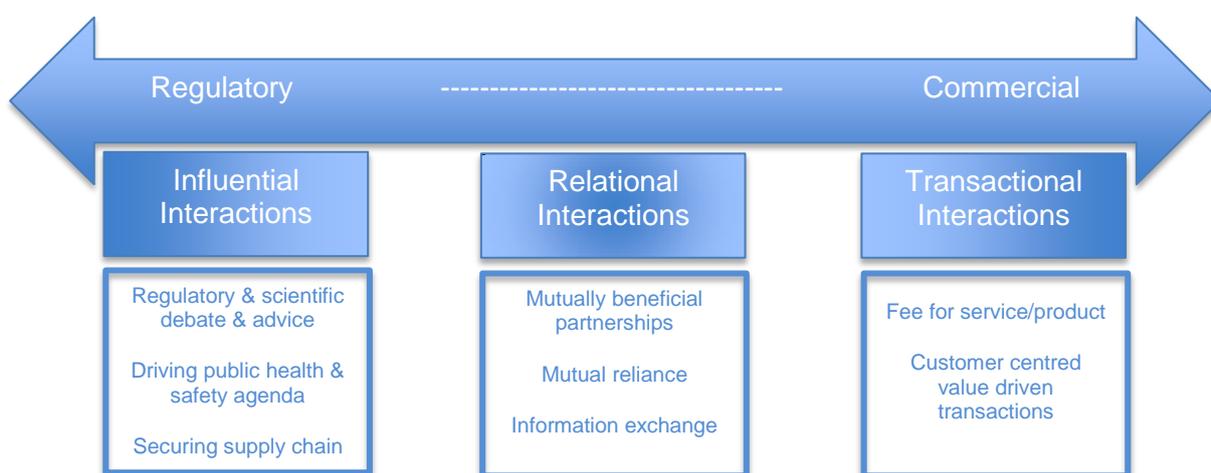
- *Align our international work, where possible and appropriate, with other government agendas, policies and strategies.*

## Prioritising our activities

Any international work must align with our Corporate and Business plans/strategies and our overarching aim to safeguard and protect the public, i.e. there should always be a public health driver or one that supports the Life Sciences agenda.

In order to consider which international activities are deemed most important, we must first consider the type of interaction. The Regulatory-Commercial Continuum (Figure 1) depicts the different spread of interactions with which the Agency might be involved. From regulatory influence, relational or two-way interactions, through to well defined commercial transactions. All have different characteristics and varying benefits.

Figure 1: Regulatory-Commercial Continuum



Once we have determined the type of stakeholder interaction from the Continuum, the relevant criteria in Figure 2 should be used in order to validate the decision to allocate resource to the international interaction.

Figure 2: Criteria to Prioritise International Interactions

The criteria below should be considered in the context of the interaction enabling us (by influence, relationship building or increased revenue) to maximise our public health impact or to support the Life Sciences agenda.

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- The country/partner has a significant role in the supply of medical products to the UK
  - Enhances the quality and safety of medical products in the global supply chain
  - Reduces substandard and falsified medical products in the global supply chain
  - There is potential for greater (regulatory or scientific) influence
  - Aligns or supports other activities ongoing across the agency/government
  - There is an opportunity to develop international or global regulatory standards
  - There is an opportunity to improve patient safety and vigilance activities on an international level
  - The activity enhances harmonisation and reduces burden
  - There are opportunities to provide advice, upskill others or learn from others
  - There are opportunities for mutual reliance or recognition
  - The interaction supports a response to a global challenge or crisis
  - There are opportunities for information exchange on e.g. legislation, safety monitoring, compliance issues, criminality etc
  - There is an opportunity for innovation or to support the life sciences industry
  - There is opportunity to market and promote the work of the Agency
  - There is potential for market penetration or market growth.
  - There are opportunities to increase sales and revenue of the Agency's products and services.
  - There are opportunities to differentiate our product and service portfolio to meet an unmet need in the market, e.g. solutions for other regulators

## Future Opportunities

Clearly, our interactions with partners in China, India, the US and Europe remain of upmost importance, as do our emerging relationships with the likes of, for example, Japan and South America.

Additionally, building on elements of our commercial and growth strategy, we should examine which otherwise non-aligned world countries we might work with and who might, in essence, purchase our regulatory capacity.

Notwithstanding some of these more longer-term objectives, more concrete and immediate potential opportunities for specific countries or stakeholder groups have been identified from the individual Division or Centre matrices as trends across the Agency.

There will be additional future opportunities with these and other countries; however these will be influenced by the outcome of Brexit negotiations, the ongoing work of the Department for International Trade and that of the Office for Life Sciences. It will be important that an iterative link is maintained between the Agency's work and these work streams as they progress.

## Measurable Outputs

It is acknowledged that the international interactions will only be undertaken if they meet the criteria presented earlier in this paper. As such, it is therefore assumed that the international work will be contributing towards our overarching aim to protect and safeguard the public. In order to determine the level of success, a number of outputs have been identified below which can be monitored and measured:

- Number of MoUs signed and maintained (and associated work progressed within agreed timescales).
- Increased number of invitations to speak, participate and contribute to influential committees, working groups, international meetings, symposia and conferences.
- Increased engagement of Industry partners, measured by contribution to liaison and working groups.
- Increased engagement with relevant Healthcare Professionals, measured by use and contribution to CPRD.
- Market growth and increased sales of Agency products and services, measured by increased revenue.
- Training and staff exchanges completed which enable the Agency to influence and improve compliance of industry activities, compliance monitoring by the authorities, approval processes, safety monitoring and device regulation. Evidenced by higher quality products leading to a reduced number of compliance issues.
- Enhanced reputation and increase in brand loyalty evidenced by Demonstrable increase in influence and an increase in support for MHRA-advocated positions/direction.
- Mutual Reliance Agreements

## Next Steps

### Resource & Finance

From an Agency perspective, the co-ordinated approach to our international work should be undertaken primarily with the current resources and due to the more aligned approach, should result in greater benefit and value, using the same resource more effectively.

It should be noted that having greater oversight and a more cohesive approach to our international work will not mean a greater level of bureaucracy. As currently managed, the Divisional or Centre Director will be responsible for overseeing international interactions for their respective Divisions or Centres. Where resource is limited, criteria presented earlier in this strategy will be used to prioritise international travel.

## Implementation

It is acknowledged that macro-environmental factors are constantly changing and while this International Strategy provides the guiding principles and prioritisation criteria, it is unrealistic to expect this document to define the work programme for any extensive period of time. Economic shocks, changing political policy, new innovative technologies and other such factors will result in a comprehensive review of the International work programme.

Therefore, in order to develop and implement the principles and criteria in this strategy effectively for long term success, Divisional and Centre representatives will be identified and will meet periodically (e.g. every 6 months) to update respective International Priority Work Matrices and to identify areas of potential overlap, to share information on visits undertaken and those forthcoming and to co-ordinate communication of the work programme to all areas of the Agency. The team will be chaired by a senior (Director Level) high profile lead for International Relations.

To facilitate these activities, a central repository will be maintained to store all visit agenda, reports and MoUs/agreements. A set of KPIs will be developed, agreed and reported to CET at least annually. In addition, Policy Division will update the representatives as and when visit requests are received, prioritising in line with those identified in this Strategy. Equally when we are proactive, Divisional or Centre representatives will keep other representatives informed, this will include the Policy Division representative. Divisional Directors remain responsible for agreeing (or not) the travel associated with international work, within their teams

The Divisional and Centre representative will together consider requests more broadly to determine if there are opportunities to promote the wider work of the Agency. International interactions (here or overseas) will be the responsibility of the lead Division for practical reasons; however Policy Division will provide support to coordinate those visits which cut across the Agency. Additionally, and as deemed necessary, advice and support will be provided by the Communications Division in order to ensure that any marketing and promotional opportunities are exploited. For example, the Communications Division may provide access to marketing collateral for Agency representatives, travelling overseas, to promote the relevant products and services of the Agency's portfolio.

## Recommended Actions

For current international interactions already planned, representatives from across the Agency will meet (by end April 2017):

- a) Reinforcing links at CEO and senior level with China to the level we have with India for the purposes of sharing information, building capacity and in relation to oversight of the supply chain, for both medicines and devices.

- b) Strengthening international links including with Australia, Switzerland, Singapore and Canada for the purposes of work sharing and regulatory co-operation;
- c) Further exploration of opportunities to work with for example, the Gates Foundation, around supporting other countries, compatible with the Agency's funding status;
- d) Further strengthen work with Japan in the innovation space, exploiting opportunities presented by existing planned visits.
- e) Reinforce links with the FDA once they have a new Commissioner given the global importance of FDA and ICMRA
- f) To identify areas of potential overlap for trips and interactions already planned for 2017/18
- g) To consider whether any of the upcoming trips, deemed to be high priority, might be enhanced by representation from elsewhere in the Agency or whether those already travelling could be briefed further
- h) To look for opportunities where additional bilateral meetings could be held in the margins of international interactions/trips already planned

Some new key areas of focus for the Agency over the next 12 months might include:

- a) Continue with our efforts to build close working relationships with key international partners by attending globally recognised meetings, such as HMA, ICMRA, PIC/s, ICH etc
- b) To consider a programme of focussed visits to China for example, with x-Agency representation.
- c) To consider the possibility of staff exchange opportunities for e.g. China, India and US and to progress with broad input from across the Agency.
- d) To consider support for training initiatives, such as those organised by the WHO, for developing countries.
- e) Following on from successfully hosting other events such as PIC/s, to consider whether there would be value in hosting another International Meeting, such as the 2019 OMCL network meeting (request has been made to the UK)
- f) To utilise industry trade groups to reach out to members to promote the work of the Agency.

Note: We must continue to ensure that we use our resource wisely, and with the right level of representation from across the Agency. It is also acknowledged that some of the proposals will be undertaken by the CEO.

## Appendix 1: Sector Snapshot

The MHRA markets cover

- Pharmaceuticals
- Medical Devices
- NIBSC market
- CPRD market

There are overlaps between these areas, particularly pharmaceuticals and devices, where there are rapid and significant developments in borderlines, companion diagnostics and genomics.

### The Pharmaceutical Market

India currently “supply 20 per cent of global generic medicines market exports in terms of volume, making the country the largest provider of generic medicines globally and expected to expand even further in coming years... India has also maintained its lead over China in pharmaceutical exports with a year-on-year growth of 11.44 per cent to US\$ 12.91 billion in FY 2015-16, according to data from the Ministry of Commerce and Industry” (IBEF, 2017).

China is the world’s largest producer of pharmaceutical ingredients and China’s pharmaceutical market value is estimated to reach \$158 billion in 2016 and \$315 billion in 2020. This increase will see China’s pharmaceutical market become the second largest in the world...China covers 40 percent of global APIs production. Low prices, good quality, and bulk production are main advantages for China being a global leader on APIs production. Now, many Chinese manufacturers are looking to strengthen ties with European and Indian markets by investing in APIs, generics, biologics, biosimilar, finished formulation, and packaging” (ITA, 2016).

The Business Monitor International Ltd reported (BMI, 2016) that:

- *“The UK is ranked as the second most attractive market to pharmaceutical investors in the Western Europe region, standing slightly below Germany and above Austria. The UK’s score is boosted by its multibillion dollar drug market and relatively high sector value growth.*
- *The leading export destinations for UK-made medicines include other developed markets, led by the US, Germany, Spain, France, the Netherlands and Italy. The leading countries of medicines imports into the UK are Belgium, Ireland, Germany, the US and Switzerland, reflecting the advanced nature of the market.*
- *The UK’s pharmaceutical industry is one of the country’s major engines of research and innovation. The country has a world class science base and a strong level of financing allows companies to leverage the generous tax-climate and build world class companies employing thousands of skilled scientists and graduates.*

- *There are approximately 450 biotech firms in the UK, representing almost 20% of the European total. This makes the UK the second most mature country in the world after the US, with annual revenues of over USD5bn.*

The BMI’s pharmaceutical SWOT analysis for the UK is presented in Appendix 2 and details, among other things, two key strengths: that “the regulatory environment is one of the fairest and most transparent in the world” and that “the government-industry relationship is mostly one of collaboration” (ibid).

The UK’s pharmaceutical market is likely to continue to grow due to factors such as the changing demographic and the increase in chronic disease and long term illnesses prevalent in the elderly population. However, government campaigns, such as those to reduce smoking and alcohol consumption, will also influence the sector growth.

The UK generics market value equates to 16.8% of the European market at a value of \$8.3bn (MarketLine, 2016), which equates to 2.6% of the global market. The UK generics drug market is forecast to steadily grow (BMI, 2016), whereas the OTC and high-value parent drug markets are expected to remain relatively static, growing only slightly. “Despite the demand for patented medicines rising, innovative drug makers in the UK will continue to face revenue pressure from government cost-containment measures” (ibid). These measures include a shift from headline price adjustments for branded medicines supplied to the NHS, a growth limit would be applied on the overall cost, making this market less attractive.

Figure 1: Europe generics market geography segmentation: % share, by value, 2016. (Source: MarketLine, 2016)

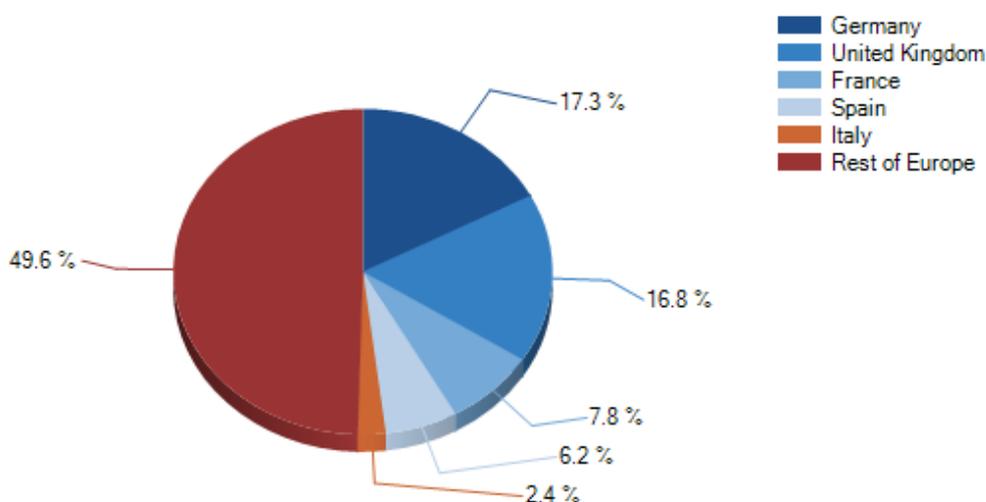
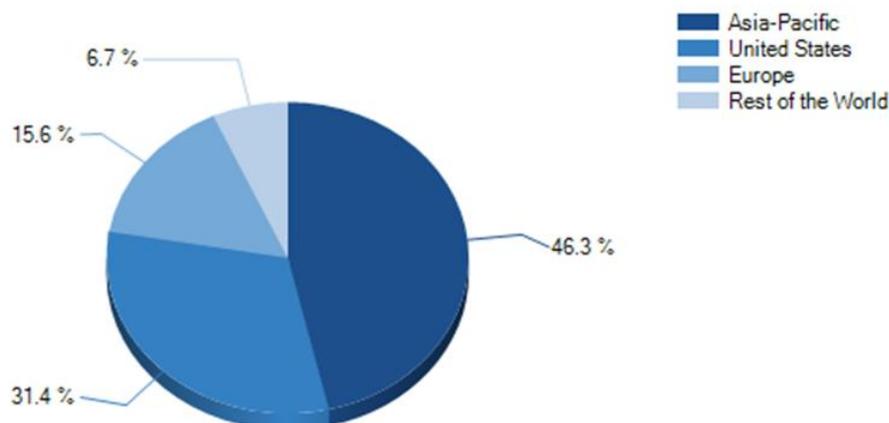


Figure 2: Global generics market geography segmentation: % share, by value, 2016. (Source: MarketLine, 2017)



The UK remains a major pharmaceutical producer and exporter. The industry's desire for cost-reduction, to maximise profits, has and will continue to result in outsourcing of production to low-cost locations, such as India and China. This outsourcing may in the long term stifle UK industry growth.

A search of the Sentinel product licensing database undertaken by the Agency's Information Centre revealed that just under half of all Product Licences (PLs), equating to approximately 6500 UK, name an Indian API site, ~2400 name an Italian site, German, UK and Chinese sites are each named on ~2000 PLs and US sites are named on ~1500 PLs.

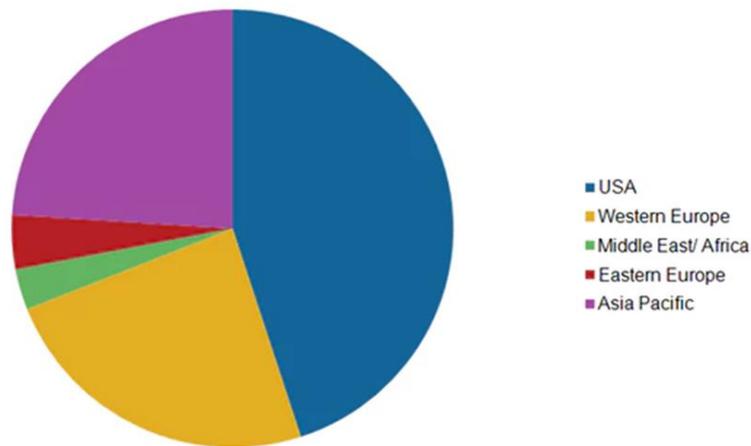
It is also worth noting the UK's position and strength as a partner with Europe, which provides opportunities for partnerships in the future. In 2016, the UK was the Reference Member State for 42% of DCP submissions, UK was rapporteur or co-rapporteur for 35 new products in the last 12 months, co-ordinator for 10% of scientific advice procedures, the UK GMDP Inspectors undertook ~25% of overseas inspections (CAPs) for Europe and ~20-25% non-CAP inspections.

### The Medical Devices Market

#### Geographic segmentation

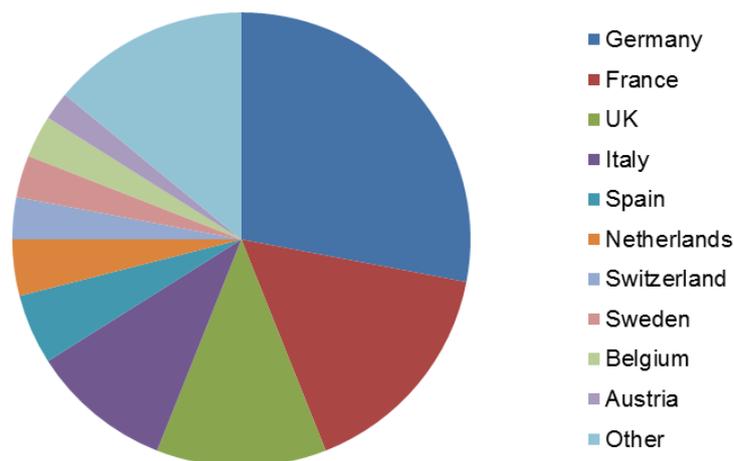
The US medical device industry is the global leader with sales of around \$136 billion, which represents approximately 45% of the global market, according to the US Government Accountability Office (or GAO) 2014 statistics. The geographical breakdown of the world market is shown in the pie chart below.

Geographic Segmentation



Source: Espicom, AMMI Analysis 2013

MedTech Europe breaks down the European market as follows:



The medical devices market is dominated by global US companies including Baxter, Beckman Coulter, Becton Dickinson, Boston Scientific, GE Healthcare Technologies, Johnson & Johnson, Medtronic, St. Jude and Stryker Corporation,. U.S. industry primarily faces competition from Germany (Siemens and Braun), Japan (Hitachi , Medical Corporation and Toshiba) and the Netherlands (Philips Electronics). In 2012, the top twelve companies in the medical devices industry controlled 45.9% of the global market.

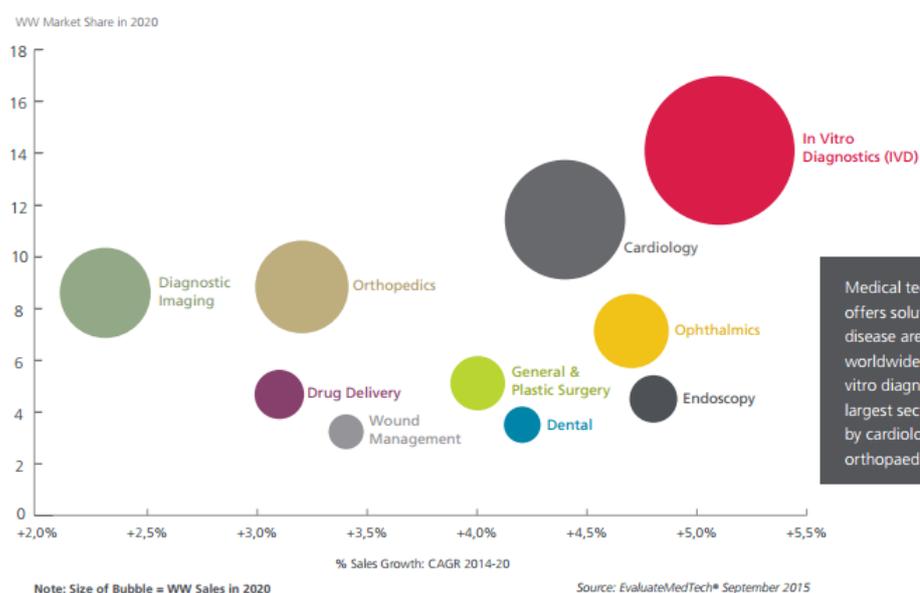
European medical technology industry employs more than 575,000 people. Germany has the highest absolute number of people employed in the medical technology sector, while the number of medtech employees per capita is highest in Switzerland and Ireland. In comparison, the US medical technology industry employs around 520,000 people while the European pharmaceutical industry employs 675,000 people.

There are almost 25,000 medical technology companies in Europe. Most of them are based in Germany, followed by the UK, Italy, Switzerland, Spain and France. Small and medium-sized companies (SMEs\*) make up almost 95% of the medical technology industry, the majority of which employ less than 50 people (small and micro-sized companies)

Medical technology is characterised by a constant flow of innovations, which are the results of a high level of research and development within the industry.

Major advances are being made in the areas of software, apps, artificial intelligence, genomics, companion diagnostics and 3D printing. These particularly contribute to forecasts of growth in the area of in vitro diagnostics

World medical technology market by area and sales growth, 2014-2020<sup>15</sup>



Medical technology offers solutions for many disease areas. On a worldwide perspective, in vitro diagnostics are the largest sector, followed by cardiology and orthopaedics<sup>15</sup>.

### The NIBSC Market

NIBSC's focus is on human biological medicines and diagnostic tests that rely on the identification and/or quantification of complex biological substances.

Biological medicines are already dominating the pharmaceutical market, with total sales of \$169bn in 2012 (IMS Health Thought Leadership, September 2013) and they are growing fast in number, clinical importance, and complexity. They are special materials which are manufactured or assayed by methods related to complex biology rather than physicochemical means, and need specific and bespoke approaches and equipment.

Biological medicines present huge opportunities but also significant, and unique, risks compared to small molecule drugs, particularly with regards to controlling their safety and potency. These risks shape the requirements of standardisation and control for biological

medicines and their dependence on biological assays for their analysis. This also necessarily implies dependence on biological standards and reference materials, and NIBSC provides over 90% of the global WHO International 'gold' Standards for biological medicines, from which the unitage for all other standards for biological medicines is derived.

The external landscape is changing rapidly, posing major challenges to standardisation and control of biologics.

- The world market for biological medicines is increasing rapidly, both in terms of overall usage and of the range and complexity of products available.
- Production of biological medicines is becoming increasingly global, with many new manufacturers entering the market from emerging economies such as China, Korea, India, Indonesia and Brazil. Sourcing of raw materials is also now global involving highly complex supply chains.
- The first generation of recombinant biologics are now at the end of their patent life opening the door to competitor products from around the world. These offer great opportunities for lower prices and increased global availability/affordability, but they also carry considerable risk, as subtle changes in manufacturing processes can dramatically affect safety and efficacy.

Medicines production is global, and NIBSC's global distribution of biological materials reflects this – we distribute materials to over 80 countries. In addition to providing measurement standards, NIBSC provides advice and regulatory input, independent batch testing of high risk biological medicinal products and collaborative research with groups from across the globe.

### CPRD Market

CPRD aims to be recognised globally as the preeminent longitudinal database of anonymised healthcare records. For more than 25 years, data provided by CPRD have been used in a range of academic, regulatory and commercial drug safety and epidemiological studies that have impacted on health care worldwide and resulted in over 1700 peer-reviewed publications. As the majority of the UK population has access to a national coordinated health service, the UK is in a unique global position to use clinical records in novel ways for patient recruitment, clinical trials management and follow up. CPRD is providing services which can capitalise on the health sector's need to deliver safer and more effective drugs in a real world setting by seamlessly integrating observational and interventional research through innovative use of clinical records. The industry is making significant investments in real world data and analytics to accelerate the bench-to-bedside process and deliver new therapies to patients. CPRD's real world services can support innovative developments and demonstrate value in both the pharmaceutical and medical device markets.

## Appendix 2: BMI Pharmaceutical SWOT Analysis for the UK

(Source: BMI, 2016)

### Strengths

- The UK's pharmaceutical market is among the 10 largest in the world.
- The UK is the main base for GlaxoSmithKline and AstraZeneca, two of the world's major multinationals, as well as a key site for most other drug majors.
- The regulatory environment is one of the fairest and most transparent in the world.
- The government-industry relationship is mostly one of collaboration.

### Weaknesses

- Government cost-cutting measures, including the promotion of generic drugs and branded product price cuts, have weighed on market growth.
- The National Institute for Health and Care Excellence (NICE)'s decisions, while not legally binding, has significantly affected reimbursement.
- The UK has lost some of its traditional appeal as a clinical trials destination, with concerns including registration times and red tape.

### Opportunities

- OTC market growth is driven by government support for self-medication and its positive attitude towards switching actives from prescribed to OTC status.
- Changes in the retail sector, such as increased pharmacy opening hours, primary care services in grocery stores and expanded pharmacy services and prescribing power for pharmacists, should help drive growth.

### Threats

- The government's cost-cutting policy, including an increasingly strict reimbursement environment, is expected to keep market growth at a modest level in the near term.
- The Brexit vote poses downside risks to the UK pharmaceutical industry, including a reduction of scientific funding in the UK and a decrease in a skilled labour force for the NHS.
- The branded drugs market is expected to be affected by the government's continuing focus on and promotion of the generic drug sector and schemes such as the Patient Access Scheme.
- Public pressure to reimburse all drugs, regardless of cost, may result in funding shortages and further cost containment measures.
- Patient access to innovative medicines, an increase in market access barriers to multinational drug makers and delays in the approvals of medicines.
- Stuttering economic performance to hamper growth of the OTC drug market.

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