



## Conference Report

The *Annual AESGP Reception in the European Parliament* in Brussels on 1 February 2011 and the AESGP Conference “*What regulation for food supplements and herbal medicinal products in Europe?*” on 2 February 2011 were again extremely well attended with well over 200 participants at each event.



In his welcome address at the *Annual AESGP Reception*, AESGP President **Hans REGENAUER** referred to the recognition of the important role of self-medication and to the numerous important political initiatives to which responsible self-care can make a major contribution, not least in the field of *active and healthy ageing* – one of the seven flagship initiatives addressed in the so-called ‘*Europe 2020 strategy*’. AESGP provided comprehensive comments to the consultation process and would be happy to be closely involved in the further process. In the last months AESGP was closely associated to the political debates on new legislation in relation to pharmacovigilance and falsified medicines. What is important now is a proper implementation of these new provisions, said Regenauer, and AESGP offered its expertise to all involved in the drafting of interpretation, guidelines or delegated acts so that the final impact would be in line with the legislator’s intentions.



**John DALLI**, the European Commissioner for Health and Consumer Policy, said in his address to the conference participants that healthcare is one of the most important social services; which is coming under increasing pressure from an ageing society, thus making a vibrant pharmaceutical industry, including the self-medication sector, more than necessary. After closing some gaps in the EU's pharmaceutical legislation in 2004 which made the decision-making process faster, more proposals were put forward in 2008, of which the aim on a more reliable system for product safety (pharmacovigilance) would - after its recent adoption - be applied from mid 2012. "It will contribute to ensuring better monitoring of, and communication on, the unwelcome side-effects of medicines and it will make the new system slimmer, safer and more reliable", said the Commissioner Dalli.

Dalli was confident that first-reading agreement on the new provisions on falsified medicines would be possible in the first quarter of 2011 following intensive negotiations between the parties last December. "I welcome the concept of a risk-based approach in the legislation. These rules apply to prescription-only medicines but offer the possibility to exceptionally include over the counter medicines on the basis of a risk evaluation." He called on AESGP and other stakeholders to continue working together on the implementation of the provisions on falsified medicines. "We are committed to a practical and cost effective implementation of the measures."

Concerning herbal medicines, Dalli mentioned that the seven-year transition period granted products on the market at the time of adoption of Directive 2004/24/EC was meant to facilitate maintaining these herbal medicines on the market. "There is no need to stress that even a long tradition of use does not exclude the possibility that there may be concerns with regard to the product's safety. Requirements for the authorisation of herbal medicines are less burdensome but this does not mean that they do not have to ensure the same level of protection of public health as the requirements for other medicines", said Dalli.

"Moving on to the specific topic of the Conference, we must not forget that food and medicines are not the same and they need to continue to be managed under a different legal framework. The distinction between medicines and food must be maintained in the interest of public health protection. At the same time we need close and coherent cooperation between the two responsible Agencies on medicines and food in assessing therapeutic indications for medicines and health claims for foods. This has to be done in full compliance with the relevant legislative frameworks."

After explaining the Commission's policy with regard to the adoption of non-botanical function claims for food, Dalli wondered what would happen to claims for botanicals. "Herbal substances or preparations can be used in food or herbal medicinal products. Different rules apply to different products; this is justified given the different statutory nature of the products. However, differences in rules can lead to important differences in the treatment of the same substance and, ultimately, in the level of information that is provided to consumers. Considering that consumers would, at least in some cases, find it difficult to see any difference in the products, there is a need for coherence across EU legislation", maintained Dalli. "We are using the time gained to consider options for the assessment and adoption of a permitted list of health claims for botanicals, one that respects the different legal frameworks, but ensures coherence and correct information of the consumers. In doing so we are conscious of the need to minimise disruption of the food supplement and herbal medicines markets as far as possible, and to keep in mind the borderline between medicines and food."

Dalli also mentioned that the Commission had launched a specific project on corporate social responsibility for non-prescription drugs. "This project, which is under the responsibility of Vice-



President Antonio Tajani, endeavours to identify the necessary elements for an informed and adequate uptake of medicines after their switch from prescription to non-prescription medicines.”

To conclude, Dalli mentioned that all EU citizens have the right to have access to the same medicines throughout the entire EU. “Industry has an important role to play in this and I count on your support. I call on you to work with me to put an end to these persisting inequalities. Only by working together will we be able to achieve our common objectives: the highest level possible of public health protection and patient’s confidence in safe, efficacious and high quality medicines.”

## WHICH CLAIMS FOR FOOD SUPPLEMENTS IN EUROPE?

### The legislative and regulatory framework for health and nutrition claims

This session was chaired by **Dagmar ROTH-BEHRENDT**, Vice-President of the European Parliament, who made it clear from the outset that she would like to see a clear distinction between medicinal products and food supplements.



Participants eagerly awaited the presentation by **Paola TESTORI-COGGI**, the Director General of the European Commission’s Directorate-General for Health and Consumers (DG SANCO), on the implementation of the [Nutrition and Health Claims Regulation](#)<sup>1</sup>, which she described as one of the most important and controversial pieces of European legislation in the food area. The implementation process proved particularly difficult as “the Member States, particularly at the beginning, did not do all the work they were supposed to do” and “overwhelmed” the European Commission with more than 44 000 ‘function’ health claims (so-called Article 13 health claims). It was therefore “unsurprising” that the process had for the time being led to negative evaluations for a large proportion of these claims by the European Food Safety Authority, the body in charge of the scientific evaluation.

The implementation of the Nutrition and Health Claims Regulation raised concerns among certain operators and Member States in particular with regard to two issues, i.e. the timing of adoption of the Community list of permitted ‘function’ claims (Article 13) and the level of scientific substantiation which is referred to in the evaluation process.

<sup>1</sup> Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods



As regards the **timing**, the European Commission had, according to Testori, “demonstrated flexibility” by deciding to abandon the process originally envisaged and based on the adoption of the Community list in multiple batches. In a [press release](#) dated 27 September 2010, the European Commission announced a restructured adoption process based on two steps, i.e. the adoption of the list of permitted health claims for all substances other than botanicals first, and subsequent consideration of claims relating to ‘botanicals’. With the evaluation by EFSA of all claims not concerning ‘botanicals’ scheduled to be completed by June 2011, the Commission hoped to be in a position to adopt the final list of non-botanical general function claims by late 2011-early 2012. “This is an ambitious project which implies a “huge amount of work” and for which the cooperation of the Member States, coupled with constructive contributions of stakeholders, will be absolutely necessary”, said Testori.

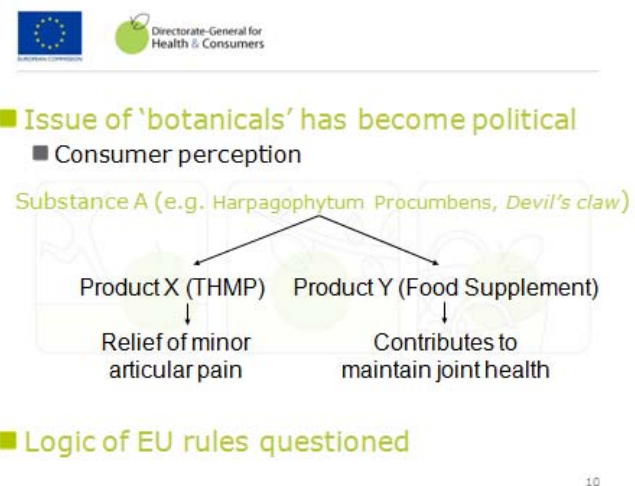
With regard to the **scientific substantiation**, Testori noted that under the Regulation the European Food Safety Authority is asked to carry out a scientific assessment of the “highest possible standard”. The European Commission does not intend to enter in the work of the risk assessor ; however it sees a need to (a) define a clearer understanding of the level of substantiation which is required, for instance through appropriate indicators and (b) envisage solutions for those “grey zones” that can be present in scientific evaluations.

Concerns had been raised by some Member States and economic operators with regard to certain ingredients mainly used in food supplements such as ‘botanicals’ and ‘substances other than vitamins and minerals’ such as glucosamine. Food supplements are more and more frequently cited as ‘borderline products’ as some of the ingredients used are common to foods and medicinal products depending on the legislation in place at EU Member State level.

The Commission has opened a particular reflection on how to deal with health claims on botanicals in light of the existing regulatory framework for the use of herbal ingredients in food supplements. Testori noted that it may happen that the same botanical ingredient e.g. *Harpagophytum procumbens* or Devil’s claw, is used in products that are placed on the market in two different legal categories, i.e. as a traditional herbal medicinal product (under the Traditional Herbal Medicinal Products Directive) on the one hand and as a food supplement (under the Food Supplements Directive) on the other. While the appreciation of the value of “traditional use” is entirely different between the two pieces of legislation, the current situation allows for the time being the use of the therapeutic indication “*relief of minor articular pain*” for Devil’s claw when used in traditional herbal medicinal products and of the health claim “*contributes to maintaining joint health*” for the same substance when used in food supplements. “Is this difference understandable for the average European consumer?”, Testori wondered, adding that the system in place should be clear for economic operators and consumers alike.

Several questions are therefore still open for the European Commission:

- Do we need to have a different treatment for botanical substances used in traditional herbal medicinal products and in food supplements?






- If no change is envisaged in the evaluation approach for health claims for botanical ingredients in food / food supplements, are we prepared to proceed with the full implementation of the Nutrition and Health Claims Regulation?
- In case a change in approach is envisaged, how can we make sure that the following elements are taken into account and treated in a balanced manner?
  - clear and understandable consumer information
  - product safety – concern for botanicals
  - product quality – linked to safety, means of extraction, preparation and manufacturing practices (“under the medicinal framework the outcome is clearly a safe and quality product – a certain level of quality has also to be guaranteed under the framework food supplements”).

In any case, concluded Testori, the European Commission will have to take the impact of any decision on the food and medicinal products market into account as well as guarantee appropriate safety and consumer information, minimise market disruption for economic operators, ensure a reasonable timing and appropriate legal robustness.

### Scientific evaluation of health and nutrition claims

The chair of the EFSA *Scientific Panel on Dietetic Products, Nutrition and Allergies* (NDA Panel), **Albert FLYNN**, presented the role of the European Food Safety Authority in relation to the scientific evaluation of health claims. In the words of the Nutrition and Health Claims Regulation, these should only be authorised for use in the Community after a “*scientific assessment of the highest possible standard*”.

**EFSA health claims evaluation progress (Jan, 2011)**



**Applications (Art 13.5/14):**

- ~ 100 adopted and published
- within legal deadlines

**Art 13.1 list:**

- **challenges** for EFSA
  - large number of claims (over 4,500)
  - poor quality of information for many claims
- **progressive adoption/publication** of opinions (over 1700 to date)
  - workload management, transparency
- complete by June 2011 (except for botanicals)

The Article 13 health claims process provided “significant challenges” for EFSA, both in terms of the large number of health claims received for scientific evaluation (over 4 500) and the poor quality of information that was submitted for many claims. For reasons of workload management and transparency, the Authority decided to adopt and publish its opinions in a progressive way and, following the publication of over 1 700 opinions to date, EFSA is now expected to complete the evaluation of all health claims other than “botanicals” by the end of June 2011.

Part of the tasks carried out by EFSA in the evaluation process lie in the further explanation / clarification of what “generally accepted scientific evidence” is given that this is not clearly spelled out in regulation. Flynn acknowledged in this context that “health claims are technically complex” and made it clear that EFSA is well aware of the need for guidance, which was already provided in many areas (e.g. [preparation and presentation of applications for Article 13.5/Article 14 health claims](#), [general principles for substantiation of health claims](#) and scientific requirements for substantiation of specific types of health claims). This is complemented by a “significant amount of dialogue between EFSA staff and applicants” before an application is accepted and during the scientific evaluation.

Flynn noted that EFSA’s work in the area of *guidance on scientific requirements for substantiation of specific types of health claims* has “no precedent” at global level as the European Food Safety



Authority is in many cases defining for the first time which scientific requirements are needed for some claims; these scientific requirements are established progressively – as claims are received and evaluated. The “significant body of opinions” already published is now in the process of being consolidated in guidance documents in selected areas (e.g. health claims related to gut and immune function), with extensive stakeholder consultation.

The complexity of the legal framework applicable to health claims and the difference of the European approach if compared to other legislations was also highlighted through the example of Article 14 health claims which refer to the reduction of a risk factor in the development of a disease (rather than to the reduction of the risk itself as is the case in the United States). EFSA has provided specific guidance on what a disease risk factor is and defined it as a “*physiological factor associated with the risk of a disease that may serve as a predictor of development of that disease*”.

The relationship of the risk factor to the development of the disease should be biologically plausible. While some risk factors are well-established, e.g. elevated LDL-cholesterol and coronary heart disease, many others are not and will be subject to a case by case judgment by the NDA Panel.

Flynn noted that pertinent studies for the substantiation of health claims are studies:

- with appropriate design and quality
- carried out with the exact food/constituent for which the claim is proposed
- with conditions of use adequately reflected in the human studies submitted
- with appropriate (i.e. generally accepted by experts in the field) outcome measures of the claimed effect, and
- with a study group representative of the target group (extrapolation to the target population is in principle possible but only after a case by case assessment).

Discussions are currently taking place between EFSA and the European Commission / Member States on the admissibility of some applications for claims that specify target population groups other than the general (healthy) population. This adds to the more general issue of the borderline between some health claims and medicinal claims (which are not allowed under European food legislation).

Conclusions

- **EFSA progress** in evaluation of health claims
  - Art. 13.5/14 applications - all within legal deadlines
  - Art 13.1 claims (except botanicals) complete by June 2011
  - EFSA is committed to maintaining the **quality** and **timeliness** of the evaluations
- Health claims are **technically complex**
  - **no precedent** for evaluation of most claims
  - EFSA defining **scientific requirements** for many claims for the **first time**
  - EFSA is committed to **assisting applicants** by providing additional **guidance** and through ongoing **dialogue**



## IMPLEMENTATION / ENFORCEMENT OF THE NUTRITION AND HEALTH CLAIMS REGULATION

Under the Chair of MEP **Antonyia PARVANOVA** (Group of the Alliance of Liberals and Democrats for Europe, Bulgaria), representatives of national authorities in the area of food control gave an insight into the Nutrition and Health Claims Regulation was implemented and enforced in their country.



**Julie UNZEITIG** of the General Directorate for Competition Policy, Consumer Affairs and Fraud Control (DGCCRF) in France explained the Member States' involvement in the adoption process of the Union list of authorised general function health claims. Work is ongoing with the European Commission on claim wordings (Member States would like the wording to stay as close as possible to the scientific formulation suggested by the European Food Safety Authority but consumer comprehension should also be taken into account) and on conditions of use. Until the Union list is adopted, the transition measures foreseen in the Claims Regulation apply and, without prejudice to the national provisions and the general conditions of Regulation 1924/2006, the responsible Authorities may request a food business operator using a health claim to produce some scientific evidence justifying the use of the claim.



### Establishing the Union list

Member States are currently working with the Commission on:

#### Claims with positive opinions

- **Claim wording and consumer comprehension**  
Must stay as close as possible to the scientific wording, but taking into account consumer comprehension (Article 5.2)
- **Conditions of use**
  - Must take into account several inputs (science, technology, safety, etc.)
  - Must be scientifically pertinent and operational (implementation + control)

#### Claims with negative opinions




**Anita LASER REUTERSWÄRD** of the National Food Administration in Sweden mentioned that up to now positive opinions had been issued by EFSA on 39 nutrients (including 13 vitamins and 14

**Questions for future on health claims:  
The food industry**

- The food industry is not very interested in using generic claims – they want exclusive marketing tools
- How will they “pick and choose” among claims for vitamins and minerals?
- Will the food industry now focus on article 10.3 claims – which will not occur on any list ?

**Article 10.3.** Reference to general, non-specific benefits of the nutrient or food for overall good health or health-related well-being **may only be made if accompanied by a specific health claim included in the lists provided for in Article 13 or 14.**

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Anita Laser R. 2 Feb. 2011

minerals. She highlighted the fact that health claims from the first three batches included 10 different claim wordings for vitamin C alone, while several nutrients had claimed to have the same effect, i.e. the “*protection of cell constituents from oxidative stress*”. According to Laser, consumers already know that they need (some) vitamins and minerals, and she wondered whether they are really interested in / actually understand functional claims which are only fragments of nutrition knowledge. She also observed that there is lack of scientific results from

consumer studies for the formulation of the wordings of health claims in the risk management process. Overall, the food industry will have to address several questions in the near future.

**Amire MAHMOOD** of the Federal Ministry of Health in Austria expressed support for a rapid adoption of the Union list of permitted Article 13 health claims and explained that the enforcement of some of the provisions included in the Claims Regulation is for the time being suspended in Austria. These are: Article 1(4) on “generic descriptors”, which will be enforced after the adoption of rules for application by the Commission; Article 10 – labelling provisions, Article 10(2)(b) on “the quantity of the food and pattern of consumption required to obtain the claimed beneficial effect” and Article 10(3) on “general non-specific claims which can only be made if accompanied by a specific claim included in the lists provided for in Article 13 or 14”, which will not be enforced until the Article 13 list is published. Mahmood also foresaw certain enforcement problems in the future (see slide above).

### Enforcement problems in the future



- Flexibility of wording
  - one example of wording in the list
  - case by case decision
- Legal status of the Art. 13 list – decisions on health claims, not on substances
- Increasing number of dietetic products for special medical purposes?
- Food supplements without claims? – Consequences?

consumption required to obtain the claimed beneficial effect” and Article 10(3) on “general non-specific claims which can only be made if accompanied by a specific claim included in the lists provided for in Article 13 or 14”, which will not be enforced until the Article 13 list is published. Mahmood also foresaw certain enforcement problems in the future (see slide above).



**Jean POTTIER** of Belgium's Federal Public Service Health, Food Chain Safety and Environment wondered whether the text of the phrase in Article 1 (Scope) of the Claims Regulation "to be delivered as such to the final consumer" referred to the "commercial communication" or to "foods". If it referred to the former, business-to-business communication and communication with health professionals would not be covered, he said. On the other hand, Recital 4 stated that "This Regulation [...] shall not apply to claims which are made in non-commercial communications, such as dietary guidelines or advice issued by public health authorities and bodies (see right), or non-commercial communications and information in the press and in scientific publications".



SPF SANTE PUBLIQUE, SECURITE DE LA CHAÎNE ALIMENTAIRE ET ENVIRONNEMENT

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**Are beauty claims within the scope?**

- If beauty is part of health, how does it fit within the regulation?

Article 5: "beneficial nutritional or physiological effect"

Article 13: Health claims describing or referring to:

- (a) the role of a nutrient or other substance in growth, development and the functions of the body; or
- (b) psychological and behavioural functions; or
- (c) (...) slimming or weight-control or a reduction in the sense of hunger or an increase in the sense of satiety or to the reduction of the available energy from the diet,

Logo of the SPF Santé Publique, Sécurité de la Chaîne Alimentaire et Environnement.

Pottier also wondered whether beauty claims would fall within the Regulation's scope (see slide on left). In the absence of a definition of "health" within the Regulation, Pottier quoted the World Health Organization's definition that "health is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity". In case "beauty" is not considered as part of "health", said Pottier, beauty claims would not be covered by the regulation and would fall under the EU's general consumer protection legislation, for instance

[Directive 2006/114/EC](#) on misleading and comparative advertising.

**Evelyn BREITWEG-LEHMANN**, of the German Federal Office of Consumer Protection and Food Safety stated that the Commission's review of the progressive adoption of the list of permitted health claims had been strongly supported in her country and that the exclusion of botanicals from the progress facilitates enforcement issues.

As one of the challenges for the enforcement authorities, Lehmann mentioned that after a positive assessment by EFSA products with substances considered as "medicinal" would appear on the market, e.g. the hormone 'melatonin' which is considered as a medicinal product in Germany. Other challenges are that EFSA does not make risk assessments in its evaluation of health claims and therefore (potential) risks to public health are not mentioned in the EFSA opinions. Given that the upper vitamin or mineral limits have not been harmonised at EU level, products with substances in concentrations with safety concerns might appear on the market following a positive assessment by EFSA, especially since the conditions of use usually only state the minimum quantity. As examples she quoted high doses of vitamin D or iron. As long as this situation persisted, said



Lehmann, Member State enforcement authorities would be confronted with non-harmonised substances representing a potential risk to the consumer.

**Ruth VEALE**, Head of the Department Food, Health, Environment and Safety at the European Consumers' Organisation (BEUC), said that from a consumer perspective it is essential that claims are generally and are not misleading. She welcomed the Nutrition and Health Claims Regulation as a major step forward that would force any claim to be substantiated by a scientific assessment and called the continued presence of unsubstantiated claims in the market unacceptable. The wording of any approved claim should lead consumers to make informed choices as it would be worded in consumer-understandable language. The setting of nutrient profiles should ensure that only healthy products can bear claims and any product that does not correspond to these profiles should be barred from making claims although they can stay on the market without claims. She supported the European Commission's approach to this and asked for an early publication of the positive list of approved claims. She regretted the postponement of the evaluation of claims on botanicals as consumers often do not make the distinction between medicinal products and food supplements.

**Basil MATHIOUDAKIS**, the Head of the European Commission's Food Law, Nutrition and Labelling Unit within DG Health and Consumers, gave an overview of the Regulation's adopted and ongoing implementation measures, including decisions on individual dossiers and guidance documents. Concerning the nutrient profiles due to be adopted as part of these implementing measures, Mathioudakis mentioned that some political pressure had delayed their adoption but that it was Commissioner Dalli's intention to go ahead with them.

What the experience to date shows, said Mathioudakis, was the importance of claims as a promotional tool and the important number of unsubstantiated claims. The criticism of the severity of the assessors is proof of their scientific rigour. Also, there was no favouritism as big companies and SMEs both got a share of the permitted and rejected claims. Mathioudakis expressed some doubt as to the motives behind the submission of this huge number of claims "were all claims actually on the market, or were operators trying to drown the regulation?", wondered Mathioudakis. And were all 10 permitted claims for vitamin C actually going to be used?

For the moment, borderline products, particularly those containing botanicals, are still on the table. However, the private sector is already anticipating regulatory outcomes by withdrawing certain claims, often following decisions by private controlling bodies and/or legal action from competitors.

In the intervention of **Juliane KLEINER**, Head of the Unit Dietetic Products, Nutrition and Allergies at the European Food Safety Authority delivered by Albert Flynn, it was pointed out that the claim evaluation status at end January 2011 was as follows (see slide on the right). Following the consultation with applicants and other stakeholders in December 2010 on gut and immune function claims, further consultations are planned on the scientific requirements for health claims related to:

**EFSA health claims evaluation status (25 January 2011)**

Claim type	Received	Withdrawn	Adopted	In progress	Under Validation
Children (Art. 14)	218	65	49 opinions covering 55 applications	9*	88
Disease risk reduction (Art. 14)	50	8	21	6**	15
New science/proprietary (Art. 13.5)	46	11	26	6***	2
Conditions of use (Art. 19)	1	0	1	0	0
<b>Total applications</b>	<b>314</b>	<b>84</b>	<b>97</b> opinions covering 104 applications	<b>22</b>	<b>105</b>
<b>Art 13 list of health claims</b>	<b>4637</b>	<b>322</b>	<b>1867</b> (1745 published)	<b>900</b> (1548 on hold)	<b>1548</b>

\* 7 in clock stop \*\* 1 in clock stop \*\*\* 0 in clock stop



- Appetite ratings, weight management and blood glucose concentrations
- Protection against oxidative damage and cardiovascular health
- Bone, joints, connective tissue and oral health
- Neurological and psychological functions
- Physical performance.

It was further announced that all application processes and regulatory workflows within EFSA are currently under review and that *more resources would be allocated to the support provided to applicants*. In this context a service point would be established for which the planning is in progress. A structural organisational change would be gradually implemented in 2011 and following years in order to increase the efficiency in EFSA, which should in turn lead to better applications.

## TOWARDS A SINGLE MARKET FOR ALL SUBSTANCES IN FOOD SUPPLEMENTS?



*Pictured at the AESGP Conference in Brussels, 2 February 2011 (from l):*

**Ana María TRONCOSO GONZÁLEZ; Emiel van GALEN; Vittorio SILANO; Basil MATHIOUDAKIS; Peter SHOTTER; Andrea LUGASI; Joris GEELLEN; Evelyn BREITWEG-LEHMANN; and Hubertus CRANZ**

In his introduction, session chair **Peter SHOTTER** of Merck Consumer Health Care, who also chairs the AESGP Food Supplements Committee, gave the general picture from an industry perspective. He pointed out that the areas of food supplements and self-medication with non-prescription medicines and traditional herbal medicinal products were partly overlapping, both in Europe and worldwide, and that there was no global harmonised framework. This makes it almost impossible to have one product form worldwide, said Shotter. Different traditions sometimes also



made it difficult for some Member States to accept a positive EFSA evaluation, leading to uncertainty for economic operators. Industry therefore needs clear frameworks, at least at regional level, for coexistence and differentiation between “self-medication” and “health maintenance”. According to Shotter, it would reduce complexity but would also require a joint industry approach to achieve.

## The use of substances other than vitamins and minerals in food supplements

In his second intervention of the day, **Basil MATHIOUDAKIS**, the Head of the European Commission’s Food Law, Nutrition and Labelling Unit within DG Health and Consumers, gave some examples of “other substances” currently on the market: Pro- and pre-biotics; Lycopene, flavonoids and other anti-oxidants; Glucosamine, chondroitin; Melatonin; “Botanicals”; Q10; and “red rice” (containing statins). Many of these are used both in foods and in medicinal products but, said Mathioudakis, there are different rules in force for medicinal products as compared to food supplements. These are related to safety and quality aspects; indications for use (“traditional use” is accepted for traditional herbal medicinal products); and the need to obtain a manufacturing license and registration. All these parameters mean that the cost of putting a medicinal product on the market is different from that of marketing a food supplement. However, any food supplements containing these other substances are subject to normal food law in so far as their definition and safety aspects are concerned. Moreover, under the legislation on fortified foods (Article 8), restrictions may be imposed on the addition to foods of substances which could be harmful to human health. Mathioudakis stressed that the Claims Regulation was not a means of deciding whether or not a product is a foodstuff but just whether a food claim can or cannot be made.

In the [Report from the Commission to the Council and the European Parliament on the use of substances other than vitamins and minerals in food supplements](#) of December 2008, the Commission concluded that the limited available scientific information would restrict the usefulness of harmonisation in the area. It nevertheless raised the possibility of partial harmonisation in the framework of the legislation adopted after the adoption of the Food Supplements Directive (for instance the legislation on fortified foods) and said that the application of mutual recognition would be a useful instrument for facilitating the free movement of the products concerned. However, more and more voices were being heard to contest these conclusions, not least from the Member States, manufacturers and consumers. In light of a possible harmonisation of the use of ‘other substances’ in food supplements, the following questions therefore remained to be resolved, concluded Mathioudakis (see slide).

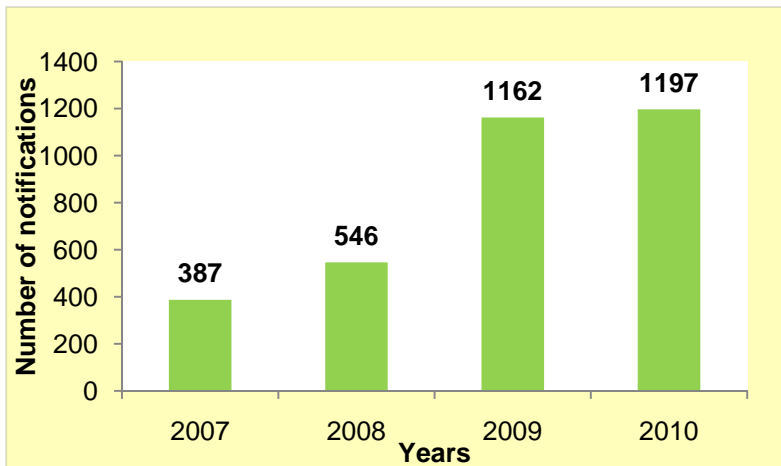
Harmonisation under food law? Questions

- such substances: acceptable as food?  
acceptable as FS
- What effect – more/less such products as food?
- What aspects for harmonisation?
  - Quality, safety, consumer information?
- Which ingredients should be given priority?

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**Ana María TRONCOSO GONZÁLEZ**, the Executive Director of the Spanish Food Safety and Nutrition Agency, explained that the final piece of legislation implementing the Food Supplements Directive in Spain - following some earlier criticism from the European Commission - was Royal Decree 1487/2009, a literal transposition of the directive. Notification to the competent authority (in the autonomous regions) should take place prior to or simultaneous with the first placing of a food supplement on the market. The number of notifications in Spain in the years 2007-2010 is shown in the graph above. Troncoso mentioned that Spain applies Regulation (EC) No 764/2008 laying down procedures relating to the application of certain national technical rules to products lawfully marketed in another Member State and only denies mutual recognition of a food supplement with 'other substances' if the product poses a serious risk to consumer health (e.g. in



case it contains more than 2 mg of melatonin or if it contains active substances not declared on the label).

A Workshop on food supplements organised under the Spanish EU Presidency in March 2010 and attended by national representatives, the European Commission and EFSA found that the main difficulties for an effective control on food supplements were:

- Lack of maximum levels for vitamins and minerals
- Lack of harmonised provisions on 'other substances'
- Borderline issues
- Difficulties of implementing mutual recognition.

It acknowledged that there were several differences in how national law had adapted Article 10 of the Directive.

According to Troncoso, the main concerns for Spain were:

- Substances other than vitamins and minerals that could be considered both as food supplements and as medicines (examples: Melatonin and Glucosamine).
- How to deal with the coexistence of traditional herbal medicinal products and botanical food supplements.
- Substances other than vitamins and minerals that could be considered as food supplements or as food for special medical purposes (example: L-carnitine) / food for sports people.

**Joris GEELLEN**, who deals with botanicals and advises on plant preparations within the Belgian Federal Public Service for Health, Food Chain Safety and Environment, explained that the presence of plants in foodstuffs is regulated in Belgium under the Royal Decree of 29 August 1997. This includes annexes with lists of (1) plants that are not allowed for use in food; (2) edible mushrooms; and (3) plants allowed in food supplements. To draw a distinction between medicinal products and food supplements, the Belgian authorities follow the indications from the European Court of Justice (ECJ) and carry out all evaluations on a case-by-case basis.

When necessary and possible, maximum levels are determined by the Federal Public Service – Department for Health, Food Chain Safety and Environment on advice of the Advisory Commission on Plant preparations. The maximum levels are a certain percentage of the Minimal



Daily Therapeutic Dose (MDTD) for a certain indication; doses are taken from scientific publications in which clinical doses are evaluated. This is based on the fact that higher levels lead to therapeutic or prophylactic properties and allows a distinction between foodstuffs and medicines to be made. For an administrative evaluation of controversial cases, the Belgian Federal Agency for Medicines and Health Products (FAMHP) installed a *Mixed Commission* responsible for providing advice on borderline issues together with the Belgian Federal Agency for the Safety of the Food Chain (FASFC).

In this session, **Evelyn BREITWEG-LEHMANN** of Germany's Federal Office of Consumer Protection and Food Safety showed in the slide that a "small" part of the use of substances in food resists harmonisation: upper limits for vitamins and minerals and 'other substances'. She mentioned that, unlike Belgium, a comprehensive list of botanicals allowed in or as food is not available in Germany, and that many were traditionally classified as medicinal products.

Bundesamt für Verbraucherschutz und Lebensmittelsicherheit

**Legal framework for substances within the EC**

We are in the year 2011. The legislation concerning substances in food or food products is harmonized .... All substances?

**No!**

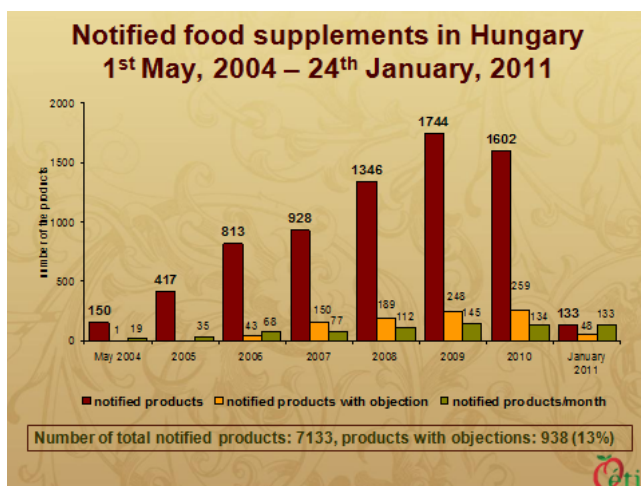
A small part resists harmonization

- Upper limits for Vitamins and Minerals
- Other substances according to Annex III of the Regulation (EC) No. 1925/2006

Under the chair of the Federal office for consumer protection and food safety (BVL), a working group made up of experts from the Federal States (ALS), the Federal Institute for Medicines and Medical Devices (BfArM) and the Federal Institute for Risk Assessment (BfR) is in the process of making a management document of herbal (botanical) substances. This will be made up of a part detailing the scope and the different categories of plants and parts of plants, as follows:

- List A: substances not recommended in food
- List B: substances recommended in food only with restrictions. This is subdivided into: A: only used as flavour; G: only used as spice; S: only used as decoration; T: only used as tea; b: Substances only used after treatment (e.g. heating, cooking); X: Food (used without restrictions)
- List C: substances under scrutiny.

The first list, which has now been published on the websites of the [BVL](#) and the BfArM, so far includes 630 plants (comments are requested by end September 2011). The list will also include a [decision tree](#) to assess a product's legal status.



**Andrea LUGASI** of the National Institute for Food and Nutrition Science (NIFNS) in Hungary showed how food supplements were regulated in her country before accession to the European Union and how the legislation had changed after 2004, with a fairly extensive notification procedure now being in place for manufacturers wishing to put products on the Hungarian market. The NIFNS carries out a safety assessment based on the data provided by the food business operator to see whether the product and the label comply with EU and Hungarian legislation. However, food safety



risks (microbiological and toxicological contamination, etc.) are not examined by the NIFNS. For the evaluation of botanicals, the NIFNS is assisted by an Expert Committee whose members come from university faculties of pharmacology, the National Institute of Pharmacy, the Hungarian Dietary Supplement Association and the NIFNS. A negative list of plants and parts of plants whose use was not recommended in food supplements with 209 items was published in 2007 based on scientific publications. The use of some plants on the list is possible in a given (restricted) dose (e.g. *Cassia acutifolia* – 10 mg / hydroxy-anthracene glycoside in daily dose of the product). The [negative list](#) (available only in Hungarian) is a guidance document and is not part of the legislation.

**Vittorio SILANO**, the Chair of EFSA's Scientific Committee, echoed the opinion of other speakers that the EU market for botanicals was relatively segmented due to the many differences in positive and negative lists adopted by several Member States to identify botanical species and parts which can or cannot be used in the manufacture of food supplements. According to official documents from 20 EU Member States plus Croatia and Switzerland summarised by AESGP in 2007, said Silano, a large number (e.g. several hundred) well-identified botanical species (out of the about 1 900 herbal species), are: (i) allowed for use as food supplements in some Member States; (ii) prohibited in some other Member States; and (iii) not considered at all in yet other Member States. To help the Member States, EFSA in 2009 published a [Guidance document on Safety assessment of botanicals and botanical preparations intended for use as ingredients in food supplements](#). Moreover, EFSA and the Member States had produced a [Compendium of botanicals that have been reported to contain toxic, addictive, psychotropic or other substances of concern](#) which is currently being further developed. It reports in a standard format the results of the available literature analysis for the botanical species included in each negative list adopted by each Member State for the presence of toxic, addictive, psychotropic or other substances of possible concern to human health. However, the Compendium also makes it clear that the presence of substances of concern in a large number of botanical species require a strict approach to risk assessment and control to ensure that adequate tools (e.g. specific extraction or distillation steps) are adopted during manufacture to avoid the presence in the final product of significant residual levels of substances of concern.

In Silano's personal opinion, the best way forward to the harmonisation of 'other substances' in food supplements would be to develop, in the framework of Directive 2002/46/EC, the adoption of an ad hoc regulation providing for a positive list of safe botanical species and plant parts (including, where necessary, relevant specifications) and of applicable harmonised descriptions of science-based intended uses.

**Emiel van GALEN** of the Department 'Botanicals & Novel foods' at the Medicines Evaluation Board in the Netherlands, found it potentially confusing that the framework for food supplements has a focus on herbal *substances*, while the regulatory framework for medicines is on medicinal *products*. He was convinced that as long as the classification of herbal products is done in a different way in different Member States, and on a case-by-case basis, a single European market for herbal food supplements will not be achieved.

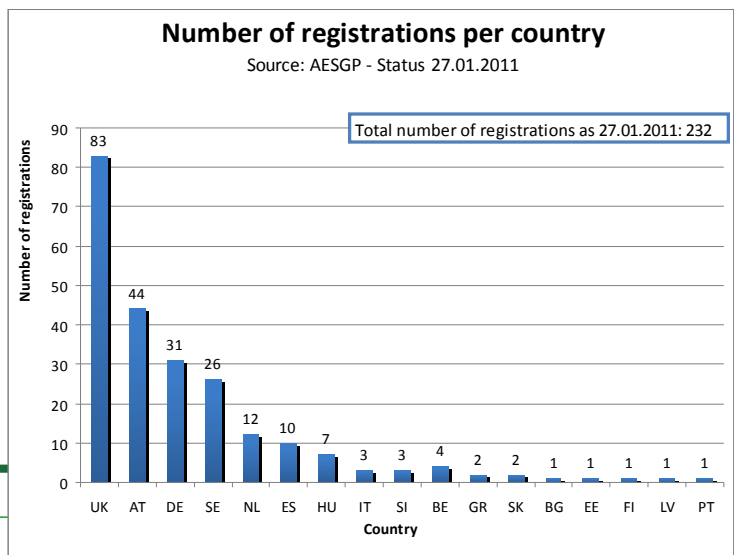


## A SINGLE MARKET FOR HERBAL MEDICINES IN EUROPE?

In this session chaired by MEP **Marina YANNAKOUDAKIS** (European Conservatives and Reformists, United Kingdom), speakers from European and national authorities looked at achievements in the area of herbal medicinal products since the adoption of [Directive 2004/24/EC of the European Parliament and of the Council of 31 March 2004 amending, as regards traditional herbal medicinal products, Directive 2001/83/EC on the Community code relating to medicinal products for human use](#).



In his introduction, **Werner BUSSE** of Schwabe Pharmaceuticals, who chairs the AESGP Herbal Medicinal Products Committee, praised the regulatory framework in place as well as the extensive guidance provided by the EMA Committee on Herbal Medicinal Products (HMPC), which had up to now led to the finalisation of approximately 80 monographs. Although more limited in number (11), the List entries adopted so far formed a reliable basis for companies to submit applications under the national, mutual recognition or decentralised procedures as they were binding on all



### Borderline issues

#### traditional herbal medicine

- 15/30 years EU use
- registration
- disclaimer
- minor indication
- dose range / duration of use
- pharmaceutical file / EP / ICH
- plausible benefits
- review: must be safe
- high costs for maintenance
- MS: due account

#### herbal food supplement

- no provision
- notification or no provision
- no disclaimer
- health benefit / third party
- usually no provision
- acc to national food legislation
- „claims“ with reference to HMP
- pretended safe if herbal
- limited costs for maintenance
- MS: free movement of goods



Member States. The number of THMP registrations per country as of end January 2011 is shown in the slide above.

Busse emphasised the requirements associated with herbal medicines (GMP, CTD, pharmacovigilance, etc) as well as the associated costs (maintenance cost, various fees). In addition, a number of elements are not harmonised at EU level such as advertising control, distribution, etc. This makes the

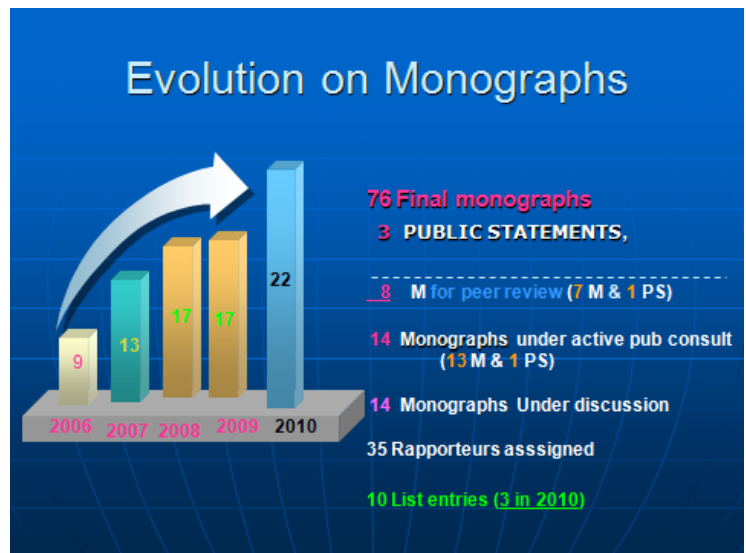
introduction of a registered / authorised herbal medicine on the market also quite complex and costly. In comparison, said Busse, food supplements are at a competitive advantage as they have to



meet lower quality requirements, have a ‘presumption of safety’, do not need registration / authorisation before placing on the market and attract limited maintenance costs.

### Scientific assessment of herbal medicines

**Ioanna CHINO**, the Vice-Chair of the EMA’s Committee on Herbal Medicinal Products (HMPC) presented the Committee’s composition, work and deliverables. The HMPC has three technical groups: the Working Party on Monographs and Lists (MLWP) which she chairs, and two Drafting Groups on respectively Quality and Organisational matters. The MLWP is in charge of the important task of developing Community monographs and List entries, which are both scientific summaries and represent the scientific opinion of the working party. The Community monograph is subject to a comprehensive development procedure including peer review and a three-month public consultation period. The number of monographs issued by the HMPC has been steadily growing over the years (see slide). Summaries of the HMPC assessment report for the public are being prepared in order to bring science to the citizens.



The HMPC counts an observer from the Council of Europe’s European Directorate for the Quality of Medicines & Healthcare (EDQM) and is itself an observer in the EDQM 13A and 13B groups. This allows close cooperation and consistency between HMPC and EDQM monographs on plants, said Chinou. The HMPC is also in direct communication with the European Food Safety Authority (EFSA).

With reference to the THMP legislation’s ‘history of use’ criteria, Chinou indicated that the MLWP

was only doing ‘science’. The ‘traditional use’ had to be thoroughly document by evidence attesting to the plausibility of the indication. This was far more complex than merely showing proof that the product had been in use for 15/30 years.

### Echinaceae purp. herba

7 March 2008

<i>Well-established use</i>	<i>Traditional use</i>
<p><u>Oral use</u></p> <p>Prevention of common cold</p> <p><b>Not recommended :</b></p> <ul style="list-style-type: none"> <li>For children below 12 years old</li> <li>For immunodeficient patients</li> <li>For patients being under therapy for                             <ul style="list-style-type: none"> <li>Infectious diseases such as tuberculosis, autoimmune illnesses (sclerosis multiplex) or</li> <li>Serious blood diseases (anaemia, leukemia, etc)</li> </ul> </li> </ul>	<p><u>Topical use</u></p> <p>THMP product for treatment of small superficial wounds</p>

Looking to the future, Chinou examined how to optimise the development of Community monographs, how to solve the ‘genotoxicity gap’ which hampers the finalisation of List entries, how to solve the paediatric gap, and how to get more experts with ‘hands-on’ experience.



As a scientist, she pointed to the confusion created by the market where food products containing herbal substances are marketed freely whilst bibliographic literature and HMPC Community monographs warn about 'interactions with other medicinal products'. In this context she showed the example of, on the one hand, the well-established use and traditional use indications of *Echinacea Purpurea* (*above*) and, on the other, the presence in the market of a freely available drink containing the same ingredient without any warning.

**Werner KNÖSS** of the Federal Institute for Drugs and Medical Devices (BfArM) in Germany, who was recently elected as the new Chair of the Committee on Herbal Medicinal Products (HMPC) but spoke in his BfArM capacity, found it unsatisfactory that the same product can have a different legal status depending on the Member State in which it is being placed on the market.

With regard to the Community monographs, Knöss mentioned that about 18-20 Member States are willing to follow them but that full uptake may still take some time. For the future, Knöss saw an increased use of the mutual recognition and decentralised procedures as a possibility once a monographs existed, although this would also entail more competition as copy products might enter the market more easily. According to Knöss, the single market for herbals may require some more time, especially in light of the existence of botanical food supplements. In this context he repeated the HMPC's openness to collaboration with EFSA.

**Reinhard LÄNGER** of the Austrian Agency for Health and Food Safety insisted that the Community herbal monographs should be legally binding in order to foster the single market for herbal medicines. He also thought there was a need for a more harmonised risk-based assessment and pragmatism in the interpretation and implementation of the legislation. To achieve this, a harmonised training of quality assessors would be an important first step.

It would also be useful, said Länger, to look at where work in the mutual recognition and decentralised procedures can be shared given that experience is still scarce. Companies should be encouraged to use these procedures, even in the absence of a monograph. The use of the centralised procedure for herbal medicines would also provide a positive experience on condition that the HMPC would be in charge of carrying out the assessment and issuing the opinion.

**Burt KROES** of the Medicines Evaluation Board in the Netherlands presented the work of the HMPC Quality Drafting group. An important part of the Drafting group's work programme for 2011 will include the revision of the guideline on the use of the CTD format to include a 'best practice guide' describing the exact location of relevant guidelines into the CTD module-3 sections and a mock up for



### 3.2.P.5 Control of drug product (name, dosage form)

- Refer to: *Notice to Applicants, Volume 2B - Presentation and Content of the Dossier - CTD Module 3 - Edition July 2004.*

#### Additional reference guidelines:

- Markers used for Quantitative and Qualitative Analysis of Herbal Medicinal Products and Traditional Herbal Medicinal Products.
- Specifications: Test Procedures and Acceptance Criteria for Herbal Substances, Herbal Preparations and Herbal Medicinal Products / Traditional Herbal Medicinal Products.
- Quality of Herbal Medicinal Products / Traditional Herbal Medicinal Products.
- Quality of Combination Herbal Medicinal Products / Traditional Herbal Medicinal Products.
- Specifications and Control Tests on the Finished Product.
- Excipients in the Dossier for Application for Marketing Authorisation of a Medicinal Product.

Burt Kroes©

10-2-2011



module 3 (quality part). He presented an example of what this would look like for section 3.2.P.5 (Control of drug product – see slide).

Coordination between the European Directorate for the Quality of Medicines & Healthcare (EDQM) and the HMPC was also mentioned on a wide range of topics (harmonisation of terminology for herbal substances and preparations, markers, classification of extracts, heavy metals and microbiological limits for herbal drugs, implementation of new assay methods, etc).

**Ilaria PASSARANI**, who is the Senior Health Policy Officer at the European Consumers' Organisation (BEUC), recalled that it was of the utmost importance that consumers had access to high-quality information that is reliable, unbiased and not misleading. Information provided in the summary of product characteristics (SPC) and leaflet should correspond to these criteria.

Consumers often use herbal medicines because they think they are less harmful than chemical medicines, but she insisted that all medicinal products should have warnings on interactions. In this context, Passarani welcomed the new pharmacovigilance legislation as an improvement over the existing situation, but she still thought that more research was needed into the use of medicines in children. "We are strongly opposed to the practice of off-label use," said Passarani.

As consumers cannot distinguish between food supplements and medicines containing the same plant, this may lead to confusion. Passarani therefore asked for a more consistent application of existing legislation.

**Tony HUMPHREYS**, the Head of the Sector Regulatory, Procedural and Committee Support at the European Medicines Agency, started by illustrating the imminent end of the transition period for the registration of traditional herbal medicinal products which were on the market when the Directive came into force. He announced that in order to increase visibility of the THMP system, the Heads of Medicines Agencies (HMA) would carry out a survey on the number of THMP registrations granted by the Member States, the use of Community monographs, etc. As one of the barriers to more national registrations being granted Humphreys mentioned that some Member States still invoked a 'serious risks to public health' even after the establishment of a Community monograph. He has also expected more List entries to be approved but thought the absence of genotoxicity data had prevented the adoption of more List entries. According to Humphreys the system should prevent different scientific opinions coming from the European Medicines Agency or EFSA on the same plant as this would be difficult to explain to consumers.

Humphreys finally asked "Quo vadis HMPC in 20 years? Will it still be revising Community monographs or will it be assessing herbal medicines applications within the centralised procedure?"



## CONCLUSIONS

At the end of the conference, **Nils BEHRNDT**, the Deputy Head of Cabinet of Commissioner John Dalli, gave an overview of the European Commission's *Work Plan in the area of medicinal products and food supplements*.

Concerning the 'pharma' package of legislative proposals put forward end 2008, the provisions on *medicines safety* (pharmacovigilance) had been adopted and published, but the 'Mediator' incident showed that medicines safety is a pressing issue, said Behrndt. "We need to give reassurance to the public that the medicines they use are safe."

Behrndt expected final agreement on the provisions on *falsified medicines* to be adopted in about two weeks' time. These will provide good guarantees to patients concerning the origin of the medicines, also in case they are purchased on the Internet. However, many of the practical arrangements to be taken in the framework of these provisions such as the nature of the safety features to be apposed and the ownership of the database in which the data will be stored have been delegated to the European Commission. In this context Behrndt mentioned that no deadline for the adoption of these "delegated acts" had been stipulated but that the Commission would draw on experience gathered during pilot projects. Once the Commission had taken a decision on these points, however, Member States would have to implement them within 36 months.

Concerning the provisions on *information to patients on prescription medicines* Behrndt mentioned that the rapporteur Christopher Fjellner had received much support for his amendments in the European Parliament. The patient information leaflets remained the main information tool for patients, and no direct contact between industry and patient was therefore needed according to Commissioner Dalli. The Commission would put forward its modified proposal in about two weeks, but given the scepticism on the part of the Member States the outcome of these provisions was as yet uncertain.

With regard to *traditional herbal medicinal products*, Behrndt referred to the Commission's 2008 [Report on the experience acquired as a result of the application of the provisions of Chapter 2a of Directive 2001/83/EC, as amended by Directive 2004/24/EC, on specific provisions applicable to traditional herbal medicinal products](#). However, so far no response had been received from the Council or the European Parliament. "As we did not want to create a third category of products between medicinal products and food supplements, we need to see how we can apply the existing legislation on *food supplements* in an intelligent manner", continued Behrndt.

Another important initiative in the area of health is the recent [European Innovation Partnership on Healthy Ageing](#) on which the Commission intended to release a concept paper in February 2011. "In spite of the wealth of research activity", said Behrndt, "we somehow fail to deliver more healthy life years. We are looking at how we can bring better care to patients, and e-health will make an important contribution to this."





The Commission also intends to revise the *Clinical Trials Directive* sometime in 2012 given that experience has proven that the rules for multicentre clinical trials are too complex and may be hampering pharmaceutical innovation. Also up for change in 2012 will be the *EMA fee regulation* to incorporate a change to the pharmacovigilance fees as well as certain other elements.

The *availability of medicines in smaller Member States* is high on Commissioner Dalli's radar screen. This may have to be accomplished by a better mutual recognition system and why not, wondered Behrndt, an automatic mutual recognition procedure for pharmaceuticals given that under current legislation it was already natural for medical devices and cosmetics to circulate freely? The Commission would think about this in the next one to two years.

According to Commissioner Dalli, *availability, affordability, innovation and dialogue* are the four most important issues on pharmaceuticals. The Commission would continue to monitor therapeutic gaps as healthcare is crucial in the Commission's 2020 Agenda. "Please let us know if you have ideas in any of these areas", concluded Behrndt.

**Hubertus CRANZ**, the Director General of AESGP, pointed out that the manufacture of high-quality products worthy of consumer trust and marketed in free competition is - and will remain – an important issue for the self-care industry. "For this to become reality we need a viable industry which is regulated in a spirit of '*smart regulation*'. "Although we may not agree on quite a few details, we do support a stable and even demanding regulatory environment."

Concerning *herbal medicinal products*, Cranz praised the work done by the EMA's Committee on Herbal Medicinal Products (HMPC). Acceptance of Community monographs by the Member States had however so far been insufficient. Cranz wondered whether the system for herbal medicines in some EU Member States was not too expensive for manufacturers given the high fee levels for authorisation / registration, maintenance and other costs. He concurred that the future role of the HMPC might well be in the evaluation of applications for central marketing authorisations for herbal medicines.

In the area of *food claims*, AESGP was happy with the Commission's revised process for the adoption of the list of general function claims in two stages, said Cranz. Further news, in particular on botanicals, is expected to be unveiled during the *AESGP 47th Annual Meeting* in Rome, Italy from 8 to 10 June 2011, in a session on 10 June. The AESGP Committees on Food Supplements and Herbal Medicinal Products will continue preparing the AESGP position in this respect based on the unique expertise of the sector. A joint meeting of both committees was to take place the next day and on 10 June 2011 to discuss the outcome of the conference and to fine-tune the Association's arguments.

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