

## ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

## CHEWING GUM BASE

**Issue**

The Dutch Competent Authority has prepared an initial opinion on an application for the authorisation of chewing gum base as a novel food ingredient under the Novel Food Regulation (EC) No. 258/97. The Committee is asked whether it agrees with the initial opinion and whether it has any comments or objections. The Committee's advice will form the basis for the UK's formal response.

**Introduction**

1. On 30 April 2009, the European Commission forwarded the Dutch Competent Authority's (CA) initial opinion on an application made by Revolymer Ltd., under Article 4(1) of Regulation (EC) 258/97, for the authorisation of chewing gum base (REV-7) as a novel food ingredient. Under the time scales set out in the regulation, the UK and other Member States have until 29 June 2009 to provide comments and/or reasoned objections to the initial opinion. The safety assessment was carried out by the Dutch Committee on the Safety Assessment of Novel Foods (known as the VNV Committee) on behalf of the Dutch Competent authority, the Ministry of Health, Welfare and Sport.

**2. Members should note following:**

- The Dutch Initial Assessment Report, (attached as **Annex 1**), indicates that the evaluation of this novel food was not straightforward and could only be completed following the provision of significant quantities of additional data by the applicant.
- The Secretariat views the Dutch Initial Assessment report to be particularly well drafted. In view of this the Secretariat has not reproduced all of its findings in detail for this paper, and Members are advised that they should

review the Dutch report in the first instance. This paper briefly summarises the issues of concern raised by the Dutch and details which of the (4) additional addendum documents contain the relevant information that Members may wish to review. The original dossier is attached at **Annex 2** (restricted), and additional data sets (Her08, Her08a, Her08c and Her09) are attached at **Annexes 3-6** (restricted) respectively.

## Background

3. '**Chewing Gum Base** 'is the raw material used in the manufacture of chewing gum and bubble gum, and consists essentially of a mixture of natural/ synthetic gums and resins. The desired sweetening, flavouring and if required colouring components are added to the base and, when the gum is chewed, these additives are more or less dissolved out of the base and ingested, leaving the original tasteless chewing gum base in the mouth. The base therefore functions as a primarily inert repository for the sweetening, flavouring and chewing components. Typically the chewing gum base will make up to 15-35 per cent of the finished product, with sugar, glucose syrup and flavourings making up the remainder.
4. This application from Revolmer Ltd, is for the placing on the market of a synthetic polymer as an ingredient for chewing gum base material as a novel food ingredient, for use in chewing gum in the EU. The novel ingredient is referred to in the application as REV-7 and is a reaction product of the polymers polyisoprene-graft-maleic anhydride (PIP-g-MA) and monomethoxy-polyethylene glycol (MPEG). REV-7 has been developed with a view to making used gum easier to remove from a variety of surfaces.
5. In accordance with the European Commission Regulation 258/97, the Dutch CA considers that REV-7 falls under the category described under Article 1(2) (e), which is a food or food ingredient with a new or intentionally modified primary structure. This corresponds to class 1.2 under Commission Recommendation 97/518/EC, which sets out the guidelines for novel food applications. The applicant's claim that the product was a class 1.1 a simple mixture of material which has previously been used in foodstuffs within the EC was rejected by the Dutch. The requirements for a submission for class 1.2 are as follows:

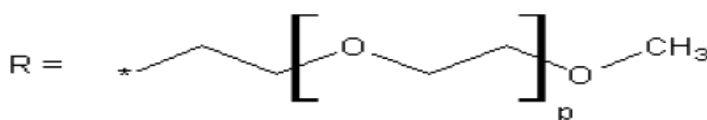
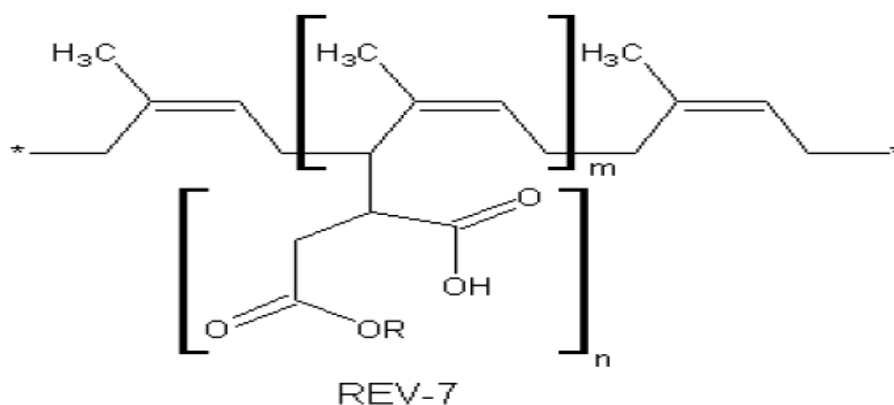
<b>I</b>	<b>Specification of the NF</b>	<b>X</b>
<b>II</b>	<b>Effect of the production process applied to the NF</b>	<b>X</b>
<b>III</b>	<b>History of the organism used as the source of the NF</b>	<b>X</b>
IV	Effect of the genetic modification on the properties of the host organism	-
V	Genetic stability of the GMO	-
VI	Specificity of expression of novel genetic material	-
VII	Transfer of genetic material from GM microorganisms	-

VIII	Ability to survive in and colonise the human gut	-
<b>IX</b>	<b>Anticipated intake/extent of use of the NF</b>	<b>X</b>
X	Information from previous human exposure to the NF or its source	-
<b>XI</b>	<b>Nutritional information on the NF</b>	<b>X</b>
<b>XII</b>	<b>Microbiological information on the NF</b>	<b>X</b>
<b>XIII</b>	<b>Toxicological information on the NF</b>	<b>X</b>

6. The key issues for consideration are presented below under these headings.

### **I. Specification of the novel food**

7. REV-7 is formed from the reaction of the polymers polyisoprene-graft-maleic anhydride (PIP-g-MA) and monomethoxy-polyethylene glycol (MPEG) with heat. PIP-g-MA and MPEG are commercially available synthetic products. MPEG consists of a linear polymer with a methoxy group at one end and the other end which reacts with the maleic anhydride side groups in PIP-g-MA to form the desired branched polymers. Excess MPEG remains in its original state in the end product.



where  $m = 366$  to  $1,248$ ,  $n = 3$  to  $15$  and  $p = 44$  to  $50$

8. The Dutch CA noted that the original dossier did not provide a clear specification for REV-7 and raised concerns about subsequent versions. The Dutch CA viewed the provision of a usable specification to be of particular importance as no further purification takes place after synthesis of REV-7 leading to the possibility of components in the starting materials being present in the end product. The safety implications of residual monomers and oligomers, solvents, additives, (heavy) metals and other impurities, of which the safety implications are reviewed in the toxicology section of the Dutch initial assessment report (Annex 1 pp 29-34).
  
9. According to the final specifications and the justifications for these submitted as Addendum 4 (Annex 4D), REV-7 consists of 30% +/- 5% free MPEG, <0.1 % free maleic anhydride, <5% moisture content. In addition the specifications include limits for heavy metals, solvent residues, additives BHT (< 570 mg/kg) and lactic acid (< 430 mg/kg), microbial limits and various impurities from raw materials including ethylene glycol <200 mg/kg, diethylene glycol <30 mg/kg, methyl glycol <3 mg/kg. An amended specification for MPEG was also provided by the applicant in Addendum 4, Annex 6D. The applicant stated that in future it intends to use MPEG to which lactic acid had been added, rather than 4-methyloctanoic acid.

10. The Dutch CA report reflects significant discussions regarding the levels of a number of parameters in the specification (see pp 8-10 of Annex 4) before they were able to accept the specification detailed on page 11 of addendum Her09 (Annex 6). The Dutch correctly state that it is up to the manufacturer to ensure compliance with the specification for all commercial batches of REV-7.

## **II. Effect of the production process applied to the novel food**

11. REV-7 is produced by heating PIP-g-MA and MPEG in fixed proportions to induce a reaction. No solvents are used in the reaction, but water is added as required at the end of the reaction to ensure that the level of intact maleic anhydride groups is consistent with the specifications by means of hydrolysis. The resulting material is then divided into pieces suitable for use in the production of chewing gum.

12. The application dossier described production at pilot scale although addendum Her08a (Annex 3) offers greater detail of the proposed scale up procedures, including that HAZOP (for process safety) and HACCP (for food safety) principles will be followed and that an accreditation on the basis of a British Retail Consortium standard would be sought, presumably before the product is produced commercially. Following concerns raised by the Dutch CA, the initial assessment records that the applicant had received assurances from the two suppliers of the raw materials to ensure that impurities were minimised. The specification described in Section I (above), together with the improved specifications and process controls detailed in Her08a (Annex3), appear to have provided sufficient reassurance to the Dutch CA that the production process does not give cause for concern, despite the absence of any purification steps following synthesis of REV-7.

13. The applicant provided data on the stability of REV-7 when stored for 12 weeks at 40°C and 75% atmospheric humidity. These data were obtained by analysing samples of the preparation taken after zero, six and 12 weeks. The applicant concluded that this indicates that REV-7 was sufficiently stable under artificial test conditions and indicated a further study was in progress to measure the product's stability when stored under normal conditions for a period of 12 months. The Dutch CA highlighted variations in moisture content, in one of the microbiological parameters, and the amount of free MPEG relative to bound MPEG, but they

concluded that they were satisfied the stability data gives no cause for concern, provided that the product continues to meet the specification. There is no indication given as to whether the results of the 12 month study were subsequently made available, but they do not appear to have been provided by the applicant. Furthermore the applicant does not indicate what is the proposed shelf life of the product REV-7 and products containing it.

### **III. History of the organism used as a source of the novel food**

14. REV-7 is a patented polymer that does not have a history of consumption in the EU as food. The applicant states that the application of synthetic polymers and natural polyisoprene as gum base ingredients is well known and refers to a number of publications discussing gum bases. A number of synthetic polymers have been licensed for use in chewing gum base material, although synthetic polyisoprene is not one of them. The use of polyisoprenes from natural sources both with cis and trans configurations is permitted.

15. The Dutch CA therefore considered the information presented by the applicant in this section as background information. The Secretariat additionally notes that the information supplied does not relate to materials used in the synthesis of REV-7 and is of little relevance.

### **IX. Anticipated intake/extent of use of the novel food**

16. REV-7 is intended to be used as part of the chewing gum base material at a level that would not exceed 15% by weight in the final product (see pp 20-21 of Annex 2).

17. The applicant uses a number of sources to estimate the levels of chewing gum usage and these are detailed in the application dossier (annex 2 pp21-22). The intake data provided are very limited and appear to reflect population averages (per capita) rather than consumption by gum users. Such data are of limited relevance when trying to determine average and high level consumption of food, particularly when the food is consumed by a relatively low proportion of the population (such as chewing gum).

18. The applicant refers to data from the chewing gum manufacturer Wrigley which is limited and appears to be based a single bar chart ([http://www.wrigley.com/about\\_us/fun\\_facts.do](http://www.wrigley.com/about_us/fun_facts.do)). The applicant reports these data as chewing gum consumption in the UK being on average 120 to 130 portions per year (360 and 390 g of gum a year, or 0.99 to 1.07 g a day). The applicant also highlighted figures reported by the Codex Committee for Food Additives and Contaminants which report similar per capita figures consumption figures in the EC at 1g/day, whilst a reference to UK consumption figures (reference not provided) states that the average consumer will eat 400-600g chewing gum per annum (1.1-1.6 per day). The applicant also reports a high user figure in a 1994 UK Government report, which reports a figure of 4.5g/day<sup>1</sup>, and regards this figure to be broadly consistent with the other figures drawing on a WHO report, which considers that high users (95<sup>th</sup> percentile) of a food consume approximately three times that of an average consumer. On this basis the applicant views high level consumption figures 3.3 – 4.8g/day to be a reasonable estimate (figures based on 3x the 'UK consumption figures'). The applicant has not attempted to estimate consumption levels for children.
19. The Dutch CA was critical of the intake estimates provided by the applicant, noting that not all the cited data sources were available for the assessment. However they agreed that the applicant had erred on the side of caution and that the high estimates of chewing gum usage and intake of REV-7 were reasonable. As REV-7 will be used in chewing gum at a maximum level of 15% by weight, the high level consumption figure of 4.8g/day equates to high level consumption of 0.72 g per day (12mg/kg body weight) of the novel ingredient. The Dutch CA also points out that where the polymers are concerned, the insoluble components of the chewing gum are not usually swallowed in significant quantities but are disposed of.
20. The Secretariat does not agree with the applicant that national dietary intake data cannot be used to estimate the intake of chewing gum. Such data are commonly employed for the assessment of the intake of novel foods and UK data can be used by food manufacturers to estimate mean and high level consumption of a range of foods and ingredients (including chewing gum) and can also be used to

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<sup>1</sup> This incorrect figure is given in the application dossier. It should read 4.3g/day

gauge differences in population age ranges. Indeed UK dietary intake data (dating back the late 1980's) were used for the UK Government report that the applicant cites. However figures derived from food diaries should be treated with caution as respondents may not regard chewing gum as 'food', and it is recognised that foods consumed out of the home and in-between meals may be less completely recorded.

21. The Secretariat has not carried out a full analysis of the most recent UK National Diet and Nutrition Survey (NDNS) intake data, but a preliminary review indicates that the mean and 97.5<sup>th</sup> percentile figures for gum users, are approximately 2.1g (15.7g) for adults; and 1.6g (6.1g) for children (4–18). Data for young children (1.5-4.5 year olds) (albeit based on data for a low number of consumers) indicate figures of 1.8 and 8.4g per day. Although these data require additional analysis in order to obtain definitive figures the preliminary figures suggest that consumption of chewing gum has been significantly under-estimated by the applicant, and high level consumption may be 3-4 times higher than the 4.8g/day figure that was accepted by the Dutch CA.
22. The Secretariat would therefore consider an accurate assessment of high level consumption of REV-7 is of the order of 2.3g in adults and 1.26g in young children. Although chewing gum base is not usually swallowed in significant quantities, these values do have implications for the low molecular weight material and possible contaminants which may leach out of the base during chewing. It is these materials which form the main basis of the toxicological assessment carried out by the applicant.
23. The Secretariat also highlights two recent EFSA opinions which have considered chewing gum consumption. A 2005 report into pulegone and menthofuran levels stated that levels of consumption of chewing gum have generally been under reported, and suggested that per capita data intakes should be increased ten-fold if they are to reflect consumption levels among gum users. The same opinion also reports intake data from Norway which indicates that high level consumption in 13 year old Norwegian children is 9.5g/day. A second opinion, published in 2008, reviewing the effectiveness of xylitol for the reduction of dental caries in children reported that the claim would be made on the basis that 2-3g of chewing gum containing the ingredient would be consumed at least 3 times per day. These

opinions, together with the provisional UK intake data described in para 21-2 all indicate that the applicant has used data sources that significantly underestimate likely consumption of chewing gum and therefore REV-8. This underestimation is of particular concern when the intake by children is considered.

#### **XI. Nutritional information on the novel food**

24. The applicant states that REV-7, like all other synthetic gum bases, has no nutritional value because it is not digested and absorbed by the human body unlike some of its other ingredients. The applicant discusses the possible presence of other substances that could be relevant to the safety assessment of REV-7 and the Dutch CA considers this information in section 3.7 of its initial assessment report.

#### **XII. Microbiological information on the novel food**

25. The application dossier includes microbiological analysis of three test batches of REV-7. The Dutch CA noted that these analyses were performed in accordance with a method given in the European Pharmacopoeia for the testing of plastics used in pharmaceutical products. The applicant has also provided data on the microbiological analyses of four batches produced after the production had been scaled up as part of the supplementary information submitted. These data were obtained partly using other established analytical methods. The applicant also states that microbiological contamination of the product was unlikely, because of the high temperatures involved in production and application of HACCP principles.

26. The Dutch CA was content that the microbiological safety of REV-7 had been adequately demonstrated and noted that the microbiological criteria adopted have been incorporated into the final specification for REV-7 (see Section 1 above).

#### **XIII. Toxicological information on the novel food**

27. In the first instance the applicant did not carry out the toxicological analyses which are routinely provided in novel food applications. Instead the applicant referred to published safety assessments, e.g. by EFSA which conclude that no adverse effects are expected with polymers whose molecular weight is greater than 1000 daltons. The polymers in REV-7 have a molecular weight in the range 25 000–85 000 Daltons (PIP-g-MA), 2 000–5 000 (MPEG) Daltons. The dossier therefore

concentrates on low-molecular-weight material and other potential contaminants which may be present in the NI. In response to a request from the Dutch CA, the applicant provided significant quantities of additional information on many of these substances and also carried out a 28 day sub-acute study using laboratory rats.

28. The Dutch CA summarises the data provided in the application dossier and each of the 4 addendum documents. The Secretariat has therefore not reproduced these in detail in this paper, but when reviewing the data Members are reminded that likely consumption of chewing gum is perhaps higher than the levels predicted by the applicant..

29. **28-day toxicological study with rats:** In response to a request from the Dutch CA the applicant submitted supplementary data from a study on laboratory rats. The research was a GLP study conducted in accordance with OECD Guideline 407. The study involved four groups each consisting of ten male and ten female rats which were given a diet containing either REV-7 in concentrations of 0, 3, 5 and 8%. This resulted in average intakes in the four groups of 0, 2394, 4160 and 6879 mg/kg bw/d in the male rats and 0, 2352, 4182 and 6844 mg/kg bw/d in the females. No adverse effects attributable to REV-7 were observed.

30. The researchers concluded that the results were indicative of a NOAEL for REV-7I of 8% in the animal feed. Averaged over the 2 sexes, the highest intake was 6862 mg/kg bw/d. According to the applicant's estimated data, a heavy user could be exposed to up to 0.72 grams of the NI per day, which corresponds to 12 mg/kg bw/d in a person weighing 60 kg. The Dutch CA calculates that in the animal research up to 572 times as much of the NI was administered. The Dutch CA therefore sees no reason to question the conclusions of the research report.

31. **Ames test:** The application dossier includes results of an in-vitro mutagenicity study of REV-7 (*Ames test*). The study did not find any signs of mutagenic activity in five strains of *Salmonella typhimurium*, with and without metabolic activation. The Dutch CA doubted the relevance of this study and saw no reason to comment on the reported research

32. **Allergenicity:** The application dossier included a separate section on the possibility of REV-7 having allergenic properties. The Dutch CA did not consider

the information relating to allergic reactions to latex as being relevant because the polyisoprene used in the production of PIP-g-MA is synthetic. The applicant provides details of research of local lymph node assays using mice conducted to assess whether REV-7 or PIP-g-MA can cause skin sensitisation (appendix 25 and 26 of dossier). The findings of the first study carried out by the supplier Kuraray indicated a value for PIP-g-MA that was exactly equal to the level above which a substance should be regarded as a sensitizer. The possibility that PIP-g-MA is capable of causing skin sensitisation could therefore not be excluded. The applicant speculates that the result for PIP-g-MA is likely to be attributable to the presence of intact maleic anhydride side groups, which are removed during the synthesis of REV-7. The applicant's follow up research demonstrates (Annex 2, Appendix 26) that REV-7 itself is not a sensitiser. The Dutch CA did not view REV-7 to have allergenic properties.

**33. Labelling.** The applicant states that as chewing gum bases do not have to be individually identified in ingredient listings, and contends that this exclusion should be extended to REV-7. This would then be the first novel food which (if approved) would not require its identification on any food products. Members may wish to comment on this aspect and whether they would regard it to be important to ensure that consumers are able to determine whether authorised novel ingredient are present in foods.

### **Committee Action Required**

34. Members are asked whether it agrees with conclusions of the Dutch CA that the REV-7 chewing gum base produced by Revolymer should be granted authorisation as a novel food ingredient for use in chewing gums, or whether it has any additional comments or objections. **Comments are requested by 26 June 2009**

**Secretariat  
June 2009**

Annexes attached:

<b>Annex 1</b>	<b>Dutch Competent Authority initial assessment report.</b>
<b>Annex 2</b>	<b>Application Dossier (Confidential)</b>
<b>Annex 3</b>	<b>Addendum 1 (Her08a) (Confidential)</b>

**Annex 4      Addendum 2 (Her08b) (Confidential)**  
**Annex 5      Addendum 3 (Her08c) (Confidential)**  
**Annex 6      Addendum 4 (Her09) (Confidential)**

If Members want to review to any additional appendices please contact the Secretariat

**ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES**

**Dutch Competent Authority's Initial Assessment Report**

**Secretariat**

**June 2009**



**ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES**

**Application Dossier (Confidential)**

**Secretariat**

**June 2009**

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**Addendum 1 (Her08a) v**

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**Addendum 2 (Her08b) (Confidential)**

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**Addendum 3(Her08c) (Confidential)**

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**Addendum 4(Her09) (Confidential)**

**Secretariat**

**June 2009**

