The Hidden Additives in Children's Medicines

action on additives

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ISBN 978-1-908924-15-5
Published by Action on Additives 2013

A PDF of this resource is available at www.actiononadditives.org

Always consult a medical practitioner before using or changing medication prescribed or recommended.

Action on Additives

Action on Additives is a campaign hosted by First Steps Nutrition Trust. First Steps Nutrition Trust is a charity which provides clear, evidence based and independent information and support for good nutrition and safe food from pre-conception to five years. Information about our work can be found at www.firststepsnutrition.org.

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Acknowledgements

The report was written by Lizzie Vann Thrasher MBE
Thanks go to Jessica Mitchell, Helen Crawley, Caroline Donovan and Zoe Keech.

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Executive Summary

Some of the UK's leading children's medicines contain particular additives – six artificial colourings – that have been withdrawn from food and drink manufacture because of links to hyperactivity and attention deficit hyperactivity disorder (ADHD) in children.

Calpol Paracetamol Infant Suspension, Boots Paracetamol 3 Months Plus Oral Suspension[1] and Anbesol Teething Gel are some of the most popular medicines that contain these additives.

Young children are seen as a special risk group in relation to the ingestion of additives because the immune system is still in development during the early years and children experience rapid growth and development. For this reason, the use of artificial colours in any foods especially prepared for infants and young children (defined as under 36 months of age) have been banned in the EU for over 20 years. EU Directive 89/398/EEC states that 'Food additives shall not be used in foods for infants and young children, including dietary foods for infants and young children for special medical purposes'[2] . New regulations covering foods for special medical purposes, including foods and drinks for infants and children, have been brought in across the EU from 2013[3] and prohibition of the use of artificial colourings remains.

However, medicines are subject to different guidance and regulations from those relating to food and drink. This report reveals that medicines which can be given to children as young as two months of age may contain colourings, and some of these are those that the UK government has requested be withdrawn from all food and drink. Artificial colours used in foods, drinks and medicines have no nutritional or safety benefits. They are used solely as cosmetic additives to boost the consumer appeal of products, for example by adding brightness or suggesting the presence of an ingredient such as a fruit.

1. The 120mg/5mg 100ml suspension contains Carmoisine but in the 3 Month Plus Oral Suspension sachets this has been replaced with carmine.
2. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32008R1333:EN:NOT
3. http://new.eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.L_.2013.181.01.0035.01.ENG

The Southampton Seven

Research funded by the Food Standards Agency (FSA) and carried out by the University of Southampton between 2004 and 2007 showed that six specific colourings and one preservative – known as the Southampton Seven additives – were linked to attention deficit disorders in children in the general population (Stevenson et al, 2007).

The artificial colourings, and the preservative, linked to behavioural problems in some children are:

- Tartrazine – E102
- Quinoline Yellow – E104
- Sunset Yellow – E110
- Carmoisine – E122
- Ponceau 4R – E124
- Allura Red AC – E129
- Sodium benzoate (preservative) – E211.

Five of these colourings have been associated with genotoxic changes (permanent genetic mutations) in some animal studies. The European Food Safety Agency (EFSA) acknowledges that there is a pattern of effects shared by them, and launched an investigation to assess their genotoxicity in June 2013.[4]

As a result of the Southampton University research, the FSA requested a voluntary withdrawal of the use of these six colourings by food and drink manufacturers in the UK. The researchers also recommended that more research was needed into the preservative sodium benzoate.

In 2008 the European Commission issued a regulation that required all foods and drinks containing the six colourings from the Southampton Seven additives be clearly labelled to show they contain ingredients that could have an adverse health effect. The wording is:
"[Name] may have an adverse effect on activity and attention in children."

However, this EU law does not apply to medicines. The Medicines and Healthcare products Regulatory Agency (MHRA) is the UK's government body responsible for regulating all medicines, including ensuring that medicines work and that they are safe. The MHRA has encouraged manufacturers of medicines to remove the Southampton Seven colourings where possible. They remark, however, that medicines are taken infrequently, and that therefore consumption of these ingredients is likely to be low. However, we have seen no studies undertaken either publicly or privately to prove that this is the case either generally, or in circumstances such as among chronically ill children requiring daily doses of, for example, a medicine used to treat epilepsy, an antibiotic or pain reliever.

Action on Additives believes the same protection offered to young children by food regulation should also apply to the regulation of medicines.

4. European Food Safety Agency (2013) Statement on Allura Red AC and other sulphonated mono azo dyes authorised as food and feed additives. http://www.efsa.europa.eu/en/efsajournal/doc/3234.pdf

Which children's medicines contain the Southampton Seven?

Action on Additives investigated prescription and over-the-counter medicines, particularly looking at medicines marketed for or prescribed to children, to find out how many medicines included one or more of the Southampton Seven additives (see Table 1). We found:

- The most frequently used colouring is Sunset Yellow (E110), used in six products.
- The red colour Carmoisine (E122) is used in four medicines, including Calpol Paracetemol Infant Suspension and Boots Paracetamol 3 Months Plus.
- Five medicines contain Quinoline Yellow (E104).
- Five medicines contain Ponceau 4R (E124).
- The preservative sodium benzoate (E211) is used even more frequently, in 37 different children's medicines.
- Four medicines contain both at least one of the Southampton Seven colours and the preservative sodium benzoate.
- Two of the six Southampton Seven colourings are not used in medicines for children.

For details of the specific children's medicines using the Southampton Seven, see Appendix 2.

Number of children's medicines found to contain one or more of the Southampton Seven additives

	Colour or preservative	E Number	Number of children's medicines with S/S colours or preservatives
1	Tartrazine*	E102	0
2	Quinoline Yellow	E104	5
3	Sunset Yellow*	E110	6
4	Carmoisine*	E122	4
5	Ponceau 4 R*	E124	5
6	Allura Red AC*	E129	0
7	Sodium benzoate (preservative)	E211	37

Note: Although the list of medicines investigated in this report does not seek to be exhaustive, it does include the great majority of regularly used and recognised medicines for children.

Background information on artificial food colours and other additives

Artificial food colours and other food additives (AFCA) have long been suggested to affect behaviour in children. Ben Feingold made his initial claims on the detrimental effect of AFCA on childhood behaviour more than 35 years ago (Feingold, 1977) and a recent review looking at potential mechanisms linking artificial food colours to abnormal behaviour concluded that *" Many questions remain about the mechanisms by which foods and food additives cause biochemical changes that lead to abnormal changes in behavior in children, though several aspects are known, [including that] AFCs can cause adverse behavioral changes in a subgroup of children with ADHD and in a subgroup of the general pediatric population as well" (Stevens et al, 2013).*

5. http://www.southampton.ac.uk/mediacentre/news/2007/sep/07_99.shtml

Professor of Psychology, Jim Stevenson, who led the 2007 University of Southampton research study, commented after their research was published[5]*: "We now have clear evidence that mixtures of certain food colours and benzoate preservative can adversely influence the behaviour of children. There is some previous evidence that some children with behavioural disorders could benefit from the removal of certain food colours from their diet. We have now shown that for a large group of children in the general population, consumption of certain mixtures of artificial food colours and sodium benzoate preservative can influence their hyperactive behaviour."*

European Food Safety Authority (EFSA) research

Widespread concerns about the observed impact on hyperactivity have prompted further reviews of the Southampton Seven additives with regard to:

- review of the safe acceptable daily intake (the ADI), and
- research into genotoxicity – the overall safety on ingestion as it relates to damage to DNA, the genetic material in every cell of our body.

Review of acceptable daily intake (ADI)

In 2009, following further review of evidence relating to specific additives, EFSA lowered the acceptable daily intake (ADI) of three of the six colours:

- Quinoline Yellow E104 from 0-10mg/kg bodyweight/day to 0.5mg/kg bodyweight/day[6]
- Sunset Yellow E110 from 0-2.25mg/kg bodyweight/day to 1.0mg/kg bodyweight/day[7]
- Ponceau 4R E124 from 0-4 mg/kg bodyweight/day to 0.7mg/kg bodyweight/day[8]

Research into genotoxicity

In June 2013, EFSA announced that it would be carrying out genotoxicity testing on the colourings listed below (five from Southampton study, plus one additional colouring, Amaranth E123):

- Tartrazine E102
- Sunset Yellow E110
- Carmoisine E122
- Ponceau 4R E124
- Allura Red AC E129
- Amaranth E123.

Dr Alicja Mortensen, Chair of EFSA's Panel on Additives and Nutrient Sources Added to Food (ANS Panel), stated after recent investigation into Allura Red that : *"In the light of all the data evaluated in this review, the Panel considers that these structurally related dyes could share a pattern of effects that deserve further investigation"* [9].

6. http://www.efsa.europa.eu/en/efsajournal/pub/1329.htm
7. http://www.efsa.europa.eu/en/efsajournal/pub/1330.htm
8. http://www.efsa.europa.eu/en/efsajournal/pub/1328.htm
9. http://www.efsa.europa.eu/en/press/news/130617.htm

Research into sodium benzoate

Sodium benzoate was linked to hyperactivity in the original 2007 research. However, the Food Standards Agency (FSA) has been less stringent in trying to reduce the use of this preservative in the food supply. The FSA felt the evidence for the hyperactivity connection was not as strong. And, because of the technical use of sodium benzoate as a preservative, it would be harder for industry to remove it from products. As a result, sodium benzoate escaped the call for a voluntary ban and the requirement for the warning label, while further research was done into its effect on child health. However, the original research showed up potential adverse health implications from its use and the researchers concluded:

"More research is needed to clarify the possible effects of sodium benzoate on behaviour, they [FSA] say. This additive was included in the Isle of Wight and Southampton Studies but its effects could not be isolated from that of the food colours and a double-blinded placebo-controlled food challenge study is called for."[10]

This work has not been carried out. The reason given recently, in direct contradiction to a call for research from its own advisers, was:

"FSA considers that, because sodium benzoate was present at the same level in both the mixes tested in the study by Southampton University, and the two mixes gave different results, it is unlikely the benzoate was responsible for the differences seen. Therefore, we have no plans for further research on sodium benzoate." (Personal communication with FSA, October 2013)

Some of the companies that Action on Additives contacted in the course of compiling this report told us they are removing sodium benzoate because of the risk of an internal reaction in some products that results in the production of low levels of the carcinogenic molecule benzene. Research elsewhere has linked sodium benzoate to allergic reactions (Asero, 2006; Nettis et al, 2004).

10. http://www.southampton.ac.uk/mediacentre/news/2008/apr/08_65.shtml

Are there alternatives to these artificial colours that can be used in medicines?

At Action on Additives we have been observing the changes in the food and drink industry since the publication of the FSA-sponsored research. The leading companies in that industry have acknowledged that parents would prefer their children not to consume potentially risky synthetic colourings. It is well known that natural alternatives have been around for many years.

After 2008, publicity around the Southampton study stimulated strong public pressure, creating new opportunities for 'better' products. At the same time the requirement to put a warning statement on products catalysed new technological developments in order to avoid having to highlight the poor quality of existing products.

In most cases, all artificial colours, including those highlighted in the Southampton study, have now been removed from the majority of food and drink products. The products still have an acceptable appearance because now the colour comes from the ingredients, boosted in many cases by 'colouring foods' (fruits, vegetables and other edible plants processed with water to produce a concentrate of the fruit and/or vegetable with its corresponding colour). However, the use of artificial colourings in foods from smaller manufacturers and in imported foods sold in the UK remains a problem, and Action on Additives continues to encourage manufacturers and retailers to remove these additives, or clearly label products, as a matter of urgency.

Medicines – regulations and labelling

There are different regulations governing the constituents of medicines. The complete ban on colourings, flavourings, sweeteners and preservatives in food and drink for young children up to the age of 36 months does not apply to medicines. Also, the voluntary withdrawal of the six Southampton colours from all food and drink, requested by the FSA, does not apply to medicines.

Medicines in the UK and the EU, are regulated under two Directives:

- The Council Directive 2001/83/EC, which regulates the licensing, manufacture and wholesale dealing in medicinal products within the EU.[11]
- The Council Directive 2003/94/EC, which lays down the principles and guidelines of good manufacturing practice for products that require Marketing Authorisation (or product licence). There has been some focus on children's medicines over recent years, as nearly half of the medicines used with children were not licensed or off-label, which means that they have been tested on adults only, and not with children.[12]

Anecdotal evidence from parents tells us that some medicines such as Calpol (which contains Carmoisine E122) are given to very young children frequently, with first intakes often associated with an infant's first immunisations at 8 weeks of age, and over extended periods of time. Backing this up is market data stating that Calpol is the fourth largest OTC brand, in the UK worth £49.4M in the UK ahead of Lemsip and Seven Seas. (source IRI All Outlets; Value Sales; 52 w/e 31st December 2011).

The European Union has issued its own guidance on the use of 'colouring agents' used in paediatric medicines, advising that special care is needed when formulating medicines for children. It highlights that the known risk of, for example, azo dyes, should be taken into consideration.[13]

In July 2013, the MHRA stated that it is committed to encouraging manufacturers to remove the colourings identified in the Southampton study. However, they also commented that until the European Union regulates the use of colourings in food, rather than merely recommending withdrawal, it is not possible to ban the use of the Southampton Seven additives in medicines.

A further document currently under review covers the need for labelling of 'excipients' and details the warnings to be shown in the patient information leaflet (excipients are ingredients of a medicine other than those that have a direct action on the disease or condition and those known to have a recognised action in their own right). Information about the Southampton list is included in that document. The document is for guidance only and is currently under review, as the European Medicines Agency (EMU), awaits new information.[14]

11. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2001:311:0067:0067:EN:PDF
12. http://ec.europa.eu/health/files/eudralex/vol-1/dir_2003_94/dir_2003_94_en.pdfhttp://ec.europa.eu/health/files/eudralex/vol-1/dir_2003_94/dir_2003_94_en.pdf
13. European Medicines Agency (2007) Guideline on excipients in the dossier for application for marketing authorization of a medicinal product. http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003382.pdf
14. Guidelines. Medicinal products for human use: Safety, environment and information. Excipients in the label and package leaflet of medicinal products for human use. http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003412.pdf

Inadequate labelling of medicines

Parents need clear labelling on products they purchase to give to their children, so that they can make informed decisions. Packaged food and drink are required to show a list of ingredients, but different regulations apply to medicines. The ingredients that need to be listed depends on how the medicine is to be applied (Directive 2001/83/EC).[15]

Requirements for showing information on ingredients on medicines

Application	What needs to be shown on the external packaging	What needs to be shown on a patient information leaflet
'Topical': parentheral, ophthalmic and topical applications – skin, inside of mouth, nose, anus, vagina. Inhaled medicines.	All ingredients	
All other medicines, including oral liquids or tablets	Active ingredients that have a direct action on the disease/condition, plus other ingredients known to have a recognized action in their own right. These include: • Tartrazine E102 • Sunset Yellow E110 • Carmoisine E122 • Ponceau 4R E124	All other ingredients, often known as excipients**

* Excipients can be colourings, flavourings and preservatives. They are considered to be inactive or inert, but regulation recognises that some of these additives do have an effect under certain circumstances.

Due to the inconsistency of these rules, it would appear that three of the Southampton Seven additives do not need to be named on the external packaging of non-topical medicines and parents are therefore unable to avoid them unless they collect or purchase the product and can then check the patient information leaflet. The three additives are:

- Quinoline Yellow (E104),
- Allura Red (E129),
- Sodium Benzoate (E211)

15. Directive 2001/83/EC.

Engaging with manufacturers and retailers of children's medicines

In May 2013, Action on Additives wrote to manufacturers of children's medicines. We also wrote to retailers about their 'own brand' products and their policies on stocking of the branded lines. In total we contacted:

- 15 pharmaceutical manufacturers currently using any of the Southampton Seven additives in the production of medicines taken by young children
- the six largest pharmacy chains in the UK, and
- the 12 largest supermarkets in the UK.

We asked each organisation what their policies were in relation to the use of the colourings and preservative identified in the Southampton Study. Below are some of our findings.

Responses from the pharmaceutical companies

- The Boots Company PLC said: *"The colourants and other additives that have been mentioned are commonly present in medicines which have been approved for use by the MHRA ... One of the MHRA's roles is to assure that colour and other additives used in medicines are safe and that the products containing these ingredients are appropriately labelled."*
- Johnson & Johnson Ltd, makers of Calpol, said: *"Carmoisine (E122) (one of the Southampton Six) and sodium benzoate are contained in many medicines which have been approved for use by the MHRA in the UK."*
- Alliance Pharmaceuticals Ltd said: *"Anbesol Teething Gel is a medicine that is licensed in the UK by the Medicines and Health Product Regulatory Agency (MHRA) … Alliance Pharmaceuticals will continue to follow the advice and guidelines provided by the MHRA and European Commission."*

Despite clear evidence of a link between the Southampton Seven and ADHD, Johnson & Johnson maintain: *"To date, no evidence has been provided to suggest additives – such as Carmoisine (E122), Sunset Yellow (E110) or the preservative E211 (known as sodium benzoate) – are associated with hyperactivity when present in children's medicines."*

As this report has shown, use of the Southampton Seven is widespread in children's medicines. Often, the pharmaceutical companies that Action on Additives contacted justified this on the basis of the lower consumption of medicines compared with food and drink.

- Johnson & Johnson Ltd, manufacturers of Calpol, said: *"the consumption of food and drink is very different to the consumption of medicines – over the counter medicines are only intended for occasional use in small quantities over a very short period of time and typically a 5ml dose of CALPOL® Infant Suspension would include less than 0.1mg of colouring."*

Pharmaceutical manufacturers also argued that colourings were necessary to allow identification of medicines:

- The Boots Company PLC said: *"Colour additives are an important component of many medicines, as the colour of the product allows patients and healthcare professionals to identify a medicine on sight."*

Although the majority of pharmaceutical companies were unwilling to acknowledge the need to remove the Southampton Seven, Rosemont commented: *"We do have a few older products which contain some of the colouring agents you mentioned (the Southampton 6 colourings), which are listed on the packaging in accordance with pharmaceutical regulations. It is our intention to remove these colours from the remaining products if possible if these products undergo reformulation.*

For all new products, it has been our policy for many years not to use any colouring agents, or in extremely rare cases we would use approved colours such as caramel.

With regards to E211, we are aware that there has been one anecdotal report of gasping syndrome in a neonate in Japan with Benzoic Acid. We are not aware of any issue with this preservative in children in general. However it is a microbial preservative that we will only use if other preservatives prove to be ineffective in a formulation."

Responses from the retailers

Supermarkets are aware of the risks associated with the Southampton Six colourings. Responding to the Action on Additives questionnaire, they all stated that they had removed the colours from their own-label food and drink products:

- An **Aldi** spokesperson said: *"'Southampton Six' colours (E102, E104, E110, E122, E124 and E129) have been linked to hyperactivity in children. Aldi understands that this is a concern to our customers and has therefore removed them from all its own label food products."*
- **ASDA** said: *"We have a strict NAFNAC (no artificial flavours and no artificial colours) for all our own label food which has been in place for many years."*
- **Tesco** said: *"None of our Tesco brands contain any artificial colours or flavours. That includes the specific additives you mention – E102, E104, E110, E122, E124, and E129 – which should not be used in any Tesco brand food, supplement or vitamin. Sodium benzoate should also not be used in any Tesco brand food, supplement or vitamin."*

However, when asked about medicines, the news from retailers was less positive:

- **Tesco** said: *"With regard to colourings and the preservative E211 in medicines, we deem the risk to be low when compared to food and drink, as medicines are used for short periods of time and also sporadically."*
- **Sainsbury's** said: *"We currently use artificial colours and Sodium Benzoate in a small number of our own-brand medicines. These medicines are subject to MHRA license and none are children's medicines."*
- **Nisa** said: *"The Nisa's adherence on the listed colourings applies to all food and drink products, but we cannot categorically state that they are not present in medicines – previously some capsules contained E104 Quinoline Yellow although we are seeking to confirm with our supplier whether this is still the case … Nisa own label medicines do not contain Sodium Benzoate."*

Call to action – what needs to happen

Regulators

Action on Additives is calling for stronger action from the Medicines and Healthcare Products Regulatory Agency (MHRA) and the European Medicines Agency (EMU):

1. **The artificial colourings (azo dyes) investigated in the Southampton research should be banned from food and medicine, not simply 'recommended for withdrawal'.**
2. In the meantime, there should be a requirement that, if a medicine includes azo dyes, this should be indicated on the outside label, and the patient information leaflet should highlight the use of azo dyes as a risk.
3. The FSA should instigate and publish the results of research into the safety of sodium benzoate and forward this to the MHRA for their own actions.
4. The EFSA should publish the results of its testing on the genotoxicity of the following additives, and forward this to the MHRA for their own actions:
   - Tartrazine (E102)
   - Sunset Yellow (E110)
   - Carmoisine (E122)
   - Ponceau 4R (E124)
   - Allura Red (E129), and
   - Amaranth (E123).
5. The MHRA should publish their long-awaited review of the safety of 'excipients' (colourings, flavourings and preservatives) in medicines.

Manufacturers of children's medicines

1. **Manufacturers of medicines sold as suitable for children but containing any of the Southampton Seven additives should take action to remove them from their products as quickly as possible.**
2. In the meantime, labelling on children's medicines should be reviewed to ensure that the Southampton Seven additives are shown on both the internal and external packaging of all medicines, and not just those topically applied. Those that contain any of the Southampton Seven additives should label their products with the same warning label used by food and drink manufacturers, that is:
   '[NAME] may have an adverse effect on activity and attention in children.'

Members of the public

1. **Members of the public can join the Action on Additives in Medicines Campaign on additives in children's medicines and share information among friends on Facebook and Twitter.**
   They can help us by protesting about the presence of the additives, and/or the poor information available on the product label and/or the lack of consistency between the protection afforded to young children, and the better labelling of food and drink.

2. **They can also share their experiences, using the Yellow Card Scheme.**
   If they suspect a child has had an adverse effect from ingesting medicine contain the Southampton Seven additives, they can use the Yellow Card Scheme, run by the MHRA and the Commission on Human Medicines. This is used to collect information from both health professionals and the general public on suspected side effects to a medicine (prescription and over the counter). They can do this online at *https://yellowcard.mhra.gov.uk/* or pick up a leaflet at the local pharmacy.
3. **They can also protest in writing.**
   If they have purchased a child's medicine that contains one of the Southampton Seven additives, they can contact the MHRA with the name of the product and the date and place of purchase, complaining about the constituents. They should write to: MHRA Enforcement and Intelligence Group at 5 Magenta, 151 Buckingham Palace Road, London, SW1W 9SZ. Tel: 020 3080 6330. Or email them at *casereferrals@mhra.gsi.gov.uk.*

The next steps

The Action on Additives in Medicines Campaign is:

- calling for retailers and manufacturers to do more about banning the use of the Southampton Seven additives in their products.
- lobbying for better regulation and sharing information as it becomes available about forthcoming changes in regulation, or new testing, and
- distributing a guide for parents to help them to avoid additives in children's medicines.

Action on Additives will continue to monitor of the use of the six colourings in foods, drinks and medicines and the use of sodium benzoate. We will also look into the safety of other colourings and additives used in children's foods, drinks and medicines.

About Action on Additives

Action on Additives provides evidence-based information and resources about the use of colourings, sweeteners, flavourings and other novel ingredients in the UK's food, drink and medicine supply. The composition, quality and safety of our foods, drinks and medicines impact on the health and well-being of the entire population, but are particularly important for pregnant women and children under the age of five.

Keep in touch with us via facebook (www.facebook/actiononadditives), our twitter feed @ActionAdditives or by email to lizzie@actiononadditives.org and let us know if you are prescribed, or buy, any children's medicines that contain any of the restricted additives.

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Appendix 1
Research methodology

The information for this report was sourced from:

- British National Formulary for Children – to identify the medicines specifically aimed at children. (Published by the Royal Pharmaceutical Society and the BMJ Group, under the authority of a Joint Formulary Committee, which comprises representatives of the two professional bodies and the Department of Health).
- Online Electronic Compendium of Medicines – to check prescription medicines in UK.
- Product labels – to check information on product labels for medicines sold in pharmacy chains and supermarkets.

Although the list of medicines covered does not seek to be exhaustive, it does include the great majority of regularly used and recognised medicines for children.

Appendix 2
Children's medicines containing the Southampton Seven additives

Name of Medicine	Manufacturer	POM, P, OTC (Prescription, Pharmacy Only or Over the Counter)	Age suitable for	Colours present	Preservative Present
OVER THE COUNTER					
Anbesol Teething Gel	Alliance Pharmaceuticals	Over the Counter	Teething babies	Ponceau 4R (E124)	
Calpol Paracetamol Infant Suspension	McNeil Products	Over the Counter	2 months to 6 years	Caromoisine (E122)	
Calpol Paracetamol Infant Suspension Sachets	McNeil Products	Over the Counter	2 months to 6 years	Caromoisine (E122)	
Calpol Paracetamol Infant Suspension Sugar Free	McNeil Products	Over the Counter	2 months to 6 years	Caromoisine (E122)	
Galenphol Paediatric Linctus	Thornton & Ross Ltd	Over the Counter	6 years plus	Sunset Yellow (E110)	
Paediatric Paracetamol Elixir	Pinewood Healthcare	Over the Counter	2-3 months	Quinoline Yellow (E104)	
Paracetamol Oral Suspension (Sugar Free)	The Boots Company PLC	Over the Counter	3 months plus	Caromoisine (E122)	
PHARMACY ONLY					
Anbesol Liquid	Alliance Pharmaceuticals	Pharmacy Only	Children, Adults, Elderly	Quinoline Yellow (E104), Sunset Yellow (E110)	
Boots Threadworm Tablets	The Boots Company Plc	Pharmacy Only	2 years plus	Sunset Yellow (E110)	
Ovex/Family Threadworm	McNeil Products Ltd	Pharmacy Only	2 years plus	Sunset Yellow (E110)	
PRESCRIPTION					
Amoxicillin 125mg Sugar Free Oral Suspension	Kent Pharmaceuticals	Prescription	All ages	Quinoline Yellow (E104)	
Amoxicillin 250mg Sugar Free Oral Suspension	Kent Pharmaceuticals	Prescription	All ages	Quinoline Yellow (E104)	
Ampicilin Oral Suspension 250mg	Kent Pharmaceuticals	Prescription	All ages	Ponceau 4R (E124)	Sodium Benzoate (E211)
Ampicilin Oral Suspension 125mg	Kent Pharmaceuticals	Prescription	All ages	Ponceau 4R (E124)	Sodium Benzoate (E211)
Cefalexin 250mg/5ml Oral Suspension	Aurobindo Pharma - Milpharm Ltd	Prescription	5 years plus	Quinoline Yellow (E104) Carmoisine (E122),	Sodium Benzoate (E211)
Epanutin Oral Suspension	Pfizer	Prescription		Sunset Yellow (E110)	Sodium Benzoate (E211)
Mucodyne Paediatric Syrup	Sanofi	Prescription	2-12 years	Red Ponceau (E124)	
Nalidixic Acid 300mg Oral Suspension	Rosemont Pharmaceuticals Ltd	Prescription	3 months plus	Ponceau 4R (E124)	
Prezista Film Coated Tablets 400mg & 600mg (only)	Janssen-Cillag Limited	Prescription	3 years or 15kg +	Sunset Yellow (E110)	

Children's medicines containing Sodium Benzoate (E211) only (1)

Name of Medicine	Manufacturer	POM, P, OTC (Prescription, Pharmacy Only or Over the Counter)	Age suitable for	Preservative present
OVER THE COUNTER				
Benylin Children's Apple Flavour Cough Syrup	McNeil Products Limited	Over the Counter	3 months - 5 years	Sodium Benzoate (E211)
Benylin Children's Cough Syrup Blackcurrant	McNeil Products Limited	Over the Counter	1 year plus	Sodium Benzoate (E211)
Benylin Children's Dry Cough	McNeil Products Limited	Over the Counter	Under 6 years	Sodium Benzoate (E211)
Benylin Children's Tickly Cough	McNeil Products Limited	Over the Counter	3 months - 5 years	Sodium Benzoate (E211)
Boots Cough Syrup	The Boots Company PLC	Over the Counter	3 months - 5 years	Sodium Benzoate (E211)
Calcough Children's Soothing Syrup Blackcurrant Flavour	McNeil Products Limited	Over the Counter	1 year plus	Sodium Benzoate (E211)
Calcough Infant Syrup Apple Flavour, Sugar & Colour Free	McNeil Products Limited	Over the Counter	3 months - 5 years	Sodium Benzoate (E211)
Care Ibuprofen for Children Oral Suspension	Thornton & Ross Ltd	Over the Counter	6 months to 12 years	Sodium Benzoate (E211)
Cough Syrup Glycerol, Apple Flavour	The Boots Company PLC	Over the Counter	3 months plus	Sodium Benzoate (E211)
Dry Cough Syrup Plus	The Boots Company PLC	Over the Counter	6 years plus	Sodium Benzoate (E211)
Non-drowsy Sudafed Children's Syrup	McNeil Products Limited	Over the Counter	6 to 12 years	Sodium Benzoate (E211)
Numark Paracetamol 120mg/5ml Oral Suspension	Numark Limited	Over the Counter	2 months plus	Sodium Benzoate (E211)
Numark Paracetamol 250mg/5ml Oral Suspension	Numark Limited	Over the Counter	6-12 years	Sodium Benzoate (E211)
Paracetamol Oral Suspension	Pinewood Healthcare	Over the Counter	2 months to 12 years	Sodium Benzoate (E211)
Sainsbury Junior Ibuprofen Suspension 100mg/5ml	Sainsbury Supermarkets Limited	Over the Counter	from 3 months	Sodium Benzoate (E211)
Simple Linctus Paediatric Sugar Free	Pinewood Healthcare	Over the Counter	Children	Sodium Benzoate (E211)
Tixylix Baby Syrup Colour Free & Sugar Free	Norvatis Consumer Health	Over the Counter	3 months - 5 years	Sodium Benzoate (E211)
Tixylix Toddler's Syrup Sugar Free & Colour Free	Norvatis Consumer Health	Over the Counter	3 months - 5 years	Sodium Benzoate (E211)

Children's medicines containing Sodium Benzoate (E211) only (2)

Name of Medicine	Manufacturer	POM, P, OTC (Prescription, Pharmacy Only or Over the Counter)	Age suitable for	Preservative present
PHARMACY ONLY				
Benylin Children's Chesty Cough (Strawberry Flavour, Sugar & Colour Free)	McNeil Products Limited	Pharmacy Only	6-12 years	Sodium Benzoate (E211)
Benylin Night Cough Raspberry Flavour, Sugar & Colour Free	McNeil Products Limited	Pharmacy Only	6-12 years	Sodium Benzoate (E211)
Lloyds Paracetamol Sugar & Colour Free Oral Suspension 120mg/5ml	Lloyds Pharmacy	Pharmacy Only	from 3 months	Sodium Benzoate (E211)
Lloyds Paracetamol Sugar & Colour Free Oral Suspension 250mg/5ml	Lloyds Pharmacy	Pharmacy Only	from 6 years	Sodium Benzoate (E211)
Boots Dry Cough Syrup Blackcurrant Flavour	The Boots Company PLC	Pharmacy Only	6 years plus	Sodium Benzoate (E211)
Tixylix Chesty Cough	Norvatis Consumer Health	Pharmacy Only	6-10 years	Sodium Benzoate (E211)
PRESCRIPTION				
Amoxil Paediatric Suspension	GlaxoSmithKline UK	Prescription	from under 6 months and plus	Sodium Benzoate (E211)
Cefalexin 125mg/5ml Oral Suspension	Aurobindo Pharma - Milpharm Ltd	Prescription	Under 5	Sodium Benzoate (E211)
Diflucan 10mg/ml & 40mg/ml Powder for Oral Suspension	Pfizer Limited	Prescription	from newborn plus	Sodium Benzoate (E211)
Revatio Powder for Oral Suspension	Pfizer Ltd	Prescription	1 to 7 years	Sodium Benzoate (E211)
Septrin 40mg/200mg Paediatric Suspension	Aspen Global	Prescription	from 6 weeks	Sodium Benzoate (E211)
Sulfasalazine 250mg/5ml Oral Suspension	Rosemont Pharmaceuticals Ltd	Prescription	2 years plus	Sodium Benzoate (E211)
Suprax Powder for Oral Suspension	Sanofi	Prescription	6 months to 10 years	Sodium Benzoate (E211)
Tamiflu 6mg/ml Powder for Oral Suspension	Roche Products Ltd	Prescription	1 year and above	Sodium Benzoate (E211)
Tixylix Toddler's Syrup Sugar Free & Colour Free	Norvatis Consumer Health	OTC	3 months - 5 years	Sodium Benzoate (E211)
VFEND Powder for Oral Suspension	Pfizer Ltd	Prescription	2 to 12 years	Sodium Benzoate (E211)

Appendix 3
University of Southampton research study on food additives

The research by a team from the University of Southampton's Schools of Psychology and Medicine provided a clear demonstration that changes in behaviour can be detected in three-year-old and eight-year-old children as a result of their consuming particular additives found in food and drink.

The research was funded by a £0.75m grant from the Food Standards Agency and published as a report to them (Stevenson et al, 2007) and as a paper in The Lancet (McCann et al, 2007). It involved studying levels of hyperactivity in 153 three-year-olds and 144 eight-year-olds living in the city of Southampton. The children were selected from the general population to represent the full range of behaviour, from normal through to hyperactive, and not for any previous behavioural problems or known sensitivities to particular foods.

The children's families were asked to put them on a diet free from the additives used in the study. Over a six-week period the children were then given a drink each day which either contained a mixture of food colours and benzoate preservative, or just fruit juice – with all the drinks looking and tasting identical.

Hyperactivity is a behaviour indicated by increased movement, impulsivity and inattention. The results of the Southampton study show that when the children were given the drinks containing the test mixtures, in some cases their behaviour was significantly more hyperactive. These results replicate and extend previous FSA-funded research by the team in Southampton.

The research team used a combination of reports on the children's behaviour from teachers and parents, together with recordings of the children's behaviour in the classroom made by an observer, and, for the older children, a computer-based test of attention. None of the participants – teachers, parents, the observer, or the children – knew which drink each child was taking at any one time.

action on additives

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