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The Relationship Between Inadvertent Ingestion and Dermal Exposure Pathways: A New Integrated Conceptual Model and a Database of Dermal and Oral Transfer Efficiencies

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Occupational inadvertent ingestion exposure is ingestion exposure due to contact between the mouth and contaminated hands or objects. Although individuals are typically oblivious to their exposure by this route, it is a potentially significant source of occupational exposure for some substances. Due to the continual flux of saliva through the oral cavity and the non-specificity of biological monitoring to routes of exposure, direct measurement of exposure by the inadvertent ingestion route is challenging; predictive models may be required to assess exposure. The work described in this manuscript has been carried out as part of a project to develop a predictive model for estimating inadvertent ingestion exposure in the workplace. As inadvertent ingestion exposure mainly arises from hand-to-mouth contact, it is closely linked to dermal exposure. We present a new integrated conceptual model for dermal and inadvertent ingestion exposure that should help to increase our understanding of ingestion exposure and our ability to simultaneously estimate exposure by the dermal and ingestion routes. The conceptual model consists of eight compartments (source, air, surface contaminant layer, outer clothing contaminant layer, inner clothing contaminant layer, hands and arms layer, perioral layer, and oral cavity) and nine mass transport processes (emission, deposition, resuspension or evaporation, transfer, removal, redistribution, decontamination, penetration and/or permeation, and swallowing) that describe event-based movement of substances between compartments (e.g. emission, deposition, etc.). This conceptual model is intended to guide the development of predictive exposure models that estimate exposure from both the dermal and the inadvertent ingestion pathways. For exposure by these pathways the efficiency of transfer of materials between compartments (for example from surfaces to hands, or from hands to the mouth) are important determinants of exposure. A database of transfer efficiency data relevant for dermal and inadvertent ingestion exposure was developed, containing 534 empirically measured transfer efficiencies measured between 1980 and 2010 and reported in the peer-reviewed and grey literature. The majority of the reported transfer efficiencies (84%) relate to transfer between surfaces and hands, but the database also includes efficiencies for other transfer scenarios,

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including surface-to-glove, hand-to-mouth, and skin-to-skin. While the conceptual model can provide a framework for a predictive exposure assessment model, the database provides detailed information on transfer efficiencies between the various compartments. Together, the conceptual model and the database provide a basis for the development of a quantitative tool to estimate inadvertent ingestion exposure in the workplace.

Keywords: dermal exposure; determinants of exposure; exposure modelling; inadvertent ingestion exposure; occupational exposure

INTRODUCTION

Inadvertent ingestion exposure

Exposure to hazardous substances in the workplace may arise by inhalation, skin contact, and ingestion. Of these three primary exposure routes, ingestion has been studied the least and has typically been controlled by providing hand washing facilities and eating areas removed from work areas (European Chemicals Bureau, 2003). Cherrie *et al*. (2006) argued that the effectiveness of this control approach has never been properly evaluated. They examined the potential importance of the ingestion route in relation to dermal and inhalation exposure. For certain substances that are absorbed through the gastrointestinal tract, inadvertent ingestion exposure due to contact between contaminated hands or objects and the mouth was identified as a potentially significant factor in workplace exposure. Inadvertent ingestion exposure can be defined as ingestion that arises from contact between the mouth or the perioral region (the area surrounding the mouth) and contaminated hands or objects, which results in ingestion of which the individual may be oblivious. This is in contrast with exposure through eating contaminated food where the person is clearly aware of ingestion of the food items (although not necessarily of the contaminant). Workers may touch their mouths, chew a pen, bite their nails or use their mouths to remove personal protective equipment (PPE), and each of these activities can contribute to ingestion exposure if the hands or objects are contaminated. Cherrie *et al.* (2006) estimated that approximately 4.5 million workers in the UK (15.6% of the UK working population) are potentially exposed to hazardous substances by inadvertent ingestion exposure at work. Inadvertent ingestion was identified as a potentially significant route of exposure for metals (~1.5 million UK workers exposed), pathogens (~1 million), high molecular weight allergens (~0.75 million), pharmaceuticals (~0.89 million), and radionuclides (~32 000). Although these figures were based on professional judgement and not on measurement data, they do suggest that inadvertent ingestion exposure warrants further investigation.

Exposure modelling

Under the European Union (EU) REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) regulations (Regulation [EC] No 1907/2006) industry is required to conduct risk assessments for workers, consumers and the environment for chemicals manufactured or imported in the EU market in quantities greater than one tonne. REACH requires estimation of exposure through all relevant routes, which may include inhalation, dermal contact and ingestion.

Even for inhalation exposure there are currently insufficient exposure data to estimate exposure for many occupational exposure scenarios. Predictive exposure models have therefore been developed to screen scenarios to identify those that require additional exposure measurements and/or control. Predictive models are available for inhalation and/or dermal exposure, including the Advanced REACH Tool (ART) (Tielemans *et al*., 2011), Metals' Estimation and Assessment of Substance Exposure (MEASE) (EBRC, 2010), ECETOC Targeted Risk Assessment (TRA) (ECETOC, 2009), STOFFENMANAGER (Marquart *et al*., 2008), Dermal Exposure Assessment (DREAM) (van Wendel de Joode *et al.*, 2003), and Risk Assessment of Occupational Dermal Exposure (RISKOFDERM) (van Hemmen *et al*., 2003). None of the available tools estimate exposure by inadvertent ingestion.

A number of attempts have been made to estimate inadvertent ingestion exposure using equations that describe the relationship between the mass of contaminant loaded on the hand or object, the frequency of hand-to-mouth contact, and the transfer efficiency of substances from hands/objects into the mouth (Deubner *et al*., 2001; Gaborek *et al*., 2001; Beyer *et al*., 2003; Stapleton *et al*., 2008). These estimates typically assume uniform loading of contamination across the entire hand or object. A similar approach has been used to estimate ingestion exposure from hand or object-to-mouth contact among children (Zartarian *et al*., 2000; Hemond and Solo-Gabriele, 2004; Hore *et al.*, 2006; Canales and Leckie, 2007). Equations estimating inadvertent ingestion are of the general form as shown below:

$$E_{\text{ii}} = \text{Ld} \times \text{SA} \times \text{TE} \times N \qquad (1)$$

where, E_{ii}: exposure by inadvertent ingestion exposure (mg); Ld: loading of substance on hand or object (mg cm^{-2}); SA: surface area of hand or object that comes in contact with the mouth (cm^2); TE: transfer efficiency of substance from hands or object to the mouth (proportion) N: number of hand or object-to-mouth contacts.

Christopher (2008) developed an initial predictive screening model of occupational inadvertent ingestion based on the inadvertent ingestion exposure conceptual model described by Cherrie *et al*. (2006). The conceptual model differentiated between inadvertent ingestion arising from hands/objects directly into the mouth (direct exposure) and between hands/objects and the perioral area and subsequent transfer to the oral cavity during lip licking (indirect exposure).

Christopher (2008) calculated direct oral exposure using an equation of the general form of equation (1) and also modelled indirect exposure using the following equation:

$$E_{\text{ii, indirect}} = \text{Ld} \times \text{TE}_{\text{perioral/hand}} \times \text{TE}_{\text{oral/perioral}} \times F_{\text{hand/object}} \times N \qquad (2)$$

where, $E_{\text{ii, indirect}}$: inadvertent ingestion exposure by indirect contact (mg); Ld: loading of substance on hand or object (mg); $\text{TE}_{\text{perioral/hand}}$: transfer efficiency from hand or object to the perioral area (proportion); $\text{TE}_{\text{oral/perioral}}$: transfer efficiency from the perioral area to the oral cavity (proportion); $F_{\text{hand/object}}$: proportion of the hand or object involved in contact (proportion); N: number of hand or object-to-perioral contacts.

Christopher (2008) estimated the total mass of material on the hand or object (instead of the mass per unit area) and therefore included a term describing the proportion of the hand or object involved in contact ($F_{\text{hand/object}}$) instead of a surface area term.

Relationship between dermal and ingestion exposure

Because one of the main pathways for inadvertent ingestion exposure is hand-to-mouth contact, it cannot be considered in isolation from dermal exposure. The mass of contamination on the hands influences the mass that transfers to the mouth during contact. Hand-to-mouth contact can also affect dermal exposure as contamination is removed from the skin, and contact with the mouth can affect the subsequent re-loading of the hands as they may become moistened, which can lead to increased transfer of materials from surfaces to hands (Freeman *et al.*, 2005). Therefore, dermal and inadvertent ingestion predictive exposure models would both be improved by integration with one another.

In most inadvertent ingestion exposure predictive models, dermal loading has been either estimated using dermal exposure measurements (Deubner *et al.*, 2001; Hemond and Solo-Gabriele, 2004; Stapleton *et al.,* 2008) or modelled based on the mass of contaminant loaded on surfaces (surface loading) (Zartarian *et al.*, 2000; Gaborek *et al.*, 2001; Beyer *et al.*, 2003; Hore *et al.*, 2006; Canales and Leckie, 2007; Christopher, 2008). Such modelling of dermal loading has typically used equations of the following form:

$$\text{Ld}_{\text{hand}} = \text{Ld}_{\text{surface}} \times \text{SA} \times \text{TE} \times N \qquad (3)$$

where, Ld_{hand}: loading of substance on hand (mg); $\text{Ld}_{\text{surface}}$: loading of substance on surface (mg cm^{-2}); SA: surface area of hand in contact with contaminated surface (cm^2); TE: transfer efficiency of substance from surface to the hands (proportion); N: number of hand-to-surface contacts.

While contact between hands and contaminated surfaces is an important determinant of exposure, dermal exposure is a complex process which is affected by much more than hand-to-surface contact. Deposition of substances on the skin also plays a role, as do direct immersion and spills/splashes. There are also interactions between hands, surfaces, and clothing that can affect the loading of a substance on the skin. Several predictive models are available that can be used to estimate dermal exposure, either qualitatively or quantitatively (e.g. ECETOC TRA, STOFFENMANAGER, MEASE, RISKOFDERM and DREAM), which take many of these factors into consideration. Some of these predictive models are based on underlying conceptual models describing the pathways and processes through which exposure can occur. The development of a conceptual model describing the relationship between dermal and inadvertent ingestion exposure could guide the development of a tool to estimate both dermal and inadvertent ingestion exposure.

Transfer efficiency

Transfer efficiency estimates are used in the development of both dermal and inadvertent ingestion exposure predictive models as demonstrated in equations (1)–(3). These are typically derived from laboratory experiments in which known masses of test substances are spiked onto surfaces (or objects, hands, etc.) and then measured on hands (or the mouth, the perioral area, etc.) following predefined contact. However, in some predictive models, due to a lack of appropriate available data, randomised uniform transfer efficiency distributions between 10 and 50% or 0 and 100% have been assumed (Zartarian *et al.*, 2000; Hemond and Solo-Gabriele, 2004; Canales and Leckie, 2007; Beamer *et al.*, 2009), or transfer efficiency estimates have been based on professional judgement (Hore *et al.*, 2006). Transfer efficiencies can be affected by the substance characteristics, level of surface loading, or circumstances of the contact (contact pressure, duration, etc.) (Brouwer *et al.*, 1999; Rodes *et al.*, 2001; Cohen Hubal *et al.*, 2005; Christopher, 2008). Furthermore the transfer efficiency of contaminants from surfaces to clothing differs from the transfer efficiency from surfaces to bare skin. The carrying capacity for contamination on clothing may also differ from skin. The further development of inadvertent ingestion exposure predictive models will benefit from the inclusion of different transfer efficiencies to apply to different scenarios.

Aims and objectives

We describe work that has been undertaken to progress the field of inadvertent ingestion exposure modelling. This work is part of a wider study funded by the UK Health and Safety Executive (HSE) to further advance the predictive model for estimating occupational inadvertent ingestion exposure developed by Christopher (2008) and to incorporate the updated predictive model into a predictive risk assessment tool for inadvertent ingestion exposure. To aid in the development of this predictive model the objectives of the work presented in this manuscript were (i) to develop a conceptual model of dermal and inadvertent ingestion exposure to enable future development of combined dermal/ingestion exposure modelling tools and (ii) to develop a searchable database of reported transfer efficiencies that can be used in dermal and inadvertent ingestion exposure modelling.

CONCEPTUAL MODEL

Cherrie *et al.* (2006) and Schneider *et al.* (1999) have published conceptual models for inadvertent ingestion and dermal exposure, respectively. The conceptual model by Cherrie *et al.* (2006) was used by Christopher (2008) to develop an inadvertent ingestion exposure predictive model. The conceptual model by Schneider *et al.* (1999) has been widely accepted in the field of occupational dermal exposure assessment. It has been used to guide measurement techniques and in the development of dermal exposure predictive models, including DREAM (van Wendel de Joode *et al.*, 2003) and RISKOFDERM (van Hemmen *et al.*, 2003).

Both the conceptual models describe the transfer of contaminants between compartments *via* episodic events. In the present paper the processes described in the two conceptual models are integrated to create a combined dermal/ingestion exposure conceptual model, which is presented in Fig. 1.

The inadvertent ingestion exposure conceptual model by Cherrie *et al.* (2006) includes five compartments: surfaces, hands, the perioral area, the oral cavity, and 'contamination from elsewhere in the environment'. The dermal exposure conceptual model developed by Schneider *et al.* (1999) consists of six compartments: source, surface contaminant layer, air, outer clothing contaminant layer, inner clothing contaminant layer, and the skin contaminant layer. The term 'layer' was used by Schneider *et al.* (1999) for some compartments to indicate that contaminants form a layer on the surface of the compartment. In both the conceptual models, substances can move between compartments, be absorbed (through the skin or by swallowing), or exit the system by 'decontamination' (exhaust ventilation, surface cleaning, skin washing, or spitting).

The oral cavity is the only compartment in the inadvertent ingestion exposure conceptual model that is not included in the dermal conceptual model. The hand and perioral compartments are both included within the skin contaminant layer, and 'contamination from elsewhere in the environment' is likely to come either directly from the source or from the air.

In the new integrated conceptual model, an oral compartment has been added to the dermal exposure conceptual model developed by Schneider *et al.* (1999), and the skin contaminant layer compartment has been split into two separate compartments: hands/arms and perioral. The eight mass transport processes described by Schneider *et al.* (1999) have been retained: Emission (E) from the source to other compartments (i.e. by immersion, spills or splashes); Deposition (Dp) from the air to surfaces, clothing and skin; Resuspension or Evaporation (L) from surfaces, clothing and skin into the air; Transfer (T) from surfaces or clothing toward the worker's clothing, skin or oral cavity by direct contact; Removal (R) from skin or clothing

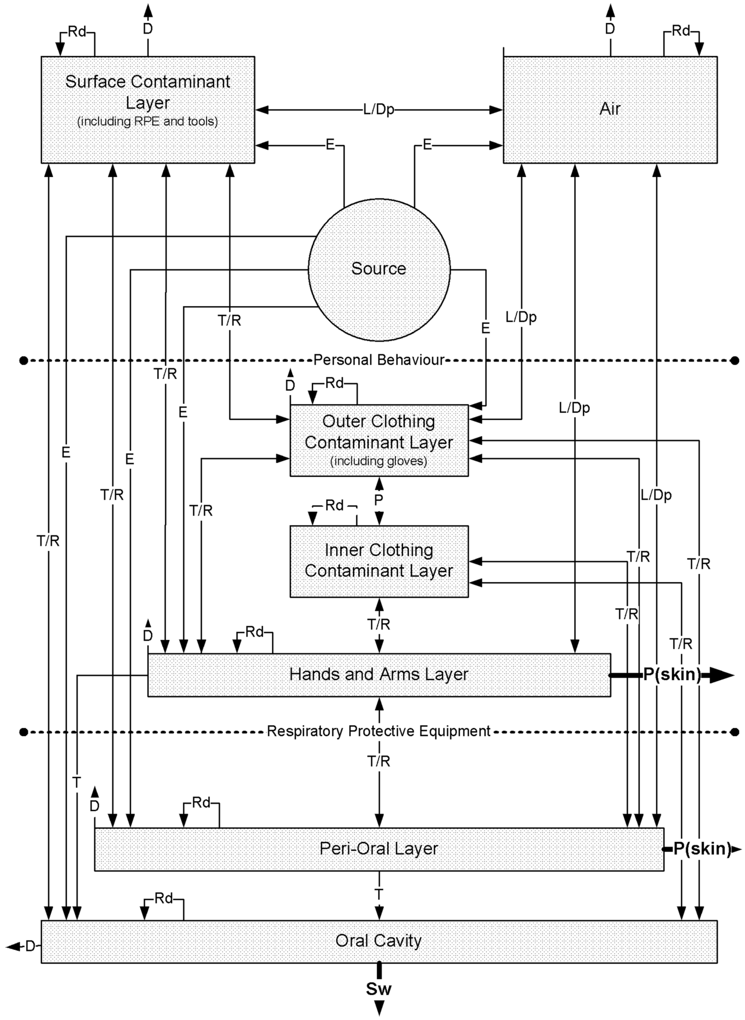

Fig. 1. Integrated dermal and ingestion conceptual model. Note: E, emission; Dp, deposition; L, resuspension or evaporation; L/Dp, deposition and resuspension/evaporation (opposite directions); T, transfer; R, removal; T/R, transfer and removal (opposite directions); Rd, redistribution; D, decontamination; P, penetration and permeation; Sw, swallowing. T/R between the surface contaminant layer and the oral cavity is depicted by a dashed line to indicate that transfer by this pathway is only likely to occur for surfaces that are portable and capable of being placed into the mouth.

by direct contact with surfaces or clothing; Redistribution (Rd) of substances within compartments; Decontamination (D) or removal of contamination from the system by ventilation of air, cleaning of surfaces, washing of skin, or spitting (it is assumed that workers will spit into sinks, toilets or tissues and not onto model compartments); and Penetration and Permeation (P) of substances through clothing or the stratum corneum.

An additional mass transport process, Swallowing (Sw), has been added to describe the ingestion of materials that have entered the oral cavity.

Personal behaviour and respiratory protective equipment

Two horizontal lines are included in the conceptual model to describe the points at which personal behaviour and respiratory protective equipment (RPE) influence the movement of contamination between compartments. The personal behaviour line is included in the dermal exposure conceptual model and continues to be relevant to the integrated conceptual model. The personal behaviour line separates compartments that are part of the individual from compartments that are part of the work environment.

This line emphasises the strong effect of frequency of contact and personal behaviour on the amount of material transferred to and between the clothing compartments, the skin, and the oral cavity. Transfers between the air, source and surface contaminant layer compartments are less strongly influenced by personal behaviour.

The RPE line has been added to demonstrate that workers who wear RPE will be restricted in their ability to touch their faces or mouths while working. The respiratory protection line is only intended to highlight the effect that RPE will have on the transfer of contaminant to the oral and perioral compartments from the other compartments. It is not intended to describe the transfer of contamination from the RPE to the skin, or from the air to the RPE. Within the conceptual model, RPE is simply defined as a surface.

Skin contaminant layers within the integrated conceptual model

Two separate skin compartments are included in the integrated conceptual model. Hands and arms are combined to form a single compartment, and the perioral area comprises the second compartment. Dermal surfaces of other parts of the body are unlikely to contribute to ingestion exposure and, in most cases, will be covered with clothing, minimising the transfer of contamination between the skin surfaces included in the conceptual model (hands, arms, and perioral) and the other skin surfaces.

Hands play a central role in inadvertent ingestion exposure but arms also contribute as they can be wiped across the face to remove sweat or to scratch the nose or mouth, and, therefore, both hands and arms are included in the integrated conceptual model. When modelling inadvertent ingestion exposure, it is useful to include the perioral area as a compartment, separate from the rest of the skin, as this allows the consideration of both direct and indirect inadvertent ingestion exposure. The conceptual dichotomy is important when considering exposure among adults who may be less likely to intentionally place contaminated hands or objects in the mouth than brush such items against the face.

Surfaces within the integrated conceptual model

The surface compartment includes any RPE and all surfaces within the work environment that are not clothing, skin, or part of the source. This includes work equipment, tools, vehicles, and work surfaces. For the purpose of inadvertent ingestion exposure modelling, it may be useful to consider portable and non-portable surfaces separately. Portable surfaces (including pens, paper, and many other tools) can, in principle, be inserted into the mouth, in contrast with non-portable surfaces (such as tables or machinery), which cannot be inserted into the mouth. The inclusion of these surfaces allows the consideration of ingestion exposure scenarios where dermal exposure does not play a role, such as the holding of a contaminated notepad in the mouth while climbing stairs or chewing on a pen. Within the conceptual model, direct transfer between the surface contamination layer and the oral cavity is depicted by a dashed line to demonstrate that it is only likely to involve portable surfaces.

Clothing within the integrated conceptual model

The conceptual model for the inadvertent ingestion exposure by Cherrie *et al.* (2006) did not include clothing or PPE. The integrated conceptual model allows the inclusion of these compartments. The transfer efficiency of contaminants from surfaces to clothing differs from transfer to bare skin, and the carrying capacity for contaminants of clothing materials also differs from that of skin. Clothing can also be placed on to the perioral area or into the oral cavity, and the transfer of contamination during these events may differ from transfer due to contact with bare skin. The outer clothing layer is likely to be more important to ingestion exposure than the inner clothing contaminant layer.

TRANSFER EFFICIENCY DATABASE

Literature review

A literature review was carried out to identify all available transfer efficiency data reported in the grey and peer-reviewed literatures. The search terms used included the following: 'Ingestion Exposure', 'Dermal/Skin', 'Transfer Efficiency', 'Transfer Factor', 'Reconstituted Epidermis', 'Loading', 'Surface contamination', 'Occupational', 'Industrial', 'Chemical', 'Determinants of Exposure', 'Personal Protective Equipment', 'Non-dietary ingestion', 'Hand-to-mouth', and 'Behaviour'. Combinations of the above search terms were entered into the Pubmed, Toxline, Web of Science, and Google Scholar databases. Searches were limited to studies involving humans and the English language. Review articles were included and no year restrictions were imposed. The titles and abstracts of all articles identified in database searches were screened for inclusion. Articles were identified for further consideration if the titles suggested that they reported on either of the following themes:

- transfer of substances from surfaces to skin, from the skin to other parts of the skin, mouth, or oral cavity;
- inadvertent ingestion exposure.

The titles of articles in the reference lists of papers that were identified from the initial screening were also screened using the inclusion criteria described above, and those that qualified were considered further. A total of 169 articles were identified for further consideration. The full text of the 169 articles was then reviewed and screened to identify articles that reported empirical data on transfer of substances from the following:

- surfaces to skin or clothing;
- skin or clothing to other parts of the body;
- objects or hands to the perioral area;
- objects or hands to the oral cavity.

Twenty-eight articles reporting relevant data were identified and were included in the transfer efficiency database. These studies were published between 1980 and 2000 and were conducted in the USA, the UK, Canada, the Netherlands, Mexico, and Germany.

Database building and data entry

An exposure assessment scientist (MGN) reviewed all 28 articles and recorded relevant data in a Microsoft® Office Access 2003 (Microsoft Corporation, Redmond, WA, USA) database. When reported transfer efficiencies were averages from several experiments, the number of observations and standard deviation were also recorded, but, where available, data from individual observations were recorded. All reported averages were arithmetic means.

Two methods of calculating transfer efficiency were found in the literature, the calculated transfer efficiencies from the two methods are not equivalent. Consequently two alternate transfer efficiency definitions were used in the database:

1. **Mass per unit area**: The mass per unit area detected on the receiver divided by the mass per unit area present on the surface area involved in contact.
2. **Total mass**: The mass detected on the receiver divided by the total mass present on the donor (not only on the surface area involved in transfer).

In some cases, transfer efficiencies were not explicitly reported, and the data from the study were used to calculate the transfer efficiency based on one of the two definitions above (depending upon the nature of the reported data). Within the database transfer efficiencies are labelled as calculated by either the authors of the original paper or the database developers.

Contextual information were recorded for each transfer efficiency, including information on the reference source (including authors, journal, institution, publication date, and a link to an online source for the reference) and details of the circumstances of the transfer (including the substance involved, the donor and the receiver). The identified reports indicated that a number of factors may influence transfer efficiency. These influencing factors were also recorded when available and left blank if unavailable. Potential influencing factors recorded included particle size of powders (Kissel *et al.*, 1998; Rodes *et al.*, 2001), the level of contamination on the donor surface prior to contact (Brouwer *et al.*, 1999; Cohen Hubal *et al.*, 2005; Christopher, 2008), the time between application of material to the donor surface and contact (Scott and Bloomfield, 1990; Sattar *et al.*, 2001), the presence or absence of friction during contact (Sattar *et al.*, 2001; Cohen Hubal *et al.*, 2005; Knobben *et al.*, 2007), the duration of contact (Brouwer *et al.*, 1999), the number of contacts (Cohen Hubal *et al.*, 2005; Christopher, 2008), the contact pressure (Cohen Hubal *et al.*, 2005), and moistness of the skin (Brouwer *et al.*, 1999; Edwards and Lioy, 2001; Rodes *et al.*, 2001; Cohen Hubal *et al.*, 2005; Christopher, 2008).

In the database user interface, users can view a database overview form that was designed to allow users to scroll through the available contextual information reported for each transfer efficiency (Fig. 2). Users can also access a search tool that was developed to allow database users to identify relevant transfer efficiencies for a scenario of interest based on the substance of interest and a selection of transfer efficiency influencing factors. Data recorded for influencing factors were categorised for use in the search function. Dropdown lists on the search screen allow users to select a category for each influencing factor. The database data are then filtered based on the search criteria. Users can scroll though data relevant to their search and press a button to display the mean, the standard deviation, the 75th, 95th, and 99th percentile transfer efficiency of these data calculated based on Visual Basic code developed for the database. Transfer efficiencies recorded in the database as averages of several observations are weighted by the number of observations in percentile calculations. The influencing factors used in the search function, the categories selected, and the justification for their selection and categorisation are presented in Table 1.

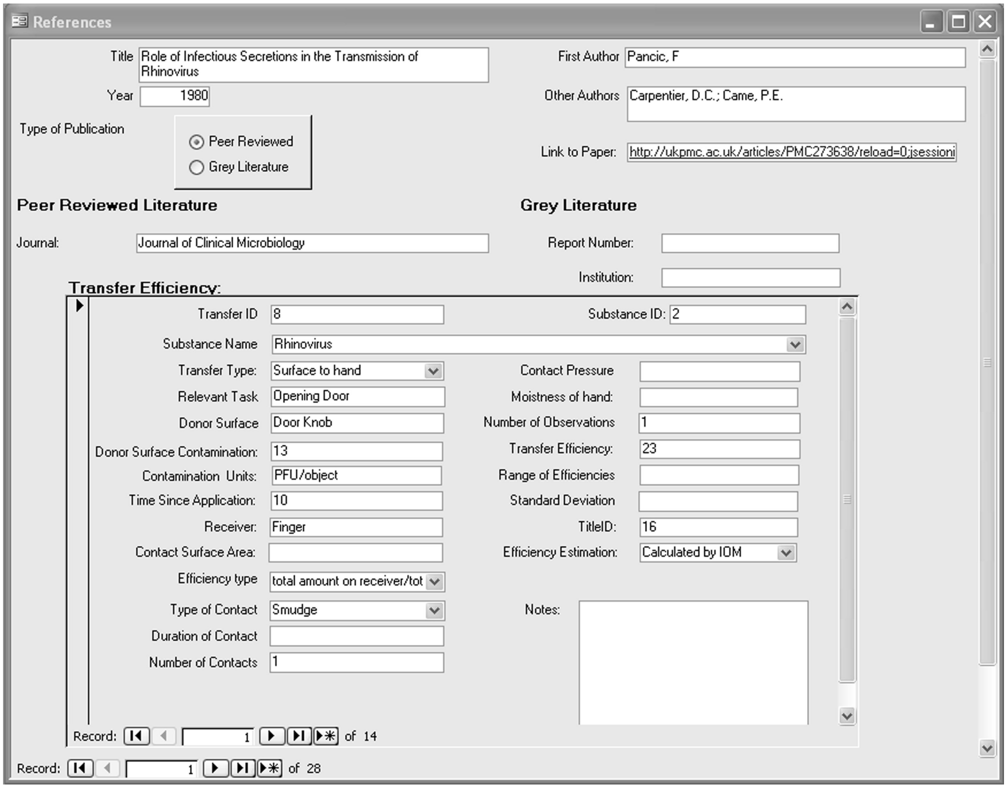

Fig. 2. Transfer efficiency database overview screen displaying data for a transfer efficiency reported by Pancic *et al*. (1980). The arrows at the bottom right of the screen are used to scroll through all transfer efficiencies reported in the selected reference (1–14), or to scroll between the different references (1–28)

Database summary and discussion

The transfer efficiency database was designed as a resource for inclusion in the inadvertent exposure assessment predictive model but may also be used by risk assessors and exposure scientists as a resource for use with other tools to estimate dermal/inadvertent ingestion exposure, including equations (1)–(3) presented above. It is publically available for download at http://www.iom-world.org/research/transfer_efficiencies.php. The database is intended to be a work in progress, and it will continue to be populated by the authors as new data become available.

Presently, 534 transfer efficiencies are recorded in the transfer efficiency database. The majority (84%) report transfer efficiencies for surface-to-hand contacts, and most transfer efficiencies (91%) were calculated based on the 'mass per unit area' definition. All volunteers in transfer simulation studies were adults. The genders of the volunteers associated with individual transfers were rarely reported and were not recorded in the database. Transfer efficiencies are recorded for 38 substances: 12 biological substances, 11 liquids, 8 solids dissolved in solution, 6 powders, and 1 radioisotope. All substances for which transfer efficiencies are recorded are listed in Table 2. The liquids and solids in solution are predominantly pesticides.

The number of data points by type of transfer, transfer efficiency definition, and physical state of substance along with maximum, minimum, and median transfer efficiencies for each category are presented in Table 3. There are many blank cells in Table 3, indicating gaps in the currently available data. For example, there are no available data on transfer of liquids or solids in solution from one section of skin to another, which may make it difficult to estimate hand-to-perioral transfer for liquids or solutions. There are also very little available data on hand-to-mouth and perioral-to-oral transfer or none on the transfer between objects and the mouth.

It is also important to note the different transfer efficiency definitions used in different studies. Even within the transfer efficiencies characterised by the mass per unit area definition some variability was

Table 1. Transfer efficiency influencing factors in database search function.

Search factor	Categories	Justification for inclusion and categorisation
Substance	Liquid Powder Biological solid in solution	Substances are organized by physical state, but users can also search by individual substances. No data on transfer of fibres were available.
Particle size (powders only)	<50 µm 50–150 µm >150 µm	Rodes *et al.* (2001) did not find a large difference in transfer efficiency between particles <10 and 40–80 µm in diameter but did find that transfer efficiencies decreased above 80 µm. Kissel *et al.* (1998) found decreasing TE with particle size for particle diameters ranging from <150 to 250 µm.
Transfer type	Hand-to-mouth Hand-to-perioral Perioral-to-oral Skin-to-skin Surface-to-clothing Surface-to-hand Surface-to-glove	All transfer types reported in the references were included as individual categories.
Donor surface type	Smooth Rough Carpet Food Skin Textile	Large differences in transfer efficiency have been observed between smooth, rough, and porous surfaces (Scott and Bloomfield, 1990; Rodes *et al.*, 2001; Cohen Hubal, 2005) There are also expected to be wide variability between different types of porous surfaces, so these have been split into subcategories (carpet, textile, food, skin).
Surface loading level	*Liquids, powders, and solids in solution* <0.0002 mg cm^{-2} 0.0002–0.002 mg cm^{-2} 0.002–1 mg cm^{-2} ≥ 1 mg cm^{-2} *Biological substances* <29 CFU cm^{-2} 29–440 CFU cm^{-2} 441–1000 CFU cm^{-2} >1000 CFU cm^{-2}	Brouwer *et al.* (1999), Cohen Hubal *et al.* (2005) and Christopher (2008) all found that surface loading was related to exposure. Data were categorised into quartiles. The units of surface contamination for biological substances (CFU cm^{-2}) differed from the units for liquids, powders and solids in solution (mg cm^{-2}) so biological substances were categorised separately.
Time since application (liquids and biological substances only)	*Liquids or solid in solution* 0–3 h 3–12 h >12 h *Biological substances* 0–60 min >60 min	For biological substances, Scott and Bloomfield (1990) found a difference in the survival of pathogens on surfaces between 0, 4 and 24 h. Sattar *et al.* (2001) found that the levels of pathogens on a surface decreased after 60 min. In the database 60 min is the third quartile of time since application data for biological substances. Data were grouped into 0–60 and >60 min.For liquids Ross *et al.* (1990) found decreasing levels of pesticides on surfaces and decreasing transfer efficiencies with increasing time, the relationship was nearly linear. Data were grouped into quartiles (12 h is the median and third quartile).Time since application is not relevant for powders as the powders used do not decay over short periods of time.
Type of contact	Press Smudge Grasp	This variable takes into account the effect of friction on transfer efficiency. Ivancic *et al.* (2004) found that friction increased the hand surface area involved in transfer and consequently increased total mass transferred. The smudge and grasp represent contacts with friction and the press represents contacts without friction.
Moistness of hand	Dry Wet	Several studies (Brouwer *et al.*, 1999; Edwards and Lioy, 2001; Rodes *et al.*, 2001; Cohen Hubal *et al.*, 2005; Christopher, 2008) found that hand moistness affected transfer. Wet hands are defined as having been moistened (e.g. with water or saliva) prior to contact. None of the available studies investigated the effect of hand creams.
Number of contacts	1, 2–6, >6	Cohen Hubal *et al.* (2005) found that after 6 contacts loading of the hands did not increase with further contacts.

Table 2. Substances for which transfer efficiencies are available.

Biological (12)	Liquid (11)	Solid in solution (8)	Powder (6)	Radioisotope (1)
Rhinovirus	d-trans Allethrin	Chlorpyrifos	House dust	^{226}Ra
Escherichia coli	Malathion	Captan	Soil	
Salmonella	Diazinon	Atrazine	Tinopal	
Staphylococcus aureus	Pyrethrin I	Permethrin	Strontium	
Klebsiella aerogenes	Piperonyl Butoxide	Riboflavin	Chloride	
Human parainfluenza virus	Azoxystrobin	Uvitex	Arizona test	
Micrococcus luteus	Carbendazim	Chlorothalonil	Dust	
Phage PRD-1	Flusilazole	Cyfluthrin	Saffron	
Serratia rubidaea	Isoproturon	Tinopal		
Staphylococcus epidermidis	Tebuconazole			
Propionibacterium acnes	Pendimethalin			
Salmonella enterica				

seen in the way that transfer efficiencies were calculated. During surface-to-hand transfer from a palm press to the surface, only part of the palmar surface actually comes into contact with the surface, the proportion varying with the contact pressure and the presence or absence of friction (Ivancic *et al.*, 2004). Most transfer efficiency calculations only take into account the part of the hand involved in contact, but six studies assumed that contact surface area is equivalent to the entire surface area of the palm; transfer efficiencies calculated under this assumption are identified in a 'notes' data field within the database. These different definitions of transfer efficiency found in the published literature highlight a need to harmonise the way that transfer efficiencies are defined, calculated, and incorporated into exposure assessment predictive models.

The transfer efficiencies extracted from the literature ranged from 0 to 157%, and even within a single transfer type wide ranges were seen (e.g. reported hand-to-mouth transfers ranged from 14 to 100%, and surface-to-hand transfers ranged from 0 to 157%). Negative transfer efficiencies and transfer efficiencies greater than 100% are both the result of experimental uncertainty in the laboratory experiments. These transfer efficiencies have been included in the database for completeness. For surface-to-hand transfer efficiencies calculated as *mass per unit area* little difference in the range and median transfer efficiency was seen across different substance physical states, but there was a wide variability within physical states. This emphasises the importance of the search function within the database to enable the selection of appropriate transfer efficiencies for a given scenario. Surface-to-hand transfer efficiency can be strongly influenced by the search parameters outlined in Table 1 (e.g. surface type, time between application and contact, number of contacts, etc.), and differences in these variables contribute to the wide variability for surface-to-hand contact.

ROADMAP TO AN INTEGRATED INADVERTENT INGESTION AND DERMAL EXPOSURE MODEL

REACH risk assessment requires estimates of exposure for all routes, including ingestion. There is, therefore, a need for predictive modelling tools to estimate occupational exposure by the inadvertent ingestion route. Furthermore, it is clear that the inadvertent ingestion of hazardous substances is closely related to dermal exposure. The integration of the dermal and inadvertent ingestion predictive exposure models is important to ensure consistency between the modelling approaches. We envision the full development of such a predictive model taking place in six stages:

1. Development of an integrated dermal and inadvertent conceptual model;
2. Literature review to identify existing relevant data and collation of such data;
3. Laboratory experiments and field studies to generate data to fill in the gaps in existing knowledge;
4. Development of integrated dermal and ingestion predictive model based on conceptual model framework and empirical data, which is guided by existing models of inadvertent ingestion and dermal exposure;
5. Calibration of the model with empirical field measurements;
6. Validation of the model against empirical field measurements.

Table 3. Number of transfer efficiency records, range and median transfer efficiency by type of transfer, transfer definition, and physical state of substances involved in transfer.

Transfer definition	Physical state	Transfer efficiency													
		Powders			Liquids			Solids in solution			Biological substances			Radioisotope	
	Type of transfer	*n*	Range (%)	Median (%)	*n*	Range (%)	Median (%)	*n*	Range (%)	Median (%)	*n*	Range (%)	Median (%)	*n*	Value (%)
Mass per unit area	Surface-to-hand	62	0.15–44.7	11.0	71	0.32–83.0	6.0	206	0.01–95.6	3.8	67	0–157.0[a]	3.4	0	—
	Surface-to-glove	1	13.1	—	9	8.3–79.0	25.0	3	8.1–17.4	16.9	15	17.0–70.0	48.0	0	—
	Surface-to-clothing	0	—	—	9	2.8–34.3	5.4	9	3.1–33.3	6.6	11	29.0–80.0	50.0	0	—
	Hand-to-mouth	1	100.0	—	0	—	—	8	14.0[a]–34.0	2.9	0	—	—	0	—
	Hand-to-perioral	1	37.0	—	0	—	—	0	—	—	0	—	—	0	—
	Perioral-to-oral	1	38.0	—	0	—	—	0	—	—	0	—	—	0	—
	Skin-to-skin	0	—	—	0	—	—	0	—	—	9	0.7–10.0	4.0	1	20.0
	Total	66	—	—	89	—	—	226	—	—	102	—	—	1	—
Total mass	Surface-to-hand	5	0.7–39.0	3.4	0	—	—	5	4.5–75.0	11.0	31	0–100.0	0.1	0	—
	Surface-to-glove	0	—	—	0	—	—	1	2.0	—	1	46.6	—	0	—
	Surface-to-clothing	0	—	—	0	—	—	0	—	—	0	—	—	0	—
	Hand-to-mouth	3	10.1–21.9	15.9	0	—	—	0	—	—	0	—	—	0	—
	Hand-to-perioral	1	8.2	—	0	—	—	0	—	—	3	33.9–41.0	34.0	0	—
	Perioral-to-oral	0	—	—	0	—	—	0	—	—	0	—	—	0	—
	Skin-to-skin	0	—	—	0	—	—	0	—	—	0	—	—	0	—
	Total	9	—	—	0	—	—	6	—	—	35	—	—	0	—

[a]Reported transfer efficiencies greater than 100 or <0 are the result of experimental uncertainty in the laboratory experiments and do not accurately describe expected transfer efficiencies. These reported transfer efficiencies have been included in the database for completeness.

In this paper, we have described work on Stage 1 and 2 of this process. We have integrated two published conceptual models to develop a conceptual model, demonstrating the relationship between dermal and inadvertent ingestion exposure to provide a framework for future development of integrated dermal and inadvertent ingestion exposure predictive models. We have also compiled a database of all available published data on the efficiency of transfer of materials between conceptual model compartments (including surfaces, hands, clothing, and the mouth). The database is searchable to allow predictive model developers to identify appropriate transfer efficiencies for use in the development of exposure models.

Before predictive modelling tools incorporating inadvertent ingestion exposure can be built, there are some additional knowledge gaps that must be addressed through further study (Stage 3). The database highlights some key gaps in the knowledge. Of the 534 transfer efficiencies that were identified, the vast majority relate to transfer between surfaces and hands. Far less is known about transfer between surfaces and clothing, the hands and other parts of the body, and hands to the mouth. No data were identified to characterise transfer between objects and the mouth or clothing/gloves and the mouth. Furthermore, much of the work on dermal and oral transfer efficiencies has focussed on pesticides, and data are unavailable for several important groups of substances, including metals, solvents, and radioisotopes.

Very little is currently known about the factors that influence hand/object-to-mouth behaviour among adults. The existing data from preliminary observational work suggests that this behaviour among adults is most frequent when the hands are idle and people are at rest (Zainudin, 2004). Further observational studies should be conducted to establish typical hand/object-to-mouth contact frequencies among workers in different occupations; the difference in contact frequencies during and between tasks; the relationship between PPE use and contact frequency; the types of objects that are typically placed in or near the mouth; and the typical surface areas of hands, arms, and objects that come in contact with the mouth. Observational methods for assessing hand/object-to-mouth behaviour have been well developed and described for the study of this behaviour among children (Ferguson *et al.*, 2006).

The collection of quantitative exposure measurements will also be required to calibrate and validate inadvertent ingestion exposure predictive modelling tools (Stages 5 and 6). Although no satisfactory inadvertent ingestion exposure assessment methods have thus far been developed, the inclusion of the perioral area in the conceptual model may allow the use of perioral surface loading field measurements in predictive model development and validation. Transfer from the perioral area to the oral cavity can be studied in laboratory settings, and laboratory derived perioral-to-oral transfer efficiencies could be added on to predictive models of perioral surface loading to quantify inadvertent ingestion exposure.

This work was carried out as part of a project to develop a quantitative predictive modelling tool to estimate occupational inadvertent ingestion exposure. It has become clear that dermal and inadvertent ingestion exposure are closely linked and cannot be considered in isolation, so we have presented an integrated dermal/inadvertent ingestion conceptual model to guide the development of such predictive modelling tools. We have also presented a database of dermal and inadvertent transfer efficiency data that can be used in predictive exposure modelling. Although further work will be required to more fully understand ingestion exposure in the workplace and its relationship to dermal exposure, the conceptual model and the database provide a basis for the development of a quantitative predictive model to estimate dermal and inadvertent ingestion exposure in the workplace.

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